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EGE KLİNİKLERİ TIP DERGİSİ
THE MEDICAL JOURNAL OF AEGEAN CLINICS

«EGE KLİNİKLERİ TIP DERGİMİZ HAKEMLİ BİR DERGİDİR»

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Sahibi /Owner
İzmir Hastanelerine Yardım ve Bilimsel Araştırmaları Teşvik Derneği Adına
On behalf of the Society of Aid to Hospitals of İzmir and Fosterage of Scientific İnvestigations

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Dernek Başkanı
Chairman of the society

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GENEL BİLGİLER

Ege Klinikleri Tıp Dergisi, İzmir Hastanelerine Yardım ve Bilimsel Araştırmaları Teşvik Derneği'nin süreli yayın organıdır. Yılda üç sayı olarak yayımlanır. Basım ayları Nisan, Ağustos ve Aralık'tır. Dergide, tıbbın her dalı ile ilgili prospektif, retrospektif ve deneysel araştırmalar, olgu sunumu, editöre mektuplar ve derlemeler yayınlanır. Yayınlanan makalelerde konu ile ilgili en yüksek etik ve bilimsel standartlarda olması ve ticari kaygılarda olmaması şartı gözetilir. Yayın için gönderilen çalışmalar; orijinal, başka bir dergide değerlendirme sürecinde olmayan ve daha önce basılmamış olması koşullarıyla kabul edilir.

Dergiye gönderilen makale biçimsel esaslara uygun ise, baş editör ve en az yurt içi-yurt dışı iki danışman incelemesinden geçip gerek görüldüğü takdirde istenen değişiklikler yazarlar tarafından yapılıp hakemlerce kabul edildikten sonra yayımlanır.

BİLİMSEL SORUMLULUK

Tüm yazarlar çalışmaya direkt olarak katkıda bulunmalıdır. Yazar olarak tanımlanmış tüm kişiler çalışmayı planlamalı veya gerçekleştirmeli, çalışmanın yazılmasında, gözden geçirilmesinde ve son halin onaylanmasında rol almalıdır. Bilimsel kriterleri karşılayan bir metnin ortaya çıkması tüm yazarların sorumluluğudur.

ETİKSEL SORUMLULUK

İnsan çalışmaları ile ilgili tüm makalelerde 'yazılı onamım' alındığını, çalışmanın Helsinki Deklarasyonu'na

(World Medical Association Declaration of Helsinki http://www.wma.net/en/30/publications/10policies/b3/index.html) göre yapıldığı ve lokal etik komite tarafından onayın alındığını bildiren cümleler mutlaka yer almalıdır.

Etik Kurul Onamlarının kendisi (Etik Kurul Onam Belgesi) yayınla birlikte gönderilmelidir.

Hayvanlar üzerinde yapılan deneyleri bildirirken yazarlar; labaratuvar hayvanlarının bakım ve kullanımı konusunda kurumsal veya ulusal yönergelerin takip edilip edilmediğini mutlaka bildirmelidirler.

Ege Klinikleri Tıp Dergisi yazarların cümlelerinden sorumlu değildir. Makale bir kez kabul edildikten sonra derginin malı olur ve dergiden izinsiz olarak başka bir yerde yayınlanamaz.

İSTATİSTİKSEL DEĞERLENDİRME

Tüm retrospektif, prospektif ve deneysel çalışma makaleleri bioistatiksel olarak değerlendirilmeli ve uygun plan, analiz ve bildirimde bulunmalıdır. p değeri yazı içinde net olarak belirtilmelidir (örn, p=0.014).

YAZIM DİLİ

Derginin resmi dilleri Türkçe ve İngilizce'dir. Türkçe metinlerde Türk Dil Kurumu'nca (www.tdk.gov.tr)www.tdk.gov.tr yayınlanan Türkçe sözlük temel alınmalıdır. Gönderilmiş makalelerdeki tüm yazım ve gramer hataları sunulan verileri değiştirmeksizin editör tarafından düzeltilir. Yazım ve gramer kurallarına metin yazımı yazarların sorumluluğundadır.

TELİF HAKKI BİLDİRİMİ

Telif hakkı devrini bildirmek için kapak mektubunda 'Bu makalenin telif hakkı; çalışma, basım için kabul edilmesi koşuluyla Ege Klinikleri Tıp Dergisi'ne devredilir' şeklinde belirtilmelidir. Makaleler için yazarlara herhangi bir ücret ödenmez.

YAZI TİPLERİ

Derleme: Derlemeler yeni veya tartışmalı alanlara ışık tutar. Dergi editörü derleme yazımı için yazar veya yazarlardan istekte bulunur.

Orijinal makaleler: Orijinal makaleler temel veya klinik çalışmalar veya klinik denemelerin sonuçlarını bildirir". Orijinal makaleler 2500 kelime ve 25 kaynaktan fazla olmamalıdır.

Olgu Sunumları: Dergi, tıbbın her alanındaki belirgin öneme haiz olgu sunumlarını yayınlar. Yazar sayısı 6'yı, kaynak sayısı ise 5'i geçmemelidir.

Editör'e Mektup: Metin 400 kelimeyi geçmemeli ve kaynak sayısı ise en fazla 3 olmalıdır (kaynaklardan biri hakkında değerlendirme yapılan yayın olmalıdır)

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Tüm yazılar elektronik ortamda idhdergi@yahoo.com adresine gönderilmelidir.

Kapak mektubu: Kapak mektubu gönderilen makalenin kategorisini, daha önce başka bir dergiye gönderilmemiş olduğunu, çıkar ilişkisi bildirimini, yayın hakkı devri bildirimini ve varsa çalışmayı maddi olarak destekleyen kişi ve kurumların adlarını içermelidir.

Başlık sayfası: Bu sayfada çalışmanın tam ismi ve kısa başlığı (karakter sayısı ve boşluklar toplamı 55'i geçmemelidir) olmalıdır. Katkıda bulunanların adlarını ve çalıştıkları kurumları listeleyin. Yazışmaların yapılacağı yazar (yazışma yazarı) belirtilmelidir. Bu yazar yayının basım sürecinde dergi editörü ile iletişimde bulunacaktır. Öte yandan tüm yazarların ORCID numarası da eklenilmeli, ORCID numarası olmayan yazarlar en kısa zamanda edinmelidir. http://orcid.org adresinden bireysel ORCID için **ücretsiz** kayıt oluşturulabilinir.

Öz ve Anahtar Kelimeler: Özet 250 kelimeyi geçmemelidir. Çalışmanın amacını, yöntemi, bulgu ve sonuçları özetlemelidir. İlaveten 3 adet anahtar kelime alfabetik sırayla verilmelidir.

Giriş: Giriş bölümü kısa ve açık olarak çalışmanın amaçlarını tartışmalı, çalışmanın neden yapıldığına yönelik temel bilgileri içermeli ve hangi hipotezlerin sınandığını bildirmelidir.

Gereç ve yöntemler: Okuyucunun sonuçları yeniden elde edebilmesi için açık ve net olarak yöntem ve gereçleri açıklayın. İlk vurgulamada kullanılan araç ve cihazların model numaralarını, firma ismini ve adresini (şehir, ülke) belirtin. Tüm ölçümleri metrik birim olarak verin. İlaçların jenerik adlarını kullanın.

Bulgular: Sonuçlar mantıklı bir sırayla metin, tablo ve görüntüler kullanılarak sunulmalıdır. Çok önemli gözlemlerin altını çizin veya özetleyin. Tablo ve metinleri tekrarlamayın.

Tartışma: Çalışmanın yeni ve çok önemli yönlerine, sonuçlarına vurgu yapın. Tartışma bölümü çalışmanın en önemli bulgusunu kısa ve net bir şekilde içermeli, gözlemlerin geçerliliği tartışılmalı, aynı veya benzer konulardaki yayınların ışığında bulgular yorumlanmalı ve yapılan çalışmanın olası önemi belirtilmelidir. Yazarlara, çalışmanın esas bulgularını kısa ve özlü bir paragrafla vurgu yapmaları önerilir.

Teşekkür: Yazarlar araştırmaya katkıda bulunan ancak yazar olarak atanmayan kişilere teşekkür etmelidir.

Kısaltmalar: Kelime veya söz dizinini ilk geçtiği yerde parantez içinde verilir. Tüm metin boyunca o kısaltma kullanılır.

Tablolar: Metin içinde tablolar ardışık olarak numaralandırılmalıdır. Her bir tabloya bir numara ve başlık yazın. Tablolar fotoğraf veya grafik dosyası olarak gönderilmemelidir.

Kaynaklar: Kaynaklar metin içinde alıntılanma sırasına uygun olarak doğal sayılar kullanılarak numaralandırılmalı ve cümlenin sonunda parantez içinde verilmelidir. " Uniform Requirements for Manuscript Submitted to Biomedical Journals" formatını kullanın. Yazar sayısı altı veya daha az ise hepsini, yedi veya daha fazla ise sadece ilk üç ismi yazın ve 've ark.'ı ilave edin. Dergi isimleri tam olarak verilmelidir. Kaynak ve kısaltılmış dergi adları yazımları Cumulated Index Medicus'a veya aşağıda verilen örneklere uygun olmalıdır.

Dergi makaleleri için örnek

Sigel B, Machi J, Beitler JC, Justin JR. Red cell aggregation as a cause of blood-flow echogenicity. Radiology 1983;148(2):799-802.

Komite veya yazar grupları için örnek

The Standard Task Force, American Society of Colon and Rectal Surgeons: Practice parameters for the treatment of haemorrhoids. Dis Colon Rectum 1993; 36: 1118-20.

Kitaptan konu için örnek

Milson JW. Haemorrhoidal disease. In: Beck DE, Wexner S, eds. Fundamentals of Anorectal Surgery. 1 1992; 192-214. 1a ed. New York: McGraw-Hill

Kitap için örnek

Bateson M, Bouchier I. Clinical Investigation and Function, 2nd edn. Oxford: Blackwell Scientific Publications Ltd, 1981.

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• Makaleniz tek dosyada olmalıdır. Çalışma tasarımı sırası şu şekilde olmalıdır: Türkçe Başlık, İngilizce Başlık, Türkçe Özet ve Türkçe Anahtar Kelimeler, İngilizce Özet ve İngilizce anahtar kelimeler. Tablo/tablolar ve resim/resimler belirtilen yerde olmalıdır.

• Kapak sayfası ekteki örnekte olduğu gibi tasarlanılmalıdır.

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Yazının Başlığı:

Sorumlu Yazarlar:

Yazarların sorumlulukları:

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Yazar Adı Soyadı **İmza** **Tarih**

Determinant Role of Magnetic Resonancelmaging in Transition of Clinical Isolated Syndrome to Multiple Sclerosis

Klinik İzole Sendromda Multipl Skleroza Dönüşümde Manyetik Rezonans Görüntülemenin Belirleyici Rolü

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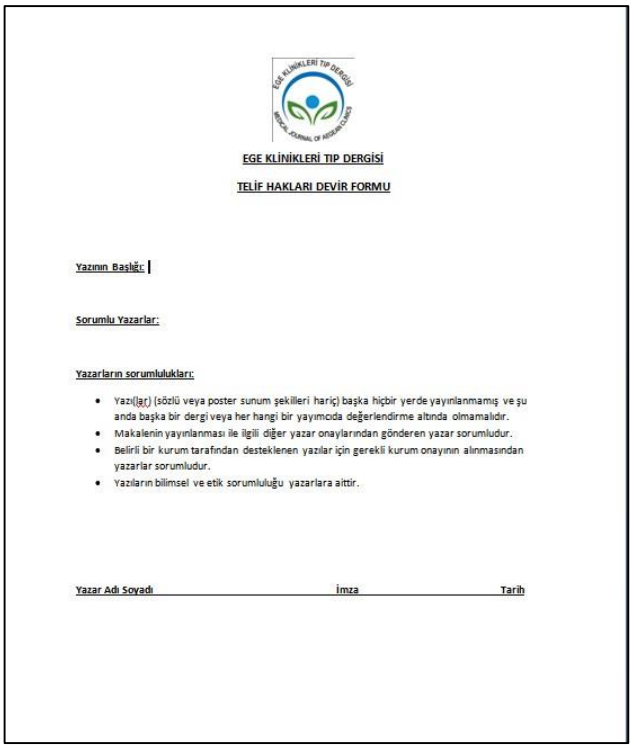

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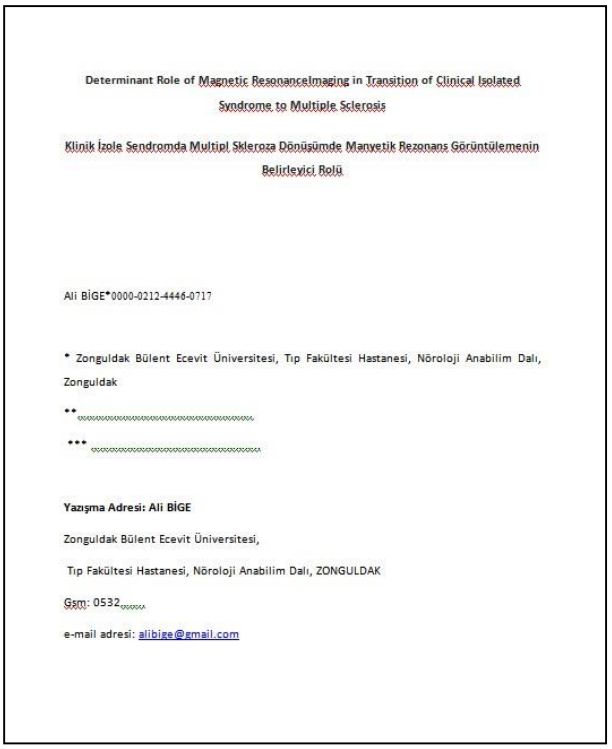

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Do We Measure Aort Right Way?

Aort'u Doğru Ölçüyor muyuz?

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Abstract

Aim: Our study aims to evaluate the effect of the different methods on ascending aortic aneurysm (AAA) diameter. In the medial section of the AAA, differences between axial, curved MPR with semi-automatic software, and para-axial measurements perfectly aligned to the aneurysm were evaluated.

Method: Images of 165 patients with a AAA diameter of over 40 mm in the axial plane in the computed tomography angiography (CTA) between 2015 and 2020 were retrospectively analyzed. In axial, curved MPR, and aligned para-axial images of the CTA, the largest AAA diameter was measured. The changes between the three measurements were evaluated with the Wilcoxon signed-rank test method for the significant value and with the t-test for the change between the measurements.

Results: AAA diameter in the axial plane was measured statistically higher than in the aligned para-axial and curved MPR images. The difference between the aligned para-axial image and the semi-automatic measurements was insignificant.

Conclusions: Since the AAA diameter can be measured higher, measurements should not be made from axial images. AAA diameter was overestimated unless the aneurysm was perfectly aligned with the image portion. As a result, AAA should be measured in curved MPR or a perfectly aligned para-axial image by automated software.

Keywords: Aortic Aneurysm; Aorta; Computed Tomography Angiography; Measurement; Accuracy

Öz

Amaç: Çalışmamızın amacı bilgisayarlı tomografi anjiyografide (BTA) aksiyel kesitte, otomatik yazılım ve aort eksenine mükemmel hizalanmış para-aksiyel görüntüler arasındaki çıkan aort anevrizması (ÇAA) çap ölçümlerindeki farklılıkları değerlendirmektir.

Yöntem: 2015-2020 yılları arasında BTA' da aksiyel planda ÇAA çapı 40 mm'nin üzerinde olan 165 hastanın görüntüleri geriye dönük olarak incelendi. BTA'nın eksenel, eğimli-çok düzlemli yeniden yapılanma (MPR) ve hizalı para-aksiyel görüntülerinde ÇAA çapı yükselen aort orta segmentinden ölçüldü. Ölçümler arasındaki değişimler anlamlı değer için Wilcoxon işaretli sıra testi yöntemi ve T-test ile değerlendirildi.

Bulgular: Eksenel düzlemde ÇAA çapı, hizalanmış para-aksiyel ve eğri MPR görüntülerinden istatistiksel olarak daha yüksek ölçüldü. Hizalanmış para-eksenel görüntü ile yarı otomatik ölçümler arasındaki fark önemsizdi.

Sonuç: ÇAA çapı daha yüksek ölçülebildiği için eksenel görüntülerden ölçüm yapılmamalıdır. Anevrizma görüntü bölümüyle mükemmel bir şekilde hizalanmadıkça AAA çapı yüksek ölçüldü. Sonuç olarak, ÇAA, otomatik yazılımla kavisli MPR görüntüde veya mükemmel şekilde hizalanmış bir para-aksiyel görüntüde ölçülmelidir.

Anahtar Kelimeler: Aort Anevrizması; Aort; Bilgisayarlı Tomografi Anjiyografi; Ölçüm; Doğruluk

Introduction

An increase in artery diameter of more than 50% is defined as an aneurysm (1, 2). An increase in the diameter of the ascending aorta is defined as an ascending aortic aneurysm (AAA) (1, 2). Ascending aortic diameter of 50 mm or more may cause emergent life-threatening pathologies such as rupture, dissection, and compression on mediastinal structures (1,3). Patients are asymptomatic for a long time, and symptoms usually develop suddenly. When patients become symptomatic, the condition is fatal. Therefore, early diagnosis is very important, and early diagnosis can be established with echocardiography (ECHO), computed tomography angiography (CTA). AAA size is important in decision-making for surgery (3,4,5). AAA diameter over 55 mm and sudden diameter increase of more than 5 mm in 6 months are among indications for operation (3,4,5). In the literature, reference diameter values for the ascending aorta have been measured from sections (6,7,8). In AAA patients, diameter measurement is performed from axial sections (3,6,9).
Our study aims to examine the changes between the aneurysm diameter measured in the axial section and the aligned para-axial images of the AAA diameter measurements.

Material and Method

Study design

Approval was obtained from the ethics committee of our hospital for our study. Our study is a retrospective archive scan of our hospital between 2015 and 2020. Patients with AAA without a history of cardiothoracic surgery and hypertensive treatment were included in the study. Patients with the bicuspid aortic valve, rheumatic aortic valve disease, mild-severe aortic insufficiency, aortic stenosis, high heart rate (>100 bpm), and respiratory artifact were excluded from the study. Patients with severe vascular wall calcification and thickening and anterior or posterior aortic rotation that would affect the measurement in the aligned para-axial images were excluded from the study as this could cause erroneous measurements. Patients with the widest aortic diameter above 40 mm in the axial plane were evaluated. The ascending aorta was evaluated from sagittal sections for tortuosity. As a result, images of 165 patients were suitable for examination.

Image processing and analyses

Measurements were made on the axial and in the aligned para-axial images of the patients. AAA maximum diameter was measured semi-automatic by software in all patients. Internal diameter measurement was made in the lumen. Measurements were made from the middle ascending aorta (the midpoint of the length between the proximal aortic arch and the sinotubuler junction). All measurements were made from the closest possible segments. The segments of the arcus aorta parallel to the vertical axis and close to the sinotubuler junction, where it is horizontal, were not evaluated due to misleading axial measurements. The widest diameter measurement was performed manually in axial sections and the aligned para-axial images. Measurements were made by two radiologists experienced in chest radiology. The most appropriate axial section measurements perpendicular to the axis were taken as reference and all measurements were compared. Analyses were made using the Somatom Definition Flash dual-source 128-slice CT scanner (Siemens Healthcare, Forchheim, Germany). In all patients, a non-ionic iodinated IV contrast agent (Ultravist 300 mg / mL, Schering, Berlin, Germany) with a density of 300 mmol was injected from the antecubital vein using an automatic injector at a rate of 3 ml/sec. The density measurement of the ascending artery was performed automatically. After measuring 120 HU in aortic density by bolus tracking method, volumetric imaging was performed in the axial plane without waiting. The whole thorax from the thoracic entrance to the lower end of the diaphragm was viewed craniocaudally. 0.7-mm thick sections were automatically created by the device in 3 separate axial, coronal, and sagittal planes and stored in a picture archiving and communication system. Siemens Syngo.via® (Siemens Healthineers, Germany) workstation was used for semi-automatic analysis. Measurements were performed on planes perpendicular to the centerline of the aorta that was manually identified. Inner-edge to inner-edge maximum diameters was measured. These measurements are accepted as reference standards.

Statistical Analysis

Data analysis was performed using SPSS 24.0 statistical software package. The method published by Bland and Altman was used to determine inter-observer agreement. Since the widest diameter in the axial plane and the aligned para-axial images were obtained from different planes from the same individual and had nominal distribution, they were statistically evaluated using the Wilcoxon signed-rank test method. The first step in the Wilcoxon signed-rank test was to calculate the differences and absolute differences of the repeated measurements. If the original difference was <0, the ranking was multiplied by -1; if the difference was positive, the ranking remained positive. The next step was to calculate W + and W-. A T-test was used to measure the change in measurements. The severity of the difference between measurements was evaluated. All data were presented as mean -/+ SD.

Results

577 patients with an ascending aortic diameter greater than 40 mm in the axial plane were examined retrospectively. Sixty patients had undergone cardiac surgery and antihypertensive therapy, 102 patients with the bicuspid aortic valve, rheumatic aortic valve disease, aortic insufficiency, aortic stenosis, high heart rate, and respiratory artifact, and 250 patients severe vascular wall calcification and thickening and anterior or posterior aortic rotation it was excluded from the study.

In our study, a total of 165 patients were examined including 44 women and 121 men (mean age 43 ± 10.6 years; range 27 to 68 years). In axial section measurements, AAA diameter was over 40-50 mm in 143 patients and over 50 mm in 22 patients. The highest axial plan AAA diameter was measured as 56 mm. In the aligned para-axial image measurements, AAA diameter was 40-50 mm in 135 patients and over 50 mm in 22 patients (Figure 1,2).

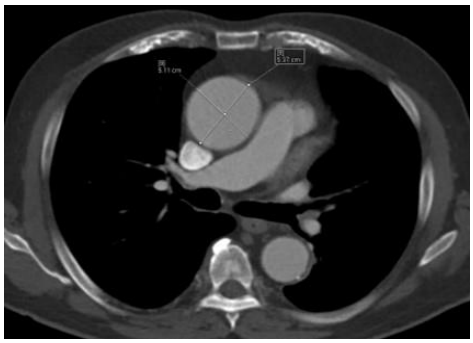
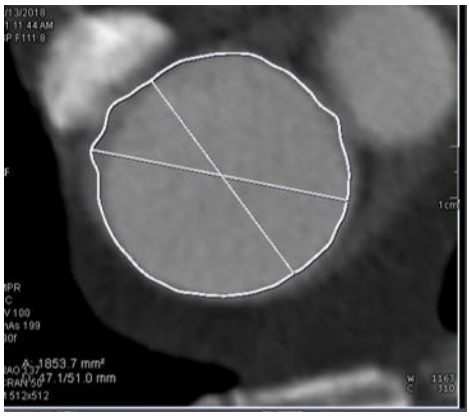


Figure 1 c

Figure 1. In a 47-year-old male patient with ascending aortic aneurysm, AAA diameter was measured in the curved MPR image (47.1 mm) (a) and in the aligned para-axial image (48.3-50.3 mm), compared to the diameter in the axial image (51.1-53, 2 mm) higher.
(a) compared to (b) when the aortic diameter was measured in two different planes.

Figure 2. In a 38-year-old male patient with an ascending aortic aneurysm, the aortic diameter was measured in three different planes in CTA images, the aortic diameter was measured 47,2 mm in the semi-automatic measurement in curved MPR image (a), and 47,8-48.4 mm in the aligned para-axial image (b), and 52,3 mm axial image. AAA diameter was measured lower in the aligned para-axial and curved MPR image.



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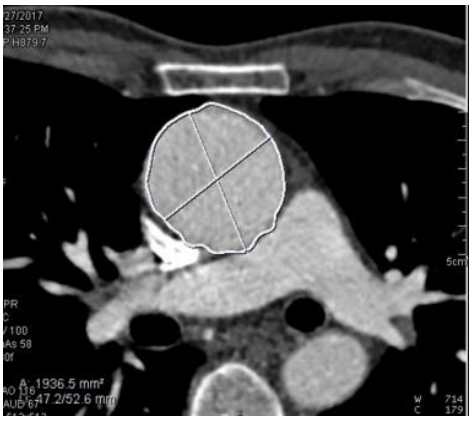

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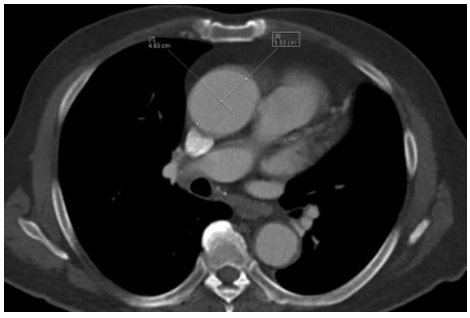

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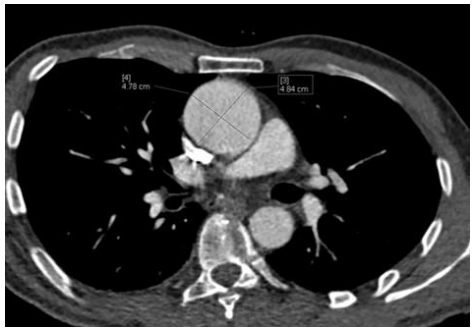

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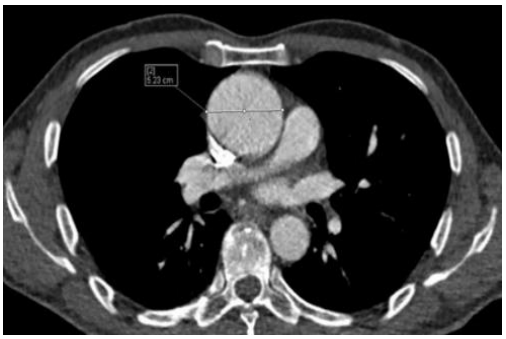
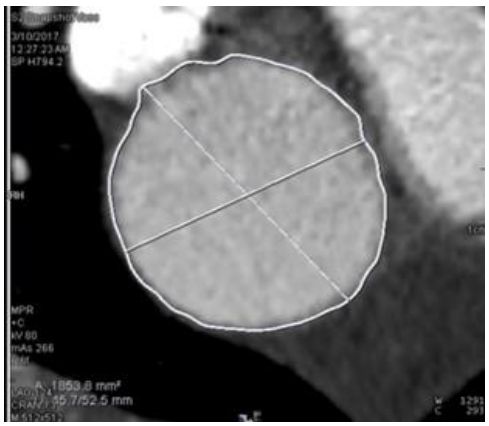


Figure 2 c

The aligned para-axial image's maximum diameter (the patient with the highest axial diameter) was 53 mm. The aortic diameter was lower than 40 mm in the aligned para-axial image measurements in 11 patients who were diagnosed with AAA (> 40 mm) in axial measurements. While the number of patients with a AAA diameter greater than 50 mm was 22 patients in axial measurements, this number was 19 in the aligned para-axial images measurements (Figure 3).

Figure 3. A 50-year-old male patient was admitted to the emergency room with chest pain. In the emergency CTA examination, an ascending aortic aneurysm was measured with a diameter of 45.7 mm curved MPR image (a) and 46.5 mm in the aligned para-axial image (b) and 53.5 mm in the axial image (c).



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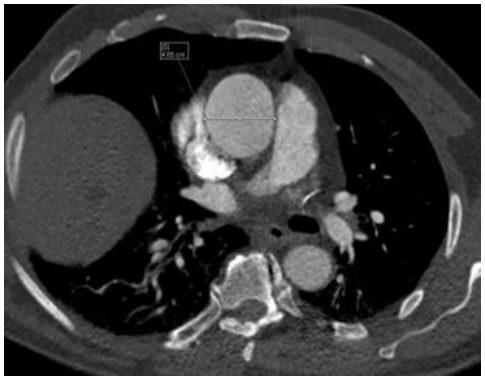

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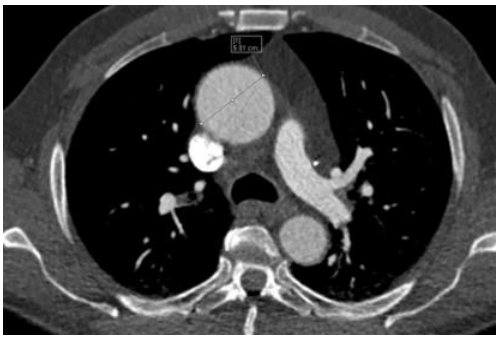

Figure 3 c

The difference between axial and aligned para-axial image values in the measurements of the patients was evaluated statistically. The change between the measurements was examined. The hypothesis test of the Wilcoxon signed-rank test was a two-tailed test and the critical z-value for directionality (95% confidence interval or 5% significance level of z=1.96) was investigated (Table 1.2).

Table 1: The standard deviation, minimum, and maximum diameter values of AAA measurements in axial, in the aligned para-axial, and curved MPR images are displayed in the table.

	N	Mean	Std. deviation	Minimum	Maximum
Axial	165	42.5345	5.21429	38.60	56.64
Para-axial	165	41.8650	4.71117	37.46	54.60
Semi-automatic	165	40,3264	3.5541	35.24	53.21

Table 2: One-Sample Kolmogorov-Smirnov test distribution is normal. The AAA diameter measurements in axial, in the aligned para-axial, and semi-automatic measurements in curved MPR images are displayed in the table.

	Axial	Para-axial	Semi-automatic
N	165	165	165
Mean	45.2659	43.6952	42,6532
Parameters	5.21429	4.71117	2,32541
Most Extreme Differences	,091	,107	,101
	,081	,107	,101
	-,091	-,071	-,023
,091	,107	0,23	
,002	,000	,000	

When a test was based on a normal distribution, it was accepted that the sample z-value must be 1.96 or higher to reject the null hypothesis. The mean inter observer variability was 3.5% (2-8 mm) (p=0,001). The significance value (p=0.091) calculated with the Wilcoxon signed-rank test was greater than the 5% significance value in our patients. For directionality, the following was found z = 1.64, 95% confidence interval (or 5% significance level). There was no significant difference between the distribution of our variable for the difference between measurements and its normal distribution in the same individuals. The distribution of our variables was normal in the spot chart. As a result of the paired T-test (p=0.104), the change in axial and in the aligned para-axial plane measurements was found to be significant (p>0.05). There was a significant difference between axial and aligned para-axial image measurements as the significance value was less than 5% for the difference between axial and aligned para-axial image measurements (Figure 4.).

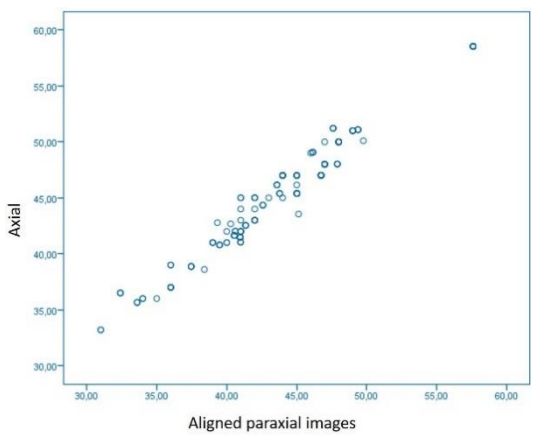

Figure 4. The distribution of axial and aligned para-axial image measurements is observed in the spot scatter plot graphic.

Since the severity of this significant difference was (D> 1), the effect severity of the difference between the two measurements was large. As a result, the measurements made in the axial plane were statistically significantly higher compared to the measurements made perpendicular to the lumen in the aligned para-axial plane, and their effect severity was greater.

Discussion

The aortic diameter measurement is important in the diagnosis and follow-up of ascending aortic aneurysm (AAA). Surgical treatment is indicated if the aneurysm diameter is greater than 55 mm or the current aneurysm diameter has increased more than 5 mm in 6 months in patients with AAA (1-5). Since AAA diameter measurement affects prognosis, accurate measurement of AAA diameter is important (10). Aortic diameter is measured from axial sections in routine contrast-enhanced thoracic computed tomography angiography (CTA) examinations (9). This study showed that there was a significant difference in the severity of the effect axial plane measurements at a level that may affect the diagnosis and treatment. Measurements made in axial sections were statistically significantly higher.

In our study, the change of AAA measurement was examined in the cross-section plane. The difference in the axial section plane is effective in diagnosis and treatment. As axial section plane measurement results are high than semi-automatic and para-axial measurements. AAA diameter measurements should be made in the correctly aligned cross-section plane. In the literature, there are CTA, magnetic resonance, and ECHO studies performed with aortic diameter measurement (4,5,7,9,11). Measurements in the oblique coronal plane and axial plane were used as a reference in large population series (1,5,6,8). In a large series of CT studies, the measurements considered as a reference for aortic diameter were performed in the axial plane without contrast, and age and aortic diameter changes were measured (7). In some studies, reference measurements of aortic diameter were made in the oblique coronal plane (6,12,13,14). There are many studies conducted with ECHO for aortic diameter in the literature (8,9,11,15). ECHO measurements were made from the sinotubuler junction and the widest diameter in visible aortic segments (14,15,16). However, the variation between axial and aligned para-axial plane measurements of AAA diameter was not investigated in these studies. According to a multicenter study, aortic diameter measurement should be made in the axial plane perpendicular to the axis. Our study shows that the aligned para-axial measurements are more reliable than axial measurements. In the literature, it is discussed which imaging methods are reliable and should be used as reference methods in measuring AAA diameter (4,7,16). According to the 2010 guide, the generally accepted method is vertical axial measurements properly aligned with the axis (9).

The results of our study show the radiological importance and clinical results of the aligned para-axial plane evaluation in the diagnosis of AAA patients with high mortality in emergencies. CTA is used in the diagnosis and follow-up of AAA (1,2). AAA measurements are performed as the axial widest diameter (3). This measurement may cause inaccurate measurement of AAA diameter. In axial plane measurements, we found that the AAA diameter was statistically higher (z=1.96). In the AAA diameter measurement (p=0.004), the change in axial and in the aligned para-axial plane measurements was significant. In patients followed up with a diagnosis of AAA, diameter measurements should be made in the aligned para-axial images. In our study, AAA measurement exceeding the limit of 50 mm in the axial plane in 35 patients was 50 mm lower when it was repeated in thein the aligned para-axial images. Since AAA diameter measurement values are lower in the aligned para-axial images compared to the axial plane, aligned para-axial image measurements must be accepted real diameter in cases with borderline values (4,7).

Our study had some limitations. The most significant limitations were that the measurements were performed by two radiologists, the results could not be confirmed surgically and pathologically, and the number of cases was low. An important limitation was that measurements could not be made according to heart phases. The reason for the low number of cases was the exclusion of patients with a history of hypertension treatment from the study.

The short duration of clinical and radiological follow-up is an important limitation. Another limitation of our patients is the lack of clinical follow-up. Surgical treatment was not performed in the patients for whom measurements were performed. ECHO findings of the patients could not be examined. This is another important limitation of our study.

Conclusions

AAA measurements in axial and aligned para-axial images were compared in our study. In conclusion, we found that the axial plane widest diameter measurements were statistically higher than the widest diameter measurements perpendicular aligned para-axial images in patients with AAA. There was no difference between semi-automatic software and aligned para-axial image measurements. Correct diameter values are important for prognosis in AAA patients with high mortality. Axial measurements may be incorrect due to the vertical course of the aorta within the thorax; therefore, AAA measurements should be made from correctly aligned para-axial images. The next step in our study should be the measurement of the AAA diameter with larger patient series in the measurement of aortic diameter using advanced software in a long-term clinical and radiological follow-up. In this way, a positive contribution will be made to the prognosis with the most accurate measurement method in AAA patients.

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Comparison of the Renal Effects of Carbetoxin and Oxytocin in Hemorrhage Prophylaxis in Elective Cesarean Delivery

Elektif Sezaryen Doğumlarda Hemoraji Profilaksisinde Karbetoksin ve Oksitosinin Renal Etkilerinin Karşılaştırılması

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Abstract

Objective: The hemodynamic effects and the renal outcome of patients undergoing elective cesarian section with Oxytocin and carbetocin for postpartum haemorrhage prophylaxis are evaluated.

Methods: One hundred patients without risk factors for postpartum haemorrhage undergoing elective cesarean delivery, under spinal anaesthesia, were randomly allocated to receive either a single dose of carbetocin (100µg/3 mL) (n = 50) or Oxytocin intravenous injection (3 IU/3 mL) (n=50). The primary outcome was blood loss and hemodynamic effects. The secondary parameter evaluated was the renal effects of drugs.

Results: Regarding the hemodynamic effects, intraoperative (243±116.91 ml vs 311.30±130.23 ml, p=0.002) and second-hour postoperative blood loss (24.72 ± 9.43 ml vs 35.54 ± 19.4 ml, p=0.003) were significantly lower in the carbetocin group. At two hours postoperatively, urine osmolality (322.66±211.67 vs 401.45±218.08, p=0.028) was significantly higher in the oxytocin group. Conversely, postoperative urine sodium was higher in the carbetocin group at the twenty four hours in the carbetocin group (51.90±36.74 vs 42.42±41.63, p = 0.004).

Conclusion: Carbetocin is easy to use with lower blood loss and less requirement of additional uterotonics compared to Oxytocin. Both drugs cause minimal changes in renal parameters at physiological limits. The renal effects might be far more different with higher doses of both drugs that necessitate further research.

Keywords: Carbetocin, Oxytocin, cesarean section, postpartum haemorrhage, renal parameters

Öz

Amaç: Doğum sonu kanama profilaksisi için Oksitosin ve karbetosin ile elektif sezaryen uygulanan hastaların hemodinamik etkileri ve böbrek sonuçları değerlendirilmektedir.

Metot: Spinal anestezi altında elektif sezaryenle doğum yapan doğum sonu kanama için risk faktörü olmayan yüz gebe, tek doz karbetosin (100µg/3 mL) (n=50) veya intravenöz Oksitosin enjeksiyonu (3 IU/ 3 mL) (n=50). Birincil sonuç, kan kaybı ve hemodinamik etkilerdi. Değerlendirilen ikincil parametre ilaçların renal etkileriydi.

Bulgular: Hemodinamik etkiler açısından, intraoperatif (243±116,91 ml - 311,30±130,23 ml, p=0,002) ve ameliyat sonrası ikinci saat kan kaybı (24,72 ± 9,43 ml - 35,54 ± 19,4 ml, p=0,003) karbetoksin grubunda kadınlarda anlamlı olarak daha düşüktü. Ameliyattan iki saat sonra, oksitosin grubunda idrar ozmolalitesi (322.66±211.67'ye karşılık 401.45±218.08, p=0.028) anlamlı olarak daha yüksekti. Tersine, ameliyat sonrası idrar sodyumu karbetosin grubunda yirmi dört saatte karbetosin grubunda daha yüksekti (51.90±36.74'e karşı 42.42±41.63, p = 0.004).

Sonuç: Karbetosin Oksitosine göre daha düşük kan kaybı ve daha az ek uterotonik gereksinimi ile kullanımı kolaydır. Her iki ilaç da fizyolojik sınırlarda renal parametrelerde minimal değişikliklere neden olur. Böbrek etkileri, daha fazla araştırma gerektiren her iki ilacın daha yüksek dozları ile çok daha farklı olabilir.

Anahtar Kelimeler: Karbetosin, Oksitosin, sezaryen, doğum sonrası kanama, böbrek parametreleri

Introduction

Postpartum haemorrhage (P.P.H.) remains the primary cause of maternal mortality and morbidity in developing countries. It is responsible for 25% of maternal deaths globally, and an estimated 140,000 deaths occur annually due to haemorrhage [1,2]. The primary P.P.H. is defined as blood loss more than 500 mL after vaginal delivery and more than 1000 mL after cesarean section [2]. The risk factors for P.P.H. are prolonged or augmented labor, severe anaemia, eclampsia, antepartum bleeding, intrapartum blood loss, previous history, polyhydramnios, and inadequate management of the third stage of the labor [3,4]. Active management of the third stage with the administration of pharmacologic uterotonic agents has been proven efficient in preventing uterine atony, which is the leading cause of P.P.H. [5].

Oxytocin is the first choice uterotonic agent for the prevention and treatment of postpartum atony [6]. After binding the myometrium cell through inositol triphosphate and diacylglycerol modulated pathway, Oxytocin causes phasic contractions. Diacylglycerol causes prostaglandins synthesis, promoting uterine contractions and increasing uterine tonus, thereby reducing blood loss [7]. Nevertheless, due to its short half-life, Oxytocin is administered intramuscularly (I.M.) at a dose of 10 I.U. or as an intravenous (IV) infusion in the third stage of labor for the prevention of P.P.H. [8]. Intravenous infusion of Oxytocin has some dose-dependent hemodynamic consequences [9-12].

Carbetocin is a long-acting synthetic oxytocin analogue with similar pharmacological features. Carbetocin affects oxytocin receptors on the smooth musculature of the uterus, and it appears to be a promising alternative to Oxytocin for P.P.H. [13]. Notwithstanding, the half-life is 40 minutes (around 4-10 times longer than Oxytocin) and produces tetanic uterine contractions within two minutes, lasting six minutes, followed by rhythmic contractions a further hour [14]. Following the infant's extraction, a single dose implementation is adequate to maintain sufficient uterine contraction, thus preventing uterine atony [15]. Clinical trials revealed that carbetocin lowers the risk of P.P.H., significantly decreases the need for additional uterotonic agents, and achieves better uterine contractility in both cesarean and vaginal deliveries [16].

Hence, in this study, we aimed to evaluate the efficacy of carbetocin in terms of blood loss, additional uterotonic need, and adverse effects. In addition, as a secondary outcome, the renal parameters (diuresis, urine sodium levels, and urine osmolality) for carbetocin and oxytocin use in C-section for P.P.H. prophylaxis were also evaluated. Oxytocin is known to have antidiuretic properties through increasing osmotic water transport in microdissected renal inner medullary collecting ducts, mediated by Arginine Vasopressin (AVP) receptors [17-19]. From a clinical perspective, water retention and hyponatremia have been reported with the induction of labor with oxytocin [20]. Like Oxytocin, carbetocin can bind to the renal vasopressin V_2 receptor [21]. Nevertheless, the possible antidiuretic properties of carbetocin have not been documented in clinical studies. In this study, all the outcomes, including renal parameters of carbetocin, were compared with Oxytocin for P.P.H. prevention.

Methods

The study was conducted in a university hospital setting between May 2019 and February 2020. 122 patients were enrolled, and informed consent was obtained from all participants. Post hoc power analysis was applied with the G * Power 3.1.9.2 program at the end of the study. The study's power was applied considering the blood loss, the 2nd-hour value, and the power of the study was determined as 96 per cent at the 0.05 significance level.

Ethical approval was granted by the Ethics Committee of Education and Research Hospital (reference number: 1499/2017) and registered at clinicaltrials.gov (NCT03939806).

The study population consisted of elective C-section cases undergoing surgery after 37 weeks of gestation for malpresentation or previous C-section. The exclusion criteria were multiple pregnancies, preterm birth (<37 weeks), patients with chronic diseases (hypertension, heart disease, renal pathologies, liver disease), pregnancies complicated with preeclampsia or gestational diabetes mellitus, cases with a single kidney, and cases with contraindications for carbetocin or oxytocin use. In addition, cases with a high risk for P.P.H. [grand-multipar (>5 previous deliveries), accompanying myomas, severe anaemia, polyhydramnios, macrosomic fetus (4500 g), low molecular heparin use] were also excluded. After randomization, 59 participants received carbetocin (Group I), and 61 received oxytocin (Group II). The sealed envelope system performed randomization. The surgeon who performed all operations was blinded to the protocol.

All patients' demographic data (age, B.M.I., gravidity, parity) medical and obstetric histories were recorded. Routine preoperative laboratory parameters (including haemoglobin levels, sodium, BUN, and glucose levels) were obtained. Body mass index (B.M.I.) was calculated as kg/m^2. Serum osmolality is calculated using the formula = (2x Na) +(BUN/2.8) + Glucose /18).

Anaesthesia and intraoperative drug application

Hemodynamic data [systolic (S.B.P.), diastolic (DBP), and mean blood pressure (M.B.P.), heart rate (H.R.)] were recorded before starting surgery (**T0**). The intraoperative fluid replacement was started at T0 with Ringer Lactate given at 10 mL/kg during the first 20 minutes after that; maintenance fluid was given throughout the surgery in both groups. All cases had spinal anaesthesia with a standard protocol. Hyperbaric bupivacaine 5 mg/mL (Marcain Spinal Heavy %0,5, AstraZeneca, Sweden) of 10 mg/2mL were given at L2-L3 intervertebral space 25-gauge spinal needle (Spinocan, Braun, Melsungen, Germany). All the patients had a Foley catheter and urine bag before the start of surgery. After completion of spinal anaesthesia, hemodynamic data was recorded every 2 minutes. In case of hypotension (S.B.P. <90 mmHg, M.B.P. <60 mmHg or decrease in S.B.P.>%20), 10 mg ephedrine was given intravenously, and in case of bradycardia, intravenous 1mg atropine was given.

At the start of surgery (**T1**) and before umbilical cord clamping (**T2**), diuresis and S.B.P., DBP, and H.R. were recorded. After clamping the umbilical cord, Group I received Carbetocin (Pabal®, Ferring Pharmaceuticals, Germany), a single dose of 100µg/3 mL bolus applied at 60 seconds, and Group II received 3 IU/3 mL oxytocin (Synpitan® Forte; Deva Holding AS, Turkey) bolus applied at 60 seconds. The obstetrician assessed the uterine tone 60 seconds after the first dose of the uterotonic drug application (**T3**). With the aid of using a numeric rating scale that ranged from 0 to 10. The score of 0 intended 'no effect,' 10 elucidate 'maximal uterus contraction,' and 7 meant 'clinically convincing contraction.' As previously described [22]. If uterine tonus scoring was <7, 3 minutes after uterotonic drug application (**T4**), then the second dose of Oxytocin was given at the same amount. If required, this dose has been repeated a maximum of three times.

Afterwards, patients in Group II received 100mL/h intravenous infusion of Oxytocin 3IU/3mL in 1000 mL Ringer Lactate. During surgery, hemodynamic values and uterine tonus were recorded every three minutes (**T5, T6, T7**). Rescue uterotonics (intramuscular ergonovine and rectal misoprostol) were used when required (uterine tonus <7) in both groups.

At the end of surgery, diuresis, the amount of intravenous fluid intake, and surgery duration were also recorded. Any adverse effects of uterotonic drugs (hypotension, nausea, vomiting, tachycardia, arrhythmia, palpitation, headache, flushing, nasal congestion, dyspnea, chest pain, xerostomia) were noted.

Postoperative follow-up

Postoperatively, uterine tonus and fluid intake were checked at 2h, 12h, and 24h. The amount of urine, urine sodium levels, and urine osmolality were recorded at postoperative 2h, 12h, and 24h, and the urine catheter was removed at the postoperative 24 h. Urine osmolality is calculated using =2 x (urine Na) + Urine K + (urinary urea nitrogen/2.8) + (urine glucose/18). The need for extra uterotonic and haemoglobin levels were recorded. The blood loss was calculated by comparing the haemoglobin values on admission with the measure at 2 h, 12h, and 24 h after the operation. Estimated blood loss was calculated with the following formula: 0.75x [(maternal height in cm x19.5) + (maternal weight in kg x 55)] x (preoperative HCT- postoperative HCT) / preoperative HCT (21). S.B.P. and DBP and plasma sodium, BUN, Glucose, and blood osmolality were also checked at 2h, 12h, and 24h.

Statistical analysis

Collected data were analyzed by SPSS 22.0 (SPSS Inc., Chicago, IL) package program. P-value <0.05 was considered statistically significant. Categorical variables were expressed as the number of observations (per cent), while continuous variables were shown as mean ± standard deviation. A Chi-square test was used to compare categorical variables. The suitability of the data to normal distribution was tested with the Shapiro Wilk test. In the comparison of the mean of continuous variables, the T-Test was used in case of conformity to the normal distribution, and Mann Whitney-U Test was used for variables that did not conform to the normal distribution. Repeated Measures ANOVA was utilized to compare the averages of continuous variables over time, and the Friedman Test was used for variables that did not find suitable for the normal distribution.

Results

At the start of the study, 122 women were enrolled, but 2 patients were not meeting the criteria and were excluded. Subsequently, 59 patients in the carbetocin group and 61 patients in the oxytocin group were allocated. During the study, 16 patients were excluded (7 in the carbetocin and 9 in the oxytocin group) as the spinal anaesthesia was altered to general anaesthesia. Besides, 4 patients were excluded (2 cases in each Group) drug application was not applied according to the study design (Figure 1). Following that, the data of 100 patients were eligible for analysis (Carbetocin group n=50, Oxytocin group n=50). There were no statistically significant differences between groups regarding the demographic data (age, gravidity, parity, B.M.I., previous surgeries, preoperative haemoglobin, hematocrit), as summarized in Table 1.

Figure 1. Recruitment flow chart for a randomized trial of intravenous bolus carbetocin compared to oxytocin in cesarean section

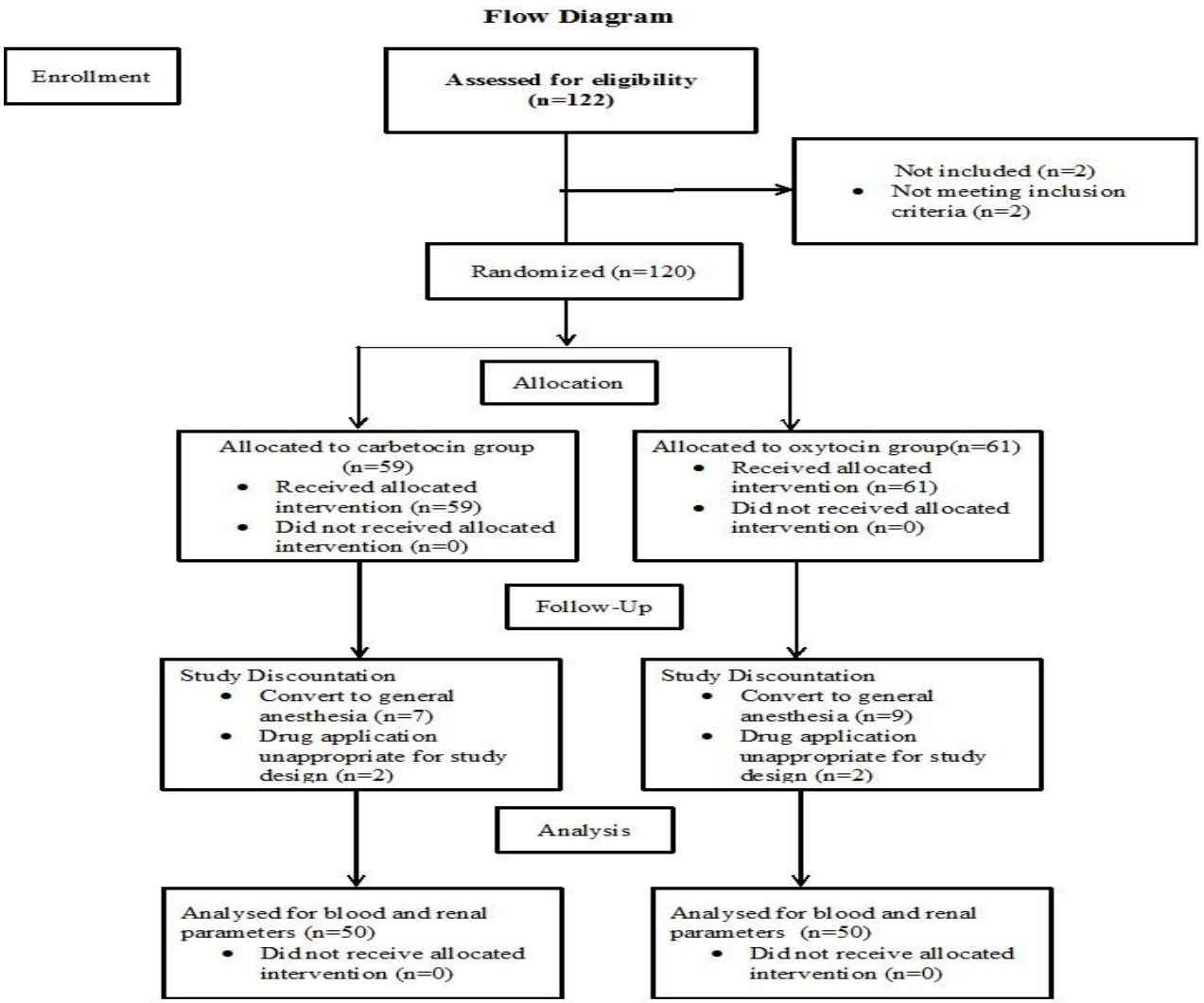


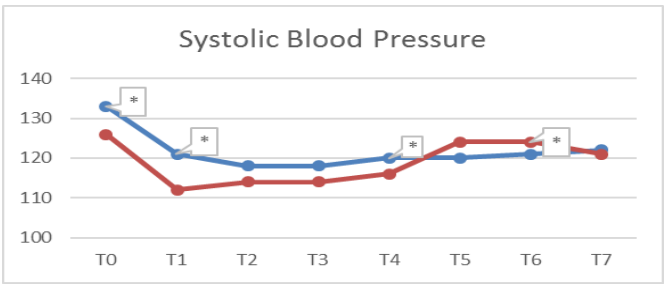
Table 1. Demographical and preoperative data of the groups

	Carbetocin (n=50)	**Oxytocin (n=50)**	***P***
Maternal age (years) Mean ± sd	31.00±5.42	30.92±5.83	NS
Gravidity Mean ± sd	2.16±0.90	2.30±1.05	NS
Parity Mean ± sd	0.91±0.75	1.14±1.06	NS
BMI (kg/m2) Mean ± sd	29.36±4.66	31.45±3.32	NS
Previous Surgeries n(%)	30(%60)	32(%64)	NS
Hematocrit (%) Mean ± sd	35.47±2.38	36.43±2.98	NS
Hemoglobin (g/dL) Mean ± sd	12.23±0.86	12.11±1.25	NS

NS: Not significant,p>0.05
BMI: Body Mass Index

The intraoperative vital signs of the groups are given in Figure 2. Intraoperative (Group I: 243±116.91 ml and Group II: 311.30±130.23ml, p=0.002) and 2nd hour postoperative blood loss (Group I: 24.72 ± 9.43 ml vs Group II: 35.54 ± 19.4 ml) were significantly lower in the carbetocin group compared to the oxytocin group (p<0.05). Concerning the intraoperative side effects, vomiting was more frequent in the oxytocin group (40% vs 6%), whereas palpitation (13% vs 10%) and xerostomia (60% vs 22%) were more frequent in the carbetocin group (p<0,05).

Figure 2. Intraoperatif systolic/diastolic blood pressure and pulse values



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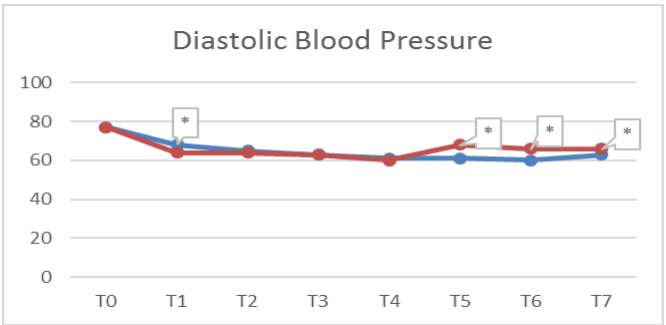

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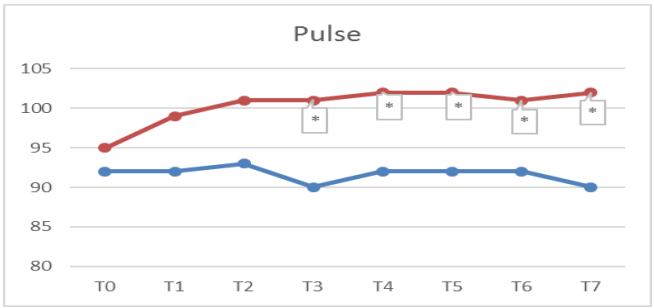

1c.

Carbetocin group Oxytocin group

*p<0.05: significantly higher in the marked group at the indicated time in surgery

None of the cases required additional uterotonics at the intraoperative and postoperative periods in the carbetocin group. However, in the oxytocin group, 30% (n=15) of the patients needed additional uterotonics intraoperatively, and the difference between the two groups was statistically significant (p = 0.001). In the oxytocin group, at postoperative 2nd hour, 20% (n=10), at 12nd hour 12% (n=6), and at 24nd hour, 4% (n=2) of the cases were given additional uterotonics due to lower uterine tonus (p=0.001). In the postoperative period, additional uterotonic needs, the difference between the two groups was statistically significant at 2h (p = 0.001) and 12h (p = 0.012) [Table 2].

Table 2. Subject characteristics of the entire study group

	Carbetocin n=50	Oxytocin n=50	*p*
Additional uterotonic	n(%)	n(%)	
Intraoperative	0 (0)	15 (30,0)	0.001*
2nd hour	0 (0)	10 (20)	0.001*
12th hour	0 (0)	6 (12)	0.001*
24th hour	0 (0)	2 (4)	0.001*
Blood loss, ml	Mean ± SD	Mean ± SD	
Intraoperative	243.40 ± 116.91	311 ± 130.23	0.002*
2nd hour	24.72 ± 9.43	35.54 ± 19.4	0.003*
12th hour	48.08 ± 20.11	49.14 ± 17.6	0.394
24th hour	44.32 ± 34.25	42.40± 18.40	0.375
Diuresis, ml	Mean ± SD	Mean ± SD	
Intraoperative	151.70 ± 136,63	148.92 ± 105.05	0.411
2nd hour	375.30 ± 264.88	400.8 ± 209.26	0.331
12th hour	1911.40 ± 521.85	1780.80 ± 627.17	0.229
24th hour	3458.0 ± 787.96	3502.6 ± 901.32	0.836
Urinary Na, mmol/L	Mean ± SD	Mean ± SD	
2nd hour	94.14±50.41	79.24±68.24	0.024*
12th hour	59.98±41.87	60.12±33.58	0.402
24th hour	51.90±36.74	42.42±41.63	0.004*
Urinary osmolality, mOsm/kg	Mean ± SD	Mean ± SD	
2nd hour	322.66±211.67	401.45±218.08	0.028*
12th hour	177.19±98.93	222.56±117.62	0.021*
24th hour	174.61±92.99	197.62±154.01	0.953
Fluid administered, ml	Mean ± SD		
Intraoperative	1330.0 ± 465.44	Mean ± SD	
2nd hour	886 ± 413.18	1387.0 ± 690.56	0.672
12th hour	2570.0±809.76	790 ± 347.44	0.170
24th hour	4487 ± 960.27	2197.0 ± 859.43	0.026*
		4532.00 ± 817.02	0.471
Systolic arterial pressure, mmHg	Mean ± SD		
Intraoperative	124.13 ± 17.78	Mean ± SD	
2nd hour	111.85 ± 13.18	114.53 ±15.77	0.031*
12th hour	106.90 ± 6.14	115.0 ± 10.74	0.527
24th hour	108.20 ± 7.20	111.80 ± 8.5	0.003*
		108.60 ± 6.70	0.278
Blood Osmolality, mOsm/L	Mean ± SD	Mean ± SD	
Preoperative	281.2 ± 3.8	279.5 ± 3.7	0.078
2nd hour	281.30 ±3.49	278.79 ± 4.65	0.002*
12th hour	280.11±4.52	270.95 ± 38.29	0.014*
24th hour	280.78±3.76	276.51 ± 13.90	0.002*
Blood Na, mEq/L	Mean ± SD	Mean ± SD	
Preoperative	136.47 ± 3.16	135.61 ± 2.11	0.082
2nd hour	137 ± 1.58	135.35 ± 4.38	0.003*
12th hour	136.50±2.08	134.88± 4.54	0.014*
24th hour	136.96±1.83	135.22 ± 4.26	0.002*

Na: Sodium
NS: Not significant,p>0.05

Regarding the urine parameters, urine output was similar at all times preoperatively and (2h,12h,24h) postoperatively [Table 2]. At 2h postoperatively, urine osmolality was significantly higher, whereas urinary sodium was lower in the oxytocin group compared to the carbetocin group [Table 2]. Additionally, it was observed that urine osmolality was found to be higher at the oxytocin group and the 12th hour ($p = 0.021$), and postoperative urine sodium was higher in the carbetocin group at 24h ($p = 0.004$) and [Table 2]. When the groups are compared regarding the blood osmolality values, the results were significantly higher in the carbetocin group than in the oxytocin group at postoperative 2h ($p = 0.002$), 12h ($p = 0.014$), and 24h ($p = 0.002$) [Table 2].

Discussion

Findings and interpretation

The data obtained from this study support the previous information that carbetocin is as effective as Oxytocin in terms of blood loss when used for P.P.H. prophylaxis. In the same line, in the meta-analysis assessing carbetocin's effectiveness for preventing bleeding, no statistical difference was found between carbetocin and Oxytocin in terms of P.P.H. incidence (11 studies, 2635 patients) [23]. In this metanalysis, three of the four studies were on women with risk factors for P.P.H., and the need for therapeutic uterotonics was significantly lower (RR 0.62; 95% CI 0.44 - 0.88) in the carbetocin group than oxytocin group, in C-section cases (1173 women) [23]. Likewise, our study shows that carbetocin can be used as a single agent for P.P.H. prophylaxis in women without risk factors for P.P.H. with no additional need for other uterotonics. Moreover, accumulating evidence in the literature indicates less blood loss after carbetocin administration. In a recent meta-analysis with seven studies involving 2012 patients, a significant reduction in P.P.H. rates was reported with carbetocin (RR 0.79; 95% CI 0.66 to 0.94; p= 0.009) [24]. In accordance with this, in our study and the previous paper in women with at least one risk factor for P.P.H. undergoing C-section by Borruto et al. [25], carbetocin was associated with less blood loss compared with Oxytocin. However, in our study and the study of Borruto et al., the amount of blood loss was too few to change the clinical scenario and management of the cases (70 ml in ours and 30 ml in Borruto et al.).

AVP is a neuropeptide like Oxytocin, central to water homeostasis by regulating urine concentration at the kidney level. AVP has different receptors, and our primary concern is the V_2 receptor of AVP that is found primarily in the kidneys [26]. After binding to the V_2 receptor, Oxytocin has an impact on renal aquaporin (A.Q.P.) water channels in the cells of the collecting duct and increases sodium excretion in urine [27].

Regarding renal parameters from this study, at postoperative 2 hours, the statistically significant difference between oxytocin and carbetocin groups regarding the serum sodium and serum osmolalities between the two groups is clinically negligible. Furthermore, the urine sodium levels in both groups are over the normal limits at all times (2h, 12h, and 24h). We may speculate that the increased excretion of sodium postoperatively can be explained by intravenous fluid supplementation during and after surgery. Moreover, the ADH-like effect of both molecules can have an additive effect on this result. Notwithstanding, the higher urine osmolality in the oxytocin group compared to carbetocin at 2 hours postoperatively might explain the increased blood loss in this Group. Another remarkable finding from this study is urinary osmolality at postoperative 2 hours in both groups. The fall in the urine osmolality at 12 and 24 hours can be due to the end of the drug effect on the kidneys. Consecutively, the reestablishment of the fluid balance was observed as low urine osmolality.

Similarities and differences in relation to other studies

To our knowledge, this is the first study examining the renal effects of carbetocin and Oxytocin in such a comprehensive manner. All parameters were monitored, and their results

were compared extensively.

Study limitations

The limited number of participants in this study weakens the generalizability of the results. Another limitation is that measurements related to different blood electrolyte balance systems, other than the renal system, are not included in the study. Besides, the patients' long-term follow-up was not performed, and the follow-up was terminated at the 24th hour after the operation.

Clinical implications

Both drugs cause minimal changes in renal parameters at physiological limits at the dosages mentioned here. However, comparing carbetocin to Oxytocin stands out as an easy-to-use agent that causes less blood loss and less additional uterotonics.

Future research

Further studies are needed as renal effects may be different at higher doses.

Conclusion

In conclusion, the data obtained from this study show that Oxytocin and carbetocin are safe and effective agents in preventing P.P.H.

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KLİNİK ÇALIŞMA / CLINICAL TRIAL
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ADC Measurement in Diffusion-Weighted Imaging; Compatibility Comparison in PACS and Workstation

Difüzyon Ağırlıklı Görüntülemede ADC Ölçümü; PACS ve İş İstasyonunda Uyumluluklarının Karşılaştırılması

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Abstract

Objective: The aim of the study is to compare the compatibility of the mean and minimum ADC values measured in dedicated workstation and PACS.

Methods: In this study, a total of 1918 patients who were reported to have malignant lesions in abdominopelvic MRI examinations were retrospectively evaluated. Among the 1918 patients scanned, 203 patients after exclusion criteria were found to have 351 lesions, 216 of which were malignant and 135 of which were benign. Two radiologists evaluated the images in consensus. Mean and minimum ADC measurements were made using ROI both in PACS and in the workstation in the same session.

Results: Mean ADC values of all lesions measured on PACS ranged from 0.30 to 3.80 (1.46 ±0.85) x10^{-3} mm^2/s, while the mean ADC values measured on the workstation ranged from 0.32 to 3.75 (1.46 ±0.86) x10^{-3} mm^2/s. The ICC value between mean ADC values of all lesions measured in both systems was 0.99. According to the Bland-Altman graph, 95% minimum and maximum compatibility limits for all lesions were found to be -0.12 x10^{-3} mm^2/s and +0.12 x10^{-3} mm^2/s. Minimum ADC values of all lesions measured on PACS ranged from 0.08 to 3.60 (1.03 ±0.74) x10^{-3} mm^2/s, while minimum ADC values measured at the workstation ranged from 0.08 to 3.56 (1.01 ±0.74) x10^{-3} mm^2/s. Minimum ADC values of all lesions measured in both devices were found to be ICC 0.99. According to the Bland-Altman graph, 95% minimum and maximum compatibility limits for all lesions were found to be -0.11 x10^{-3} mm^2/s and +0.14 x10^{-3} mm^2/s.

Conclusion: As a result, mean and minimum ADC measurements can be made directly over PACS without the need for a workstation.

Keywords: DWI, ADC measurement, PACS, Workstation

Öz

Amaç: Çalışmanın amacı, iş istasyonunda ve PACS'de ölçülen ortalama ve minimum ADC değerlerinin uyumluluklarının karşılaştırmaktır.

Gereç ve Yöntem: Bu çalışmada abdominopelvik MRG incelemelerinde malign lezyon raporlanan toplamda 1918 hasta retrospektif olarak değerlendirildi. Taranan 1918 hasta içerisinden, dışlama kriterleri sonrasında 203 hastada saptanan toplamda 351 lezyondan, 216 malign, 135 bengin lezyondu. İki radyolog, görüntüleri consensus ile değerlendirdi. ROI kullanılarak hem PACS'de hem de iş istasyonunda aynı oturumda ortalama ve minimum ADC ölçümleri yapıldı.

Bulgular: Çalışmada tüm lezyonlarda PACS'ta ölçülen ortalama ADC değerleri 0.30- 3.80 (1.46 ±0.85) x10^{-3} mm^2/s arasında, workstation'da ölçülen ortalama ADC değerleri ise 0.32-3.75 (1.46 ±0.86) x10^{-3} mm^2/s arasında değişmekteydi.

Tüm lezyonlar için her iki sistemde ölçülen ortalama ADC değerleri arası ICC değeri 0.99 olup Bland-Altman plot grafiğine göre tüm lezyonlar için minimum ve maksimum %95 uyum sınırları -0.12 x10^{-3} mm^2/s ve +0.12 x10^{-3} mm^2/s olarak bulunmuştur. Tüm lezyonlarda PACS'ta ölçülen minimum ADC değerleri 0.08- 3.60 (1.03 ±0.74) x10^{-3} mm^2/s arasında, iş istasyonunda ölçülen minimum ADC değerleri ise 0.08-3.56 (1.01 ±0.74) x10^{-3} mm^2/s arasında değişmekteydi. Tüm lezyonlar için her iki cihazda ölçülen minimum ADC değerleri ICC 0.99 olup Bland-Altman plot grafiğine göre tüm lezyonlar için minimum ve maksimum %95 uyum sınırları -0.11 x10^{-3} mm^2/s ve +0.14 x10^{-3} mm^2/s olarak bulunmuştur.

Sonuç: Sonuç olarak, iş istasyonuna gerek kalmadan direkt PACS üzerinden mean ve minimum ADC ölçümleri yapılabilir.

Anahtar Kelimeler: DWI, ADC ölçümü, PACS, iş istasyonu

Introduction

Diffusion-weighted imaging (DWI) was first used in the imaging of the central nervous system (CNS) in cases of acute ischemia (1). Due to the developments in technology and the acquisition of stronger diffusion gradients and faster imaging sequences, DWI has also found use besides the CNS (2). Aside from stroke cases in the CNS, it is currently widely used in the detection and characterization of lesions in the abdomen and pelvis, as well as in the assessment of treatment response (3,4).

DWI essentially reflects the random motion of water molecules. Since DWI is successful in demonstrating tissue cellularity and the permeability of cell membranes to water, it provides useful information in the characterization of the lesion, both qualitatively as a visual and quantitatively by measuring the "apparent diffusion coefficient" (ADC). ADC measurements have traditionally been performed on a dedicated workstation provided by the magnetic resonance imaging (MRI) company, and these measurements are regarded as reference values. Switching to a different device (possibly in a different room) to perform ADC measurements increases the workload and causes time loss. The location of the MRI and the location where the images are interpreted can sometimes be completely different due to teleradiology. All of these indirectly limit the use of ADC, which is useful in the characterization of lesions.

Mean ADC values are generally used in lesion characterization. However, there are numerous publications that investigate minimum ADC values (5–14). There are only a few studies in the literature that compare the compatibility of mean ADC measurements in PACS and a dedicated workstation (3,15,16). However, to the best of our knowledge, this is the first study to compare the compatibility of minimum ADC measurements. The aim of the study is to assess the compatibility of the mean and minimum ADC values measured in a dedicated workstation and "picture archiving and communication system" (PACS) where images are evaluated.

Methods

This study was approved by our hospital ethics committee (Date: 22.12.2021, Number: 366). The need for signed informed consent was waived due to the retrospective nature of the study.

In this study, a total of 1918 patients who were reported to have malignant lesions in abdominopelvic MRI examinations at X X University, X Training and Research Hospital, between April 1, 2020, and January 1, 2021, were retrospectively evaluated. Incidentally detected benign lesions were also noted in patients with malignant lesions. The study excluded 25 lesions less than 1 cm in size and 16 lesions whose ADC map was not optimal for evaluation or could not be visualized on the ADC map. Furthermore, three patients were excluded due to a lack of DWI. The three largest lesions were evaluated in patients who had multiple lesions with similar characteristics. Among the 1918 patients scanned, the remaining 203 patients after exclusion criteria were found to have 351 lesions, 216 of which were malignant and 135 of which were benign.

MRI examination of all patients was performed using 1.5T MRI device GE Signa Explorer 1.5 Tesla (GE Medical system, Milwaukee, WI, USA). DWIs were obtained in the axial plane by applying diffusion sensitive gradients in all three directions (x, y, z) using the breath-hold SSh-TSE-EPI sequence, with 4 different b values (b=0, 50, 800, and 1000 s/mm^2). ADC maps of images were created automatically by the device. The ADC values of the lesions were created on the second console of the MRI.

Two radiologists with 9 years of experience in abdominal radiology (F.C) and 4 years of radiology experience (M.F.K) who were blinded to the pathology results evaluated the images in consensus. Images were transferred to the GE Signa Explorer software workstation for evaluation. Out of a total of 351 lesions included in the study, mean and minimum ADC measurements were made using circular region of interest (ROI) both in PACS (Infinitt PACS; Infinitt Healthcare, Seoul, Korea) and in the workstation in the same session. Both ROIs were measured from lesions with the emphasis on them being from the same cross-sectional image, being in a similar area of the lesion, and having the same shape and size (Figures 1 and 2). ADC measurement was made from the hyperintense area of the DWI at high b values (b=1000 s/mm^2) and the corresponding hypointense area in the ADC map. In heterogeneous lesions, measurements were taken from the solid component of the lesion.

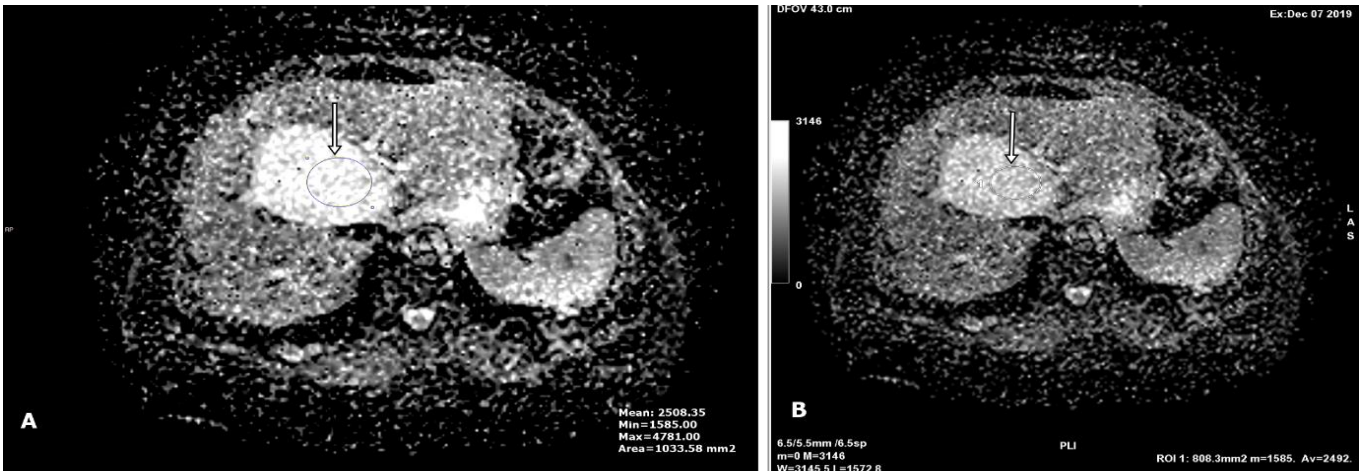

Figure 1. A 54-year-old female patient with Gharbi type 1 granular echinococcal lesion in liver. **(A)** Minimum and maximum ADC values on PACS were measured as 2.51 x10^{-3} mm^2/s and 1.58 x10^{-3} mm^2/s, respectively. **(B)** The same values were measured as 2.49 x10^{-3} mm^2/s and 1.58 x10^{-3} mm^2/s on the workstation, respectively.

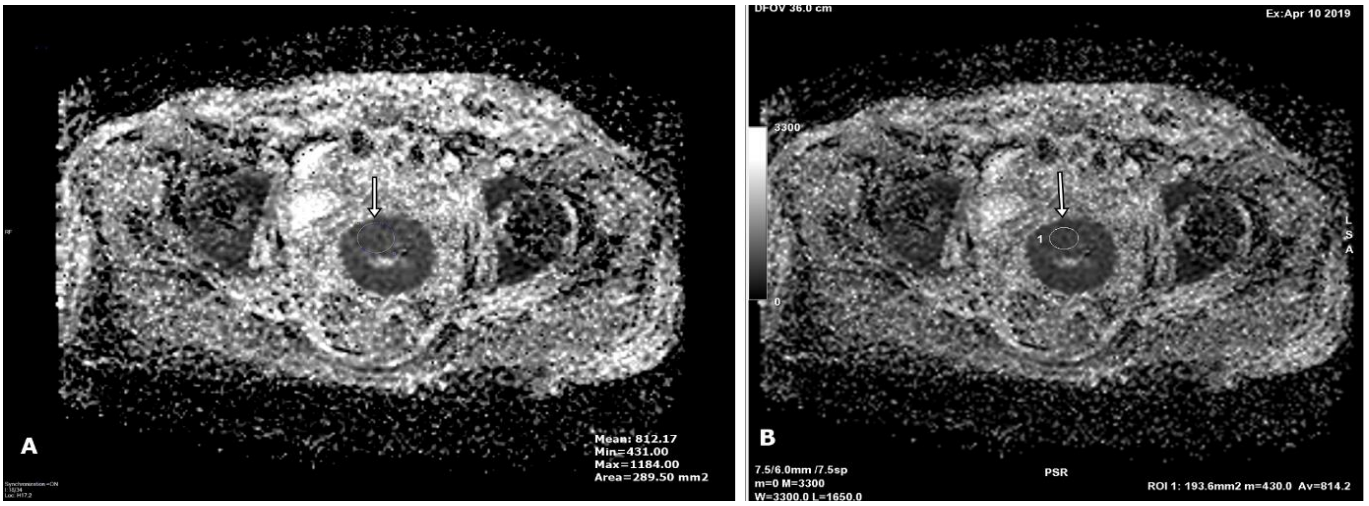

Figure 2. A 59-year-old patient with a squamous cell carcinoma of the uterine cervix. **(A)** Minimum and maximum ADC values on PACS were measured as 0.81 x10^{-3} mm^2/s and 0.43 x10^{-3} mm^2/s, respectively. **(B)** The same values were measured as 0.81 x10^{-3} mm^2/s and 0.43 x10^{-3} mm^2/s on the workstation, respectively.

For categorical variables, the results of the study are presented as numbers and percentages, and for continuous variables, as mean, standard deviation (SD), median, minimum, and maximum. The Shapiro-Wilk Test was used to determine whether the continuous variables were normally distributed, and the difference between the methods was compared using the Paired Sample t test in the case of normal distribution and the Wilcoxon test in the case of non-normal distribution.

To determine the significance, direction, and strength of the relationship b etween the measurements Pearson Correlation Analysis was used in the case normal distribution, and Spearman Correlation Analysis was used in the case of non-normal distribution. Compatibility between methods was calculated with intraclass correlation coefficients (ICC) and Bland-Altman graphs were drawn to visualize the data.

ICC values less than 0.5 were considered poor, values between 0.5 and 0.75 were considered moderate, values between 0.75 and 0.9 were considered good, and values greater than 0.9 were considered excellent (17). The data were analyzed with SPSS 24.0 and MedCalc software. The confidence interval was set at 95%, and the analysis results were interpreted by comparing them to the level of $p<0.05$.

Results

Following the exclusion criteria, our study group included a total of 203 patients with a mean age of 57, 122 women (60%) and 81 men (40%). Of total 351 lesions found in 203 patients, 216 were malignant and 135 were benign. Of the malignant lesions; 43 were liver metastases, 29 were renal cell carcinoma (RCC), 22 were rectal adenocarcinoma, 20 were malignant ovarian tumor, 15 were bladder urothelial carcinoma, 15 were lymphoma, 10 were endometrial carcinoma, 9 were pancreatic adenocarcinoma, 9 were metastatic LAP, 8 were colon adenocarcinoma, 7 were squamous-cell carcinoma (SCC) of the uterine cervix , 6 were gastric adenocarcinoma, 5 were peritoneal implant, 4 were cholangiocellular carcinoma (CCC), 3 were hepatocellular carcinoma (HCC), 3 were gallbladder adenocarcinoma, and 8 were other [adrenocortical carcinoma, malignant gastrointestinal stromal tumor (GIST), malignant neuroendocrine tumor (NET), retroperitoneal liposarcoma, uterine leiomyosarcoma] lesions. Of the benign lesions, 42 were Bosniak type 1 and 2 renal cortical cysts, 16 were hepatic hemangiomas, 13 were simple hepatic cysts, 9 were pancreatic serous cystadenomas, 7 were benign ovarian tumors, 7 were adrenal adenomas, 7 were physiological proliferative endometrium and endometrial polyps, 6 were abscesses, 5 were granular echinococcus, 4 were tuberculosis lymphadenitis, 3 were retroperitoneal peripheral nerve sheath tumors, 15 were other (renal angiomyolipoma, hemorrhagic renal cortical cyst, adrenal cyst, stomach GIST, desmoid tumor, focal nodular hyperplasia of the liver, tubular adenoma of the colon, adrenal myelolipoma, pancreas NET, renal oncocytoma, renal hemangioblastoma and branch-duct type IPMN of the pancreas) lesions. In 142 of the malignant lesions, the diagnosis was made histopathologically, and in 74 malignant and 135 benign lesions, the diagnosis was made based on typical imaging features, clinical and laboratory findings, and follow-up. In GIST and NET cases, malignancy was determined based on a high histological grade or whether the case had metastases.

Mean ADC values of all lesions measured on PACS in the study ranged from 0.30 to 3.80 (1.46 ±0.85) $x10^{-3}$ mm^2/s, while the mean ADC values measured on the workstation ranged from 0.32 to 3.75 (1.46 ±0.86) $x10^{-3}$ mm^2/s. Mean ADC values of malign lesions measured on PACS ranged from 0.40 to 2.64 (0.98 ±0.32) $x10^{-3}$ mm^2/s, while the mean ADC values measured on the workstation ranged from 0.42 to 2.64 (0.98 ±0.32) $x10^{-3}$ mm^2/s. Mean ADC values of benign lesions measured on PACS ranged from 0.30 to 3.80 (2.21 ±0.89) $x10^{-3}$ $mm^2/$, while the mean ADC values measured on the workstation ranged from 0.32 to 3.75 (2.22 ±0.89) $x10^{-3}$ mm^2/s (Table 1). The mean ADC values of malignant lesions were found to be statistically significantly lower than the mean ADC values of benign lesions ($p<0.001$).

Table 1. Mean and minimum ADC values (x 10^{-3} mm^2/s) on PACS and Workstation

	Mean ADC			Minimum ADC		
	All lesions (n:351)	Benign lesions (n:135)	Malignant leions (n:216)	All lesions (n:351)	Benign lesions (n:135)	Malignant lesions (n:216)
PACS	0.30-3.80 (1.46 ±0.85)	0.30-3.80 (2.21 ±0.89)	0.40-2.64 (0.98 ±0.32)	0.08-3.60 (1.03 ±0.74)	0.12-3.60 (1.65 ±0.81)	0.08-2.21 (0.64 ±0.28)
Workstation	0.32-3.75 (1.46 ±0.86)	0.32-3.75 (2.22 ±0.89)	0.42-2.64 (0.98 ±0.32)	0.08-3.56 (1.01 ±0.74)	0.09-3.56 (1.63 ±0.81)	0.08-2.21 (0.63 ±0.28)

PACS; picture archiving and communication system. ADC; apparent diffusion coefficient

Values are expressed as minimum-maximum (mean ± standard deviation)

The ICC value between mean ADC values of all lesions measured in both systems was 0.99, and it was found to be excellently compatible. The ICC value for both malignant and benign lesions was 0.99, and it was found to be excellently compatible. There was no statistically significant difference between the mean ADC values measured in both devices. (p=0.875). According to the Bland-Altman graph, 95% minimum and maximum compatibility limits for all lesions were found to be -0.12 $x10^{-3}$ mm^2/s and +0.12 $x10^{-3}$ mm^2/s. The same values for benign and malignant lesions were found to be -0.14 $x10^{-3}$ mm^2/s and +0.13 $x10^{-3}$ mm^2/s, -0.097 $x10^{-3}$ mm^2/s and +0.101 $x10^{-3}$ mm^2/s, respectively (Figure 3).

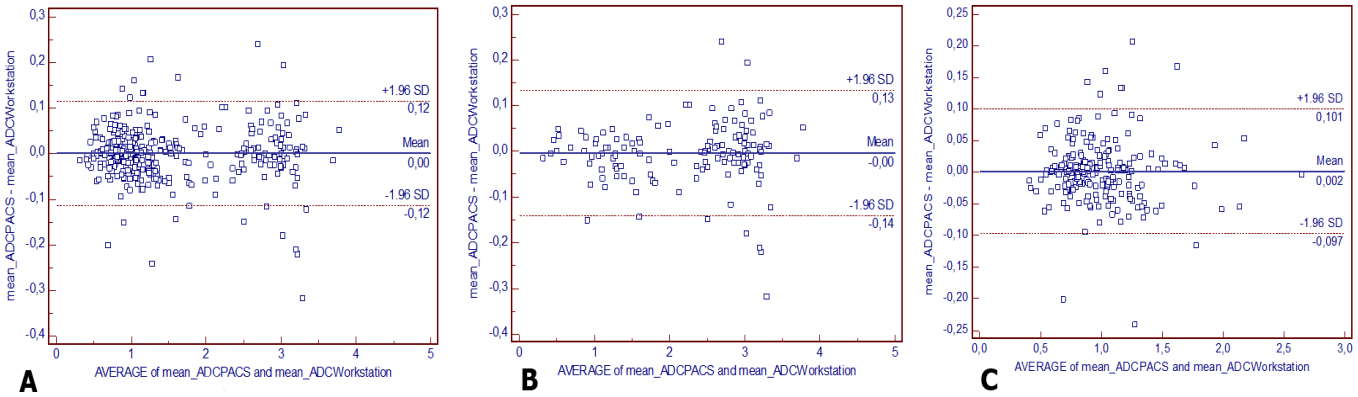

Figure 3. Bland-Altman graph of **(A)** all lesions, **(B)** benign lesions, **(C)** malignant lesions. The graph depicts the compatibility between the mean ADC values measured in the workstation and those measured in the PACS.

Minimum ADC values of all lesions measured on PACS in the study ranged from 0.08 to 3.60 (1.03 ±0.74) $x10^{-3}$ mm^2/s, while minimum ADC values measured at the workstation ranged from 0.08 to 3.56 (1.01 ±0.74) $x10^{-3}$ mm^2/s. Minimum ADC values of malign lesions measured on PACS ranged from 0.08 to 2.21 (0.64 ±0.28) $x10^{-3}$ mm^2/s, while the minimum ADC values measured on the workstation ranged from 0.08 to 2.21 (0.63 ±0.28) $x10^{-3}$ mm^2/s. Minimum ADC values of benign lesions measured on PACS ranged from 0.12 to 3.60 (1.65 ±0.81) $x10^{-3}$ mm^2/s, while the minimum ADC values measured on the workstation ranged from 0.09 to 3.56 (1.63 ±0.81) $x10^{-3}$ mm^2/s (Table 1). The minimum ADC values of malignant lesions were found to be statistically significantly lower than the minimum ADC values of benign lesions ($p<0.001$).

Minimum ADC values of all lesions measured in both devices were found to be ICC 0.99, and they were found to be excellently compatible. Furthermore, the ICC value was 0.99 in benign lesions and 0.98 in malignant lesions, and they were found to be excellently compatible. According to the Bland-Altman graph, 95% minimum and maximum compatibility limits for all lesions were found to be -0.11 $x10^{-3}$ mm^2/s and +0.14 $x10^{-3}$ mm^2/s. The same values for benign and malignant lesions were found to be -0.14 $x10^{-3}$ mm^2/s and +0.18 $x10^{-3}$ mm^2/s, -0.075 $x10^{-3}$ mm^2/s and +0.106 $x10^{-3}$ mm^2/s, respectively (Figure 4).

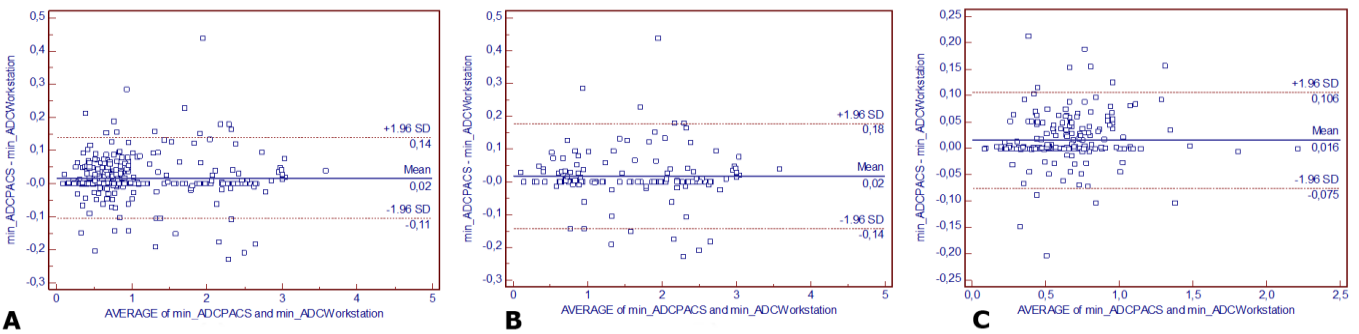

Figure 4. Bland-Altman graph of **(A)** all lesions, **(B)** benign lesions, **(C)** malignant lesions. The graph depicts the compatibility between the mean ADC values measured in the workstation and those measured in the PACS.

Discussion

DWI is becoming more commonly performed besides the CNS, and particularly in abdominal examinations. DWI is being added to routine abdominal MRI protocols by an increasing number of clinics because it does not require the use of intravenous contrast material, has a short scanning time, and adds data to conventional MRI sequences.

Image reporting with the widespread use of PACS, enabled the scanning to be performed from a location other than the hospital. Furthermore, image evaluation on PACS is more practical than dedicated workstation. Although both systems use the same algorithm (the Stejskal-Tanner equation) to acquire ADC maps, PACS providers use different post-processing processes (e.g., thresholding, motion correction, echo planar imaging distortion correction) to obtain the ADC map (15). As a result, it is critical that the image analyses and measurements performed in both systems are compatible and reproducible.

In the study of Fanariotis et al. with a total of 100 breast lesions, 59 malignant (46 mass, 13 non-mass lesions) and 41 benign (28 mass, 13 non-mass lesions) in the literature, they found ICC to be 0.98 for all lesions of ADC measurements in workstation and PACS, indicating that they were excellently compatible (15). The ICC was found to be 0.98 in benign mass lesions, 0.97 in benign non-mass lesions, 0.96 in malignant mass lesions, and 0.96 in malignant non-mass lesions. The Bland-Altman graph demonstrated that there are narrow limits of compatibility between measurements in their work. They discovered that the 95% compatibility limits for all lesions are -0.07 $x10^{-3}$ mm2/s at the minimum and 0.09 $x10^{-3}$ mm2/s at the maximum, with the same values for mass lesions being -0.07 $x10^{-3}$ mm2/s and 0.09 $x10^{-3}$ mm2/s, respectively, and for non-mass lesions being -0.13 $x10^{-3}$ mm2/s and 0.15 $x10^{-3}$ mm2/s. In addition, in the study of Clauser et al. conducted with the evaluation of 2 independent radiologists in 41 breast lesions, (31 malignant and 10 benign), ICC was found to be 0.97 (for radiologist 1) and 0.99 (for radiologist 2) in all lesions, indicating that they were excellently compatible (16). For all lesions, 95% compatibility limits were found to be minimum -0.17 $x10^{-3}$ mm^2/s, and maximum 0.19 $x10^{-3}$ mm^2/s (16). The Bland-Altman graph revealed narrow limits of compatibility between measurements in both studies. The ICC (for both mean and minimum ADC values) in our study ranged between 0.98 and 0.99 and was found to be excellently compatible. Similarly, the Bland-Altman graph demonstrates that the compatibility limits between mean and minimum ADC measurements are narrow (Figures 3 and 4).

In the study of El Kady RM et al. conducted with 120 liver lesions in 79 patients, no statistically significant difference between mean ADC measurements on PACS and workstation was found (p=0.268) (3). We also included any other lesions found in the abdomen besides liver lesions. In our study, there was a high correlation between mean ADC measurements taken in both systems, and there was no statistically significant difference between the two measurements (p=0.875).

In addition to the evaluation of the compliance of mean ADC values measured in workstation and PACS, the compliance of minimum ADC values used in lesion characterization was also examined. The ICC value between the minimum ADC values measured in workstation and PACS was found to be 0.99 for all and benign lesions, and 0.98 for malignant lesions, and it was found to be excellently compatible.

There are publications in the literature that compare the mean ADC values measured in devices from different MRI companies and/or different MRI devices from the same company (18,19). Despite scanning with similar protocols in studies, statistically significant differences in mean ADC values were discovered and considered to be due to standardization difficulties, different coil systems used, different analysis methods used, or different software programs.

There were some limitations to our study. Firstly, it used a retrospective, single-center design. Secondly, we compared ADC measurement compliances in a single workstation and a single PACS. Comparative evaluations of MRI devices and PACS systems from a wider range of manufacturers will make additional contributions to the literature. Thirdly, ADC measurements were made by a collaboration of two radiologists, and inter-reader variability was not assessed. However, the main purpose was that measurements were taken in both systems during the same session and ROIs from the same cross-section, same area of the lesion, and similar size and shape were required for comparison. Clauser et al. discovered in their study that intra-reader compliance was excellent with 0.97 (for radiologist 1) and 0.99 (for radiologist 2) in all lesions, while inter-reader compliance was substantial with 0.682 in workstation and 0.615 in PACS (16). The main reason was that two radiologists performed ROI and ADC measurements in separate sessions, possibly in different cross-sectional images, and in different sizes and shapes. The main reason for the difference in measurements in our clinical practice was also the different sizes and shapes of the ROIs taken. The more similar the shape and size of the ROI taken, the closer the ADC value will be.

Conclusion

In our study, an excellent correlation was found between the ADC measurements taken in both systems. As a result, mean and minimum ADC measurements can be performed directly over PACS, eliminating the need for a dedicated workstation. Thus, time will be saved in a high-paced work environment, and ADC usage will increase.

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KLİNİK ÇALIŞMA / CLINICAL TRIAL
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Retrospective Evaluation of Sociodemographics, Clinical Characteristics and Intervention Methods of Pediatric Patients Presenting for Epistaxis

Pediatrik Epistaksis Nedeniyle Girişimsel Müdahale Yapılmış Olan Hastaların Sosyodemografik ve Klinik Özelliklerinin Retrospektif Olarak İncelenmesi

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Abstract

Objective: Most of the pediatric epistaxis occur as a result of trauma, intranasal dryness, infection, hematological disorders, allergy and as a result of some chronic diseases. In addition; the clinical characteristics of the patient, maternal and environmental factors also have an important role in the occurence of epistaxis. The aim of this study is to examine the clinical features, maternal and environmental factors of patients with pediatric epistaxis who applied to our clinic and to analyze the relationship of these variables with the treatment methods.

Materials and Methods: The data of 142 pediatric patients with epistaxis who applied to our clinic between 01/03/2020 and 01/03/2022 were evaluated retrospectively. Age, gender, topical emolient usage, indoor humidifier usage, history of nasal trauma, nose picking habit, smoking status, history of foreign body, admission time, and the type of treatment modality datas were collected. Descriptive statistical analyses, chi-square and Pearson correlation tests were used.

Results: 142 patients were included in the study. 89 (62.7%) of the patients were evaluated as recurrent epistaxis. There was no statistical relationship between the independent variables of the study and the type of treatment modality. It was observed that interventional methods were used more frequently in the recurrent epistaxis group (p: 0.046). No statistically significant difference was observed between the two groups for non-interventional treatment methods.

Conclusion: Interventional epistaxis methods are statistically more commonly used in patients with recurrent epistaxis. No relationship was found between other treatment modalities and epistaxis type. Interventional methods, primarily chemical cauterization, can be used in recurrent pediatric epistaxis.

Keywords: Pediatric epistaxis, retrospective studies, treatment

Öz

Amaç: Pediatrik epistaksislerin büyük bir kısmı travma, burun içi kuruluk, enfeksiyon, hematolojik bozukluklar, allerji ve bazı kronik hastalıklar sonucunda oluşur. Epistaksisin gerçekleşmesinde bu sebeplerin yanında hastanın klinik özelliklerinin, maternal faktörlerin ve çevresel faktörlerin de önemli rolü mevcuttur. Bu çalışmanın amacı; kliniğimize başvuran pediatrik epistaksis hastalarının klinik özelliklerini, maternal ve çevresel faktörlerini incelemek ve bu değişkenlerin uygulanan tedavi yöntemleri ile olan ilişkisini analiz etmektir.

Araçlar ve Yöntem: Kliniğimize 01/03/2020 ile 01/03/2022 arasında epistaksis nedeniyle başvuran 142 pediatrik hastanın verileri retrospektif olarak değerlendirilmiştir. Hastaların yaş, cinsiyet, topikal veya ev içi nemlendirici kullanımı öyküsü, nazal travma öyküsü, burun karıştırma öyküsü, ev içi sigara içimi, buruna yabancı cisim sokma öyküsü, başvurmuş olduğu ay ve yapılmış olan tedavi bilgileri toplanmıştır. İstatistiksel olarak tanımlayıcı istatistik analizlerin yanında, kikare ve Pearson korelasyon testi kullanılmıştır.

Bulgular: Çalışmaya 142 hasta dahil edildi. Hastaların 89 tanesi (% 62,7) rekürren epistaksis olarak değerlendirildi. Cinsiyet, ev içi nemlendirici kullanımı, topikal nemlendirici kullanımı, burun karıştırma alışkanlığı, yabancı cisim aspirasyon öyküsü, nazal travma öyküsü, ev içi sigara içimi bağımsız değişkenlerinin hastaya uygulanan tedavi yöntemi tipi ile arasında herhangi bir istatistiksel ilişki saptanmadı. Rekürren epistaksis grubunda girişimsel yöntemlerin istatistiksel anlamlı olarak daha fazla kullanıldığı görüldü (p: 0,046). Girişimsel olmayan tedavi yöntemleri için ise her iki grup içinde anlamlı bir istatistiksel fark gözlenmedi.

Sonuç: Girişimsel epistaksis işlemleri rekürren epistaksis hastalarında istatistiksel olarak daha sık uygulanmaktadır. Diğer tedavi yöntemleriyle epistaksis tipi arasında herhangi bir ilişki saptanamamıştır. Rekürren epistaksis şikayeti ile başvuran çocuklarda kimyasal koterizasyon başlıca olmak üzere girişimsel yöntemler daha uygun bir tedavi seçeneğidir.

Anahtar Kelimeler: Pediatrik epistaksis, retrospektif çalışmalar, tedavi

Introduction

Epistaxis is a frequently observed condition in emergency, pediatrics and otolaryngology departments. It is seen at a rate of 30 % in the first 5 years of age, and it is seen nearly 30 % above at the age of 5 years. It is rarely seen under 2 years of age, unless there is any underlying trauma or coagulation problems.[1] Epistaxis arise mostly from the anterior nasal septum. The majority of epistaxis are managed by clearing blood clots and simple digital compression maneuvers.[2] Sometimes epistaxis cannot be managed with simple interventions and recurrent epistaxis episodes can be observed. In such cases, patients need to apply to the otolaryngology, pediatrics or emergency departments for detailed evaluation.

The main causes of pediatric epistaxis are: common diseases such as rhinosinusitis, habitual nasal picking, nasal trauma, allergic rhinitis, septal deviation; rare and idiopathic causes such as coagulopathies, nasal polyps, juvenile nasopharyngeal angiofibroma, hereditary hemorrhagic telangiectasia.[3] Pediatric epistaxis can be controlled with noninvasive or invasive methods. Digital compression, topical emolients, topical vasoconstrictors, topical antibiotics are the main non-invasive methods, while chemical cauterization with silver nitrate, electrocautery, nasal tamponade application, surgery and embolization are advanced and invasive methods.[4]

It is thought that most of the pediatric epistaxis may be caused by the reasons that may lead to the dryness of the nasal mucosa, digital or external trauma of the nose. Some environmental and maternal factors can also be related with the formation of pediatric epistaxis. On the other hand, studies focusing on the epidemiological, socio-cultural and maternal factors on this topic are very limited.[5] In addition, there are not many studies describing which treatment strategy should be used for which patient. The studies about the importance and possible effects of clinical characteristics of patients in choosing the treatment strategies are lacking in the literature.

It is also thought that some meteorological factors such as air temperature, humidity, and air pollution have potential effects on the development of primary and recurrent epistaxis.[6] There are some studies showing that the decrease in air temperature and humidity increase the risks of nasal dryness and possibility of upper respiratory tract infections and it results in increasing the probability of epistaxis. There are also some studies contrary to this hypothesis in the literature, and the effect of these meteorological factors on the development of epistaxis has not been fully demonstrated.[7]

The aim of this study is to investigate the clinical features, environmental and maternal factors, the seasonal effects, treatment methods and evaluate the relationship of these parameters in pediatric patients who applied to our clinic due to primary and recurrent epistaxis. According to the obtained data, it is aimed to clarify the possible etiological factors, environmental and maternal factors on formation of primary and recurrent epistaxis. Another main objective of this study is to determine the relation of treatment methods and recurrency status of epistaxis.

Materials & Methods

This study was approved by Clinical Research Ethics Committee of XXX University (Date: 16.11.2021 Application no: 207-207-07 Decision no: 07).

The data of 142 pediatric patients who applied to the Department of Otorhinolaryngology at XXX University Training and Research Hospital between 01/03/2020 and 01/03/2022 due to epistaxis were evaluated retrospectively. Patients who had been admitted to the hospital within 3 months due to epistaxis and had a history of epistaxis in the last week were considered as recurrent epistaxis. Sociodemographic information, clinical characteristics, month of admission to the hospital and maternal factors of each case were collected via scanning the charts of the subjects in the electronic data system. Patients who were previously diagnosed with a systemic disease, patients with coagulopathy, patients with history of nasoseptal or any kind of surgery in the last 3 months, patients who had abnormal hemogram and coagulation laboratuary parameters, and patients with lack of information in the electronic database were excluded from the study.

Age, gender, history of topical emolient or indoor humidifier usage, history of nasal trauma, history of nose picking, smoking status at home, history of nasal foreign body aspiration, month of admission to the hospital, and treatment methods were evaluated in this study.

Statistical Analysis

SPSS 25.0 data program was used for statistical analysis. The data were analyzed by descriptive statistical methods, calculating the mean and standard deviation values. The relation between the datas and the applied treatment techniques were evaluated with the chi-square test. Pearson correlation test was used for correlation between datas. Statistical significance was accepted as $p<0.05$.

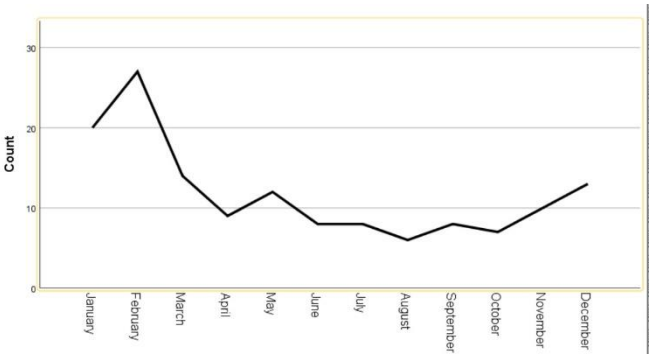
Results

There were 142 patients included in the study; 57 (40,1%) of patients were female and 85 (59,9%) of patients were male. The mean age of the patients included in the study was 7.11 ± 3,35. 89 (62,7%) of the patients were evaluated as recurrent epistaxis. 45 of the patients were using a nasal topical emolient agent at the time of admission to the hospital for epistaxis. 35 of the patients were using an indoor humidifier. 40 of the patients had habitual nose picking. 6 patients had a history of nasal foreign body aspiration. In the history of 20 patients, it was determined that they were admitted to the hospital due to nasal trauma. There was smoke exposure in 40 patients. The sociodemographic data of the patients included in the study, their recurrency status, clinical characteristics, maternal and environmental factors and the epistaxis tretament methods are explained with details in Table 1.

Table 1: The detailed table of sociodemographic data, recurrency status, clinical characteristics, maternal and environmental factors and the epistaxis treatment methods

	Primary epistaxis	**Recurrent epistaxis**
Gender	24 female, 29 male	33 female, 56 male
Indoor humidifier usage	n: 22 (41,5%)	n: 13 (14,6%)
Topical emolient usage	n: 28 (52,8%)	n: 37 (41,5%)
Habitual nose picking	n: 23 (43,3%)	n: 17(19,1%)
History of nasal foreign body	n: 2 (3,7%)	n: 2 (2,2%)
History of nasal trauma	n: 7 (13,2%)	n: 13 (14,6%)
Smoking status at home	n:14 (26,4%)	n: 26 (29,2%)

The admission times of the patients included in the study were examined and it was determined that pediatric epistaxis was more frequent in winter months in this study. 61 patient (42.9%) were admitted to the hospital during the winter season. There was no similar clustering in the other months and seasons in this study. The distribution of admission of pediatric epistaxis by months is shown in detail in Graph 1.

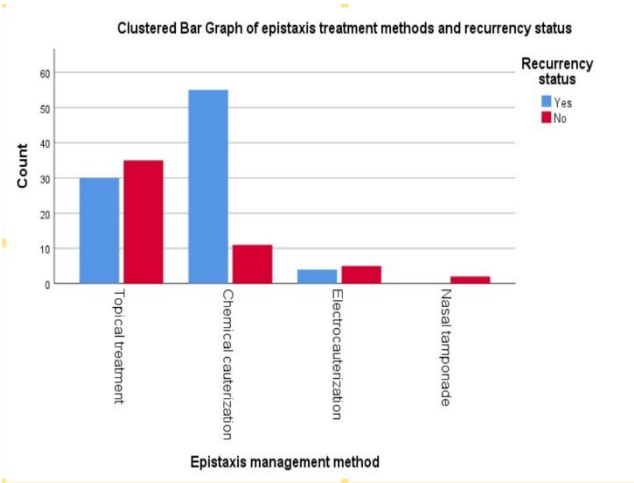


Graph 1: The graph that shows the distribution of admission of pediatric epistaxis according to months

There were 89 patients in recurrent epistaxis group. Fifteen subjects were treated with chemical cauterization and 53 received topical treatment previously. Treatment was not recommended for 21 patients because they did not have active bleeding at the time of intervention. The distribution of patients treated for primary and recurrent epistaxis according to treatment methods is shown with details in Table 2 and Graph 2.

Table 2: The distribution of patients treated for primary and recurrent epistaxis according to treatment methods

	Primary epistaxis	**Recurrent epistaxis**
Topical treatment	n: 35	n: 30
Chemical cauterization	n: 11	n: 55
Electrocauterization	n: 5	n:4
Nasal tamponade application	n: 2	n:0



Graph 2: Clustered graph that shows the relation of recurrency status and epistaxis management method

The correlations and effects of the clinical, sociodemographic and maternal characteristics of the patients with the treatment methods were analyzed statistically using chi-square and Pearson tests. Since the number of patients who underwent electrocauterization (n=9) and nasal tamponade application (n=2) was very small, two groups were formed as interventional and non-interventional methods during statistical analysis, and these methods were classified as in interventional methods together with chemical cauterization. There was no statistical relationship between the independent variables of gender, use of indoor humidifier or topical emolient, habitual nasal picking, history of nasal forieng body aspiration, history of nasal trauma, smoke exposure and the treatment methods applied to the patient. When the recurrency status of epistaxis and treatment methods were analyzed with the chi-square test, it was seen that interventional methods were used statistically significantly more in the recurrent epistaxis group (p: 0,046). The exact p values between variables are shown in Table 3.

Table 3: Table of variables according to the treatment type. Exact p values are shown in table. (*: Chi square test, Pearson correlation analysis)

	Interventional treatment	**P value**
Indoor humidifier usage	n: 11	0,078*
Topical emolient usage	n: 22	0,073*
Habitual nose picking	n: 12	0,068*
History of nasal foreign body	n: 2	-(limited number of subject p value not calculated)
History of nasal trauma	n: 8	-(limited number of subject p value not calculated)
Smoke exposure	n: 21	0,083*
Recurrency status	n: 59	0,046*

Discussion

Pediatric epistaxis is a frequently encountered condition in otolaryngology, pediatrics and pediatric emergency services. Up to 60% of children experience epistaxis at least once until the age of 10.[8] The majority of pediatric epistaxis arise from the Kiesselbach plexus in the anterior part of the nasal cavity. In most of the epistaxis seen in the pediatric age group, there is a slight bleeding and the bleeding stops spontaneously. Patients with uncontrolled epistaxis or recurrent epistaxis usually present to the hospital. The main etiological causes are digital or external trauma, nasal dryness, local infection, allergy and hematological disorders.[9] Epistaxis caused by chronic diseases and hematological disorders can be controlled by correcting the underlying disease, in addition to emergent management. Causes arising from other etiological factors can be stopped by correction of familial and environmental factors, topical emolients or antibiotics, chemical or electrocauterization, nasal tamponade application and rarely surgical interventions.[10]

In this study, individual, family and environmental factors encountered in the etiology of recurrent pediatric epistaxis and treatment options for primary and recurrent pediatric epistaxis were evaluated and their effects on each other were investigated. Patients with chronic diseases and hematological disorders were not included in the study; the relationship between other etiological factors and treatment options was evaluated.

The mean age of the patients with pediatric epistaxis evaluated in our study was 7,11 years. Damrose et al.[9] had an average of 7,3 in their study, and the average was found to be 7,8 in Brown et al.' s[10] study. When we look at the series in our country; Bilal et al.[11] found an average 10,02 in their study, Özdemir et al.[12] in their study, the average was 9,1. This study has a smaller average age than the studies in our country, but it is compatible with the international literature. In most of the studies in the literature, epistaxis is seen more frequently in males. In our study, 59.9% of the patients were males similar to the literature. There was no statistical relationship found between the age and gender distribution of the patients and the treatment methods applied to the patients.

There is no obvious fact in the literature regarding the seasonal variation in the frequency of pediatric epistaxis. Many studies emphasise that the distribution of pediatric epistaxis is similar in all seasons.[9,10,13] However; in some recent studies, it has been found that pediatric epistaxis is more common in months of autumn and winter.[14] Sowerby et al.[15] did not find any correlation with air temperature and the frequency of epistaxis, and no correlation with air humidity. Muhammad et al.[16] reported that low temperature and low humidity increased the incidence of epistaxis. In our study, pediatric epistaxis applications were more frequent in winter months, with the highest number in February. It can be attributed to the decrease in humidity in cold weather, the increase in the frequency of upper respiratory tract infections and the drying of the air due to indoor heating.

Nasal trauma history, nose picking habit and history of nasal foreign body aspiration were evaluated to determine the individual clinical characteristics of the patients. When the relationship between these parameters and treatment methods was examined, there was no statistically significant relationship. However, interventions including chemical cauterization, electrocautery and nasal tamponade application were detected more frequently in patients with a history of nasal trauma. However, we think a larger chort of subjects is needed to clarify this relatiponship. There was no relationship between history of nasal foreign body aspiration and nasal picking habit and the treatment option.

Most pediatric epistaxis cases can be treated by moistening the nasal mucosa with topical antibiotics or emolients.

It is thought that the use of topical moisturizer and indoor moisturizer will reduce the frequency and severity of pediatric epistaxis. In our study, the relationship of these parameters with the recurrence status of epistaxis and the treatment method were investigated. However, no statistically significant results were obtained. Damrose et al.[9] reported in their study that up to 56% of the patients had their epistaxis under control with topical moisturizing treatment. In our study, the use of topical moisturizer was higher in the recurrent epistaxis group. It is thought that this is due to the fact that patients receive this treatment at their first admission. It is thought that by increasing the humidity of the environment, indoor humidifier devices reduce the frequency and severity of bleeding due to dryness in the nasal mucosa.[17] In the present study, we could not find a relationship between this parameter and the treatment method. These factors are thought to reduce the risk of pediatric epistaxis, but prospective studies with large series are needed to elucidate this issue.

Although not statistically significant, smoke exposure was more common in the recurrent epistaxis group. Children are more easily affected physiologically and metabolically by changes related to humidity and air in the environment. For this reason, epistaxis may be encountered in children, in cases of smoke exposure and poor indoor air quality.[18] However; prospective studies with large case groups are needed to evaluate the effect of this parameter on the risk and development of epistaxis.

When the relationship between recurrence status of epistaxis and treatment methods were analyzed, it was seen that interventional methods were used statistically significantly more in the recurrent epistaxis group. Most of the recurrent epistaxis were treated with chemical cauterization. According to the literature, a significant portion of pediatric epistaxis can be stopped with simple interventions and topical treatments.[9] However, we think that chemical cauterization will prevent recurrence in cases of recurrent epistaxis. Especially in patients with etiological factors that increase the risk of epistaxis, chemical cauterization can prevent recurrences. Prospective studies with larger case series on this subject may be helpful in identifying possible individual and familial factors for recurrent epistaxis. Thus, the frequency of recurrent epistaxis can be reduced by chemical cauterization in patients with possible risk factors.

The major limitations of this study are the small number of cases and its retrospective nature. In order to make a clear statistical evaluation, patients with missing data were excluded from the study. Data about the familial and individual factors was obtained from the histories of the patients. We think that large case series in which these parameters are evaluated prospectively and laboratory and radiological parameters are included as additional data will contribute to this issue.

Conclusion

This study is a retrospective study about the impact of familial and individual factors on the treatment methods of patients treated for pediatric epistaxis. No relationship was found considering gender, use of indoor humidifier, use of topical moisturizer, nose picking habit, history of foreign body aspiration, history of nasal trauma, and smoke exposure analyzed in the study, with the treatment method. Interventional epistaxis methods were statistically more commonly applied in patients with recurrent epistaxis. No relationship was found between other treatment modalities and epistaxis type. In children presenting with the complaint of recurrent epistaxis, interventional methods, primarily chemical cauterization can be used. Prospective studies are needed to elucidate this issue.

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Evaluation of Epilepsy Prevalence and Clinical Correlations in Individuals aged 18 and over in Çanakkale City Center

Çanakkale İl Merkezinde 18 Yaş ve Üzeri Bireylerde Epilepsi Prevalansı ve Klinik Korelasyonlarının Değerlendirilmesi

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Abstract

Objective: Epilepsy; is a common neurological disease characterized by sudden and recurrent seizures, especially affecting the young population. The burden of epilepsy is not limited to seizures. The disease also significantly affects personal, familial and social quality of life by causing psychological problems. In this study, it was aimed to determine the prevalence of epilepsy and to determine the effect of epilepsy on quality of life and sleep hygiene in people aged 18 years and older living in Çanakkale city center.

Method: In our study, 397 participants aged 18 years and older residing in Çanakkale city center were interviewed. Sociodemographic characteristics, personal and family history, and epilepsy disease history were questioned. World Health Organization Quality of Life Scale (WHOQOL-BREF) and Sleep Hygiene Index (SHI) scales were applied to patients with epilepsy diagnosis.

Results: 2.0% (n=8) of the participants had a diagnosis of epilepsy. 75% (n=6) of patients with epilepsy were female. There was a family history of epilepsy in 62.5% (n=5) of individuals with epilepsy, a family history of febrile seizures in 25% (n=2), and a family history of consanguinity between parents in 12.5% (n=1). There was no significant difference between the groups with and without epilepsy in terms of the mean SHI scores (p=0.400). There was no difference in the WHOQOL-BREF quality of life scale in terms of bodily domain, mental domain, social domain and environmental domain sub-scores (p>0.05).

Conclusion: In our study, the prevalence of epilepsy was found to be 2%. Most of the patients were female. There was an increased rate of consanguineous marriage in the families of the patient group. Again, a devastating majority of the patient group had a family history of epilepsy or a history of febrile convulsions. Sleep hygiene and quality of life scales did not differ between the patient group and the control group. This may be due to the very small number of our patient group. There is a need for larger-scale studies on this subject in our region.

Keywords: Epilepsy, prevalence, quality of life scale,

Öz

Amaç: Epilepsi; ani ve tekrarlayıcı olarak seyreden, nöbetler ile karakterize özellikle genç popülasyonun etkilendiği sık görülen bir nörolojik hastalıktır. Epilepsinin yükü sadece nöbetlerle sınırlı değildir. Hastalık aynı zamanda psikolojik problemlere sebep olarak kişisel, ailesel ve sosyal yaşam kalitesini önemli ölçüde etkilemektedir. Bu çalışmada; Çanakkale il merkezinde yaşayan 18 yaş ve üzeri kişilerde epilepsi prevalansının saptanması, epilepsinin yaşam kalitesi ve uyku hijyenine etkisinin belirlenmesi amaçlandı.

Yöntem: Çalışmamızda Çanakkale il merkezinde ikamet eden 18 yaş ve üzeri 397 katılımcı ile görüşüldü. Sosyodemografik özellikler, öz ve soy geçmiş bilgileri ve epilepsi hastalık öyküsü sorgulandı. Epilepsi tanısı olan hastalara aynı zamanda Dünya Sağlık Örgütü Yaşam Kalite Ölçeği (WHOQOL-BREF) ve Uyku Hijyen İndeksi(UHİ) ölçekleri uygulandı.

Bulgular: Katılımcıların %2,0'sinde (n=8) epilepsi tanısı mevcuttu. Epilepsili hastaların %75'i (n=6) kadındı. Epilepsi saptanan bireylerin %62,5'inde (n=5) ailede epilepsi öyküsü, % 25'inde (n=2) ailede febril konvüzyon öyküsü, %12,5'inde (n=1) anne baba arası akrabalık öyküsü bulunmaktaydı. Epilepsi olan ve olmayan gruplar arasında UHİ puanı ortalamaları açısından anlamlı fark saptanmadı (p=0,400). WHOQOL-BREF yaşam kalitesi ölçeğinde bedensel alan, ruhsal alan, sosyal alan ve çevresel alan alt puanları açısından da fark yoktu (p>0,05).

Sonuç: Çalışmamızda epilepsi prevelansı %2 olarak saptandı. Hastaların çoğu kadın cinsiyetteydi. Hasta grubunun ailelerinde artmış oranda akraba evliliği mevcuttu. Yine hasta grubunun büyük bir çoğunluğunda ailede epilepsi öyküsü veya febril konvülziyon öyküsü saptandı. Uyku hijjeni ve yaşam kalitesi ölçekleri hasta grubuyla kontrol grubu arasında fark göstermedi. Bunun nedeni hasta grubumuzun sayısının çok az olması olabilir. Yöremizde bu konuda daha büyük ölçekli çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Epilepsi, prevelans, yaşam kalitesi ölçeği

Introduction

Epilepsy is one of the most common neurological diseases. Epilepsy occurs as a result of changes in perception, consciousness and motor activity due to abnormal discharges in the brain [1]. According to the recommendations of the epidemiology commission of the International League Against Epilepsy-ILAE; Transient seizures closely associated with acute central nervous system (CNS) injury were defined as acute symptomatic seizures or condition-related seizures. Acute symptomatic seizures are seizures that can be seen at the beginning of the disease, do not require antiepileptic treatment, or require short-term treatment. Clinically, it can be seen as complex partial, tonic-clonic or status epilepticus. It has been reported that acute symptomatic seizures increase the risk of epilepsy in some cases [2].

According to the World Health Organization data, there are 50 million people diagnosed with epilepsy [8]. The prevalence of active epilepsy is 4-10/1000, and the lifetime accumulated incidence is approximately 3% [2]. In epilepsy prevalence studies conducted in Turkey; 5.5-6.3/1000 for women and 8.6-10/1000 for men in Istanbul Küçükçekmece; It was determined as 8.5/1000 in Bursa [3]. The frequency of epilepsy; It is twice as high in low- and middle-income countries as in high-income countries. The prevalence of epilepsy in low-income countries is multifactorial. Among these factors; frequency of head trauma and CNS (central nervous system) infections and infestations such as malaria, neurocysticercosis and invasive bacterial infections [4].

The burden of epilepsy is not only limited to neurological deficits, but also causes devastating psychological and psychiatric problems, significantly affecting personal, familial and social quality of life, and can be fatal if left untreated or inadequately treated. Individuals with epilepsy generally have higher rates of disability and mortality. It is thought that the mortality rate in people with epilepsy is two to three times higher than the healthy population [5].

The epidemiology, etiology, frequency and regional differences of epilepsy will be determined by studies, etiological factors can be found, scientific approaches can be planned for diagnosis-treatment and follow-up, how to prevent these etiological factors [6]. In this study, the prevalence of epilepsy in people aged 18 years and older living in Çanakkale city center; It was aimed to determine the effect on quality of life and sleep hygiene.

Method

This study was carried out by Çanakkale Onsekiz Mart University Faculty of Medicine, Department of Neurology and Department of Public Health, on 397 individuals aged 18 years and older residing in Çanakkale City Center between August 2019 and January 2020, selected with a multi-stage cluster sampling system. This study, which was approved by Çanakkale Onsekiz Mart University Faculty of Medicine Local Ethics Committee, was conducted in accordance with the Helsinki Declaration decisions and ethical rules.

Design of the study

The population of this study is 131,367 people aged 18 and over living in Çanakkale city center (TÜİK 2018, ABPRS). The sample of the study; In the Epi Info Statcalc program, the expected prevalence of Epilepsy was determined as 9/1000, the confidence limit was 95%, the margin of error was 0.01, the pattern effect was 1 and the sample calculation formula used in cases where the population was known was determined as 342 people. The addresses of the individuals were obtained from the neighborhood headmen. Addresses were randomly selected from the address lists of 342 people who will participate in the research with the multi-stage cluster sampling method. Cluster heads are distributed proportionally to the neighborhood population.

Scales

Personal questionnaire was used in the study. This questionnaire consists of socio-demographic section, self and family history questioning, epilepsy questioning section, WHOQOL-BREF (World Health Organization Quality of Life Scale) and Sleep Hygiene Index sections. Socio-demographic section; It consists of 13 items. It was used to obtain demographic data such as age, gender, education, marital status, etc. of the participants. The section where the resume and family history are questioned; It consists of 10 items. Personal and familial characteristics that increase the risk of developing epilepsy were questioned. The section where epilepsy is questioned; It consists of 17 items.

Survey form; Karaagac et al. It was created by adding 4 questions about complex partial epileptic seizures to the questionnaire form used in the epilepsy prevalence study and proven to be valid.

WHOQOL-BREF (World Health Organization Quality of Life Scale); health-related quality of life scale developed by WHO; The validity and reliability of Eser et al. There are two versions of the scale, long (WHOQOL-100) and short (WHOQOL-27). WHOQOL-BREF consists of a total of 26 questions, one of which is the general perceived quality of life and the other two questions about the perceived health status. With the addition of a national question during Turkish validity studies, WHOQOL-BREF-TR consists of 27 questions. Physical, psychological, social, environmental and national environmental field scores are calculated using questions other than the first two general questions. Calculation is made over 0-20 points, and the higher the score, the higher the quality of life.

Sleep Hygiene Index (SHI); Mastin et al. (2006) was developed by. Its Turkish validity and reliability were determined by Özdemir et al. (2015) made by The survey consists of 13 questions. It is a five-point Likert scale (none:1, rarely:2, sometimes:3, often:4, always:5). The index aims to evaluate the presence of sleep hygiene by questioning how often the participant performs the sleep behaviors that constitute sleep hygiene. Scores ranged from 13 to 65, with higher scores indicating worse sleep hygiene status of the participant.

Statistical assessment

Data were analyzed with SPSS Package Program version 20.0. Number, percentage, mean, standard deviation, median, minimum and maximum were used in the presentation of descriptive data. Chi-square test was used to compare categorical data. The conformity of the variables to the normal distribution was evaluated with the ShapiroWilk Test and the KolmogorovSmirnov Test. The Mann Whitney U Test was used to compare the variables that did not fit the normal distribution. P<0.05 was accepted for statistical significance.

Results

A total of 397 people were included in the study. The mean age of the participants was 39.7±13.7 years, and the median was 38 years (min: 19.0-max: 80.0). 59.9% of the participants are female, 40.1% are male (n=159), 57.7% (n=229) are working, 58.2% (n=231) are university graduates, % 22.7% (n=90) were high school graduates, 7.6% (n=30) were secondary school graduates, 10.1% (n=40) were primary school graduates, and 1.5% (n=6) were was illiterate (Table-1).

Table 1. Socio-demographic characteristics of the participants

Gender	n (%)
Male	159 (40,1)
Female	238 (59,9)
Employment status	
Employed	229 (57,7)
Non-employed	119 (30,0)
Retired	49 (12,3)
Education Status	
Illiterate	6 (1,5)
Primary	40 (10,1)
Secondary	30 (7,6)
High	90 (22,7)
University	231 (58,2)
Economic-Income level	
Poor	51 (12,9)
Medium	194 (48,9)
Good	152 (38,3)
Marital Status	
Married	247 (62,2)
Single	111 (28,0)
Divorced/Widowed	39 (9,8)
Smoking	
Current-smoker	155 (39,0)
Never-smoked	193 (48,6)
Ex-smoker	49 (12,3)
Alcohol consumption	
No	189 (47,6)
Rarely	143 (36,0)
Once a week	52 (13,1)
Everyday	13 (3,3)
Chronic disease	
Yes	88 (22,2)
No	308 (77,8)

The rate of those who stated that they were diagnosed with epilepsy was 2.0% (n=8). The mean age of those who stated that they were not diagnosed with epilepsy was 39.8±13.8 years, and the median was 38.5 years (min: 19.0-max: 80.0). There was no significant difference in age between those who stated that they had epilepsy or not (p=0.339). Of those who stated that they were diagnosed with epilepsy, 75.0% (n=6) were female, 25% were male (n=2). 75.0% (n=6) were working, 12.5% (n=1) primary school, 12.5% (n=1) secondary school, 25% (n=2) high school, 50% (n=4) university graduate. 12.5% (n=1) of those who stated that they had a diagnosis of epilepsy stated that their parents were relatives (Table-2).

Table 2. Socio-demographic characteristics and habits of those who stated that they were diagnosed with epilepsy

History of epilepsy in family	n (%)
Yes	52 (13,1)
No	345 (86,9)
Degree of consanguinity who has epilepsy	
1st degree relative	19 (38,8)
2nd degree relative	13 (26,5)
3rd degree relative	12 (24,5)
4th degree relative	4 (8,2)
Family history of febrile seizures	
Yes	61 (15,4)
No	336 (84,6)
Degree of family member with febrile seizures	
1st degree relative	27 (45,8)
2nd degree relative	22 (37,3)
3rd degree relative	5 (8,5)
4th degree relative	4 (6,8)
Consanguinity marriage between parents	
Yes	34 (8,6)
No	363 (91,4)

13.1% (n=52) of the participants stated that they had a family history of epilepsy, and 38.8% (n=19) of those with a family history of epilepsy stated that their first-degree relative had been diagnosed with epilepsy. 15.4% (n=61) of the participants stated that they had a febrile seizure in their family, and 45.8% (n=27) of those who had a febrile illness in their family had a first-degree relative with a febrile illness. 8.6% (n=34) of the participants stated that there was consanguinity between their parents (Table-3). 12.5% (n=1) of those who stated that they had a diagnosis of epilepsy stated that their parents were relatives (Table-2).

Table 3. Family history characteristics of the participants

History of epilepsy in family	n (%)
Yes	52 (13,1)
No	345 (86,9)
Degree of consanguinity who has epilepsy	
1st degree relative	19 (38,8)
2nd degree relative	13 (26,5)
3rd degree relative	12 (24,5)
4th degree relative	4 (8,2)
Family history of febrile seizures	
Yes	61 (15,4)
No	336 (84,6)
Degree of family member with febrile seizures	
1st degree relative	27 (45,8)
2nd degree relative	22 (37,3)
3rd degree relative	5 (8,5)
4th degree relative	4 (6,8)
Consanguinity marriage between parents	
Yes	34 (8,6)
No	363 (91,4)

12.6% (n=50) of the participants had a head injury, 0.3% (n=1) had meningitis, 65.7% (n=261) had a hospital delivery, 89.9% (n=357) stated that they were born with a normal standard delivery, 3.0% (n=12) stated that their mother had a health problem while pregnant, and 5.5% (n=22) stated that they had a health problem during their delivery (Table-4). There was no significant difference in terms of head trauma history between those who stated that they had epilepsy or not (p=0.077). There was no significant difference in terms of meningitis history between those who stated that they had epilepsy or not (p=1,000). There was no significant difference between those who stated that they had epilepsy or not (p=1,000) in terms of their mothers having health problems during pregnancy. There was no significant difference between those who stated that they had epilepsy or not, in terms of the development of a health problem at birth (p=0.370). 62.5% of those who stated that they had a diagnosis of epilepsy and 12.1% of those who stated that they did not have a diagnosis of epilepsy stated that they had a family history of epilepsy, and this difference was significant between the groups (p=0.001). There was no significant difference in terms of having a febrile seizure in the family of those who stated that they had epilepsy or not (p=0.356). There was no significant difference between those who stated that they had epilepsy or not, in terms of their family's consanguineous marriage status (p=0.516) (Table-5).

Table 4. Childhood medical history of the participants

History of head trauma	n (%)
Yes	50 (12,6)
No	326 (82,1)
Unknown	21 (5,3)
History of meningitis	
Yes	1 (0,3)
No	384 (96,7)
Unknown	12 (3,0)
Hospital delivery	
Yes	261 (65,7)
No	121 (30,5)
Unknown	15 (3,8)
Type of delivery	
Cesarean section	37 (9,3)
Normal delivery	357 (89,9)
Head to head	1 (0,3)
Breech arrival	2 (0,5)
Health problems in the mother during pregnancy	
Yes	12 (3,0)
No	383 (96,5)
Unkonown	2 (0,5)
Delivery complications	
Yes	22 (5,5)
No	374 (94,2)
Unknown	1 (0,3)

%: column percentage

Table-5 Comparison of the answers given to the medical history questions of those who stated whether they had epilepsy or not.

	Participants with Epilepsy	Participants without Epilepsy	
	n (%)	**n (%)**	**p**
Have you had a head injury (traffic accident, crash etc.)?			0,077
Yes	3 (37,5)	47 (12,8)	
No	5 (62,5)	320 (87,2)	
Do you have a history of meningitis?			1,000
Yes	0 (0,0)	1 (0,3)	
No	8 (100,0)	375 (99,7)	
Did your mother have a history of any health problems during her pregnancy?			1,000
Yes	0 (0,0)	12 (3,1)	
No	8 (100,0)	374 (96,9)	
Did you have any health problems during your birth?			0,370
Yes	1 (12,5)	21 (5,4)	
No	7 (87,5)	366 (94,6)	
Do you have a family history of epilepsy (epilepsy, seizures)?			***0,001***
Yes	5 (62,5)	47 (12,1)	
No	3 (37,5)	341 (87,9)	
Do you have a family history of febrile convulsions?			0,356
Yes	2 (25,0)	59 (15,2)	
No	6 (75,0)	329 (84,8)	
Do you have any consanguinity between your parents?			0,516
Yes	1 (12,5)	33 (8,5)	
No	7 (87,5)	355 (91,5)	

%:column percentage, p: Ki Kare Test. Those who answered yes or no to the questions were included in the analysis.

The mean SHI total score was 15.7±7.6, and the median was 15.0 (min:0.0-max:38.0). Those who stated that they did not have a diagnosis of epilepsy had a mean SHI score of 15.7±7.6, a median of 15.0 (min:0.0-max:38.0), and those who stated that they had epilepsy had a mean SHI score of 17.8±7.4, with a median of 17. was .5 (min:7.0-max:32.0). No statistically significant difference was found between those who stated that they had epilepsy and those who did not, in terms of SHI score averages.

There was no statistically significant relationship between the groups with and without epilepsy in terms of physical domain, psychological domain, social domain, and environmental domain sub-scores of health related quality of life scale (p>0.05) (Table-6).

Table 6. Quality of life scale scores of those with and without epilepsy

	Participants with Epilepsy		Participants without Epilepsy		
	mean±s.d.	**mean rank (min-max)**	**mean±s.d.**	**mean rank (min-max)**	**p**
Physical domain (0-20)	15,5±2,7	16,0 (6,9-20,0)	13,8±3,8	15,1 (6,9-18,3)	0,206
Psychological domain (0-20)	14,8±2,6	15,3 (5,3-20,0)	13,7±3,2	15,0 (7,3-16,7)	0,332
Social domain (0-20)	14,8±3,1	14,7 (4,0-20,0)	14,7±3,2	14,7 (9,3-18,7)	0,819
Environmental domain (0-20)	14,3±2,6	14,5 (6,0-20,0)	14,2±3,9	14,8 (7,0-18,5)	0,857
Environmental domain - when the national social pressure item is included (0-20)	14,3±2,4	14,7 (6,7-20,0)	14,2±3,5	14,4 (7,6-17,8)	0,846
Physical domain (0-100)	71,7±16,9	75,0, (17,9-100,0)	61,2±23,5	69,6 (17,9-89,3)	0,206
Psychological domain (0-100)	67,7±16,1	70,8 (8,3-100,0)	60,4±19,8	68,8 (20,8-79,2)	0,332
Social domain (0-100)	67,5±19,4	66,7 (0,0-100,0)	66,7±19,9	66,7 (33,3-91,7)	0,819
Environmental domain (0-100)	64,5±16,3	65,6 (12,5-100,0)	63,7±24,2	67,2 (18,8-90,6)	0,857
Environmental domain - when the national social pressure item is included (0-100)	64,4±15,2	66,7 (16,7-100,0)	63,9±21,6	65,3 (22,2-86,1)	0,846

mean±s.d: mean±standart derivation, min-max: minimum-maximum, p: Mann Whitney U Test

Discussion

Epilepsy is a chronic neurological disease that causes recurrent, episodic, and temporary central nervous system dysfunction resulting from abnormal discharges in neurons due to various factors [7]. There are approximately 50 million epilepsy patients all over the world, including 3 million in the USA, 6 million in Europe, and 40 million in developing countries. Epilepsy; causes a significant burden on the affected individuals and their families [8].

The prevalence of epilepsy was different in developed and developing countries [9]. Studies have reported that the prevalence of epilepsy is 4-10/1000 in developed countries and 18.5/1000 in developing countries [10]. The prevalence of active epilepsy is reported as 11.5/1000 in South America, the highest lifetime epilepsy prevalence in Nigeria as 37/1000 and the lowest as 5.3/1000 in Ethiopia, 5.2 in Ethiopia [9]. In our study, we determined the prevalence of epilepsy in individuals over the age of 18 living in Çanakkale city center as 20/1000. In a study conducted in Trabzon in our country in 2019 in the 0-17 age group, the prevalence of epilepsy was; 8.6/1000, in the study conducted in Sivas city center in 1999 for all age groups; It was determined as 6.1/1000 in Bursa city center and 8.5/1000 in all age groups in 2006 [3,11,12].

The sociodemographic characteristics of the region where the studies were conducted, the date of the studies and the difference in the methodological methods used may have caused this situation. The fact that accessibility to health services has increased today and that the general population of the region is more conscious about this issue may also have been effective. On the other hand, this may indicate the need for more comprehensive studies.

Although it has been reported that epilepsy is more common in males than females in prevalence studies, it is stated that the absolute difference in gender-specific prevalence is minimal. As the most striking example of the prevalence of epilepsy in the male gender, in a study conducted in India, the prevalence of epilepsy was found to be 5.1/1000 in men and 2.2/1000 in women. The reason for this is thought to be that women with epilepsy in this population hide their symptoms or diagnoses in order to avoid social exclusion [13]. In our study, unlike the literature, 25% (n=2) of epilepsy patients were male and 75% (n=6) female. To this situation; The difference in the socio-demographic characteristics of the population in which the study was conducted and the fact that it was carried out on a limited group of individuals aged 18 years and over may have been the cause.

Low socio-economic level, accompanying chronic diseases, and structural brain anomalies increase the frequency of epilepsy [14]. About 90% of people with epilepsy live in low- and middle-income countries. This situation is in these countries; It is explained by the high frequency of head trauma, birth trauma, and central nervous system infections [15]. In our study, similar to the literature, a history of head trauma was found in 37.5% (n=3) of epilepsy patients, and complications such as jaundice during delivery or a history of incubation were found in 12.5% (n=1) of epilepsy patients. Educational status of the patients; 12.5% (n=1) primary school graduate, 12.5% (n=1) secondary school graduate, 25% (n=2) high school graduate, 50% (n=4) university was a graduate. Distribution according to income status; monthly income of 12.5% (n=1) is between 1000-1500 TL, 50% (n=4) monthly income is between 1500-5000 TL, 37.5% (n=3) is 5000 TL and above were detected. This situation was thought to be related to the fact that the study was limited to the city center.

Epilepsy causes include hypoxia, trauma, vascular pathologies, ion channel defects, as well as genetic components. Twin studies show that the genetic transmission in epilepsy is 25-70%. A recent study showed that genetic transmission in epilepsy is 23% in focal epilepsy and 36% in nonfocal epilepsy. Genetic studies have identified a large number of genes that cause monogenic forms of epilepsy. In order to fully explain the etiology of epilepsy; There is a need to identify the genes that cause familial epilepsy [16]. In our study, 62.5% (n=5) of epilepsy patients had a family history of epilepsy.

Febrile convulsions (FC) are the most common seizure type in childhood, the etiology of which is unknown. FC; It is defined as a seizure observed in children aged 3 months to 6 years who have no neurological pathology, rectal fever >38°C, intracranial infection and no previous history of afebrile convulsions. A very small proportion of these individuals develop epilepsy [17]. The rate of epilepsy in families of children with FC is higher than the normal population [18]. In our study, in accordance with the literature; family history of febrile seizures; It was found 25% (n=2) in individuals with epilepsy and 15.2% (n=59) in individuals without epilepsy. The rate of history of febrile seizures was 12.5% (n=1) in individuals with epilepsy and 5.9% (n=23) in individuals without a diagnosis of epilepsy, and this result was consistent with the literature.

Adequate sleep is important to prevent epileptic seizures and improve memory, learning and concentration. Sleep disturbance causes deterioration of seizure control, increased daytime sleepiness and poor quality of life. Patients with epilepsy; they need better sleep hygiene than normal individuals [19]. In our study; The mean SHI total score was 15.7±7.6, and the median was 15.0 (min:0.0-max:38.0).

Those who stated that they did not have a diagnosis of epilepsy had a mean SHI score of 15.7±7.6, a median of 15.0 (min:0.0-max:38.0), and those who stated that they had epilepsy had a mean SHI score of 17.8±7.4, with a median of 17.5 (min:7.0-max:32.0).

No statistically significant difference was found between those who stated that they had epilepsy and those who did not have a diagnosis of epilepsy in terms of mean SHI scores (p=0.400).

Since epilepsy causes attention, memory and cognitive problems; causes a change in the person's self-perceived health status. Compared with other chronic diseases; Emotional well-being deterioration and functional limitations are more common in epilepsy patients. The unpredictability of seizures and the exposure of epilepsy patients to social exclusion and stigmatization can be cited as the reason for this situation [20]. Problems experienced by patients when assessing quality of life in epilepsy patients; should be addressed in terms of physical, psychological and economic aspects [21]. There was no statistically significant relationship between the groups with and without epilepsy in terms of bodily domain, mental domain, social domain, and environmental domain sub-scores (p>0.05) (Table-6). It is thought that this result is due to the fact that our target audience is individuals living in the city center and the socioeconomic level of the city we are in and the individuals with epilepsy in our study are relatively high.

Limitations; The relatively low number of epilepsy patients detected in our study weakened our analysis of quality of life and sleep hygiene index.

Conclusion

Prevalence studies are one of the preferred research techniques because they predict the relationship of common diseases with risk factors that may cause social and economic burden. There are many international and national studies examining the prevalence of epilepsy in the literature. The results obtained vary due to the differences in the methodological features of the studies and the characteristics of the region where the studies were conducted. Periodic prevalence studies will help to determine the prevalence in different parts of the population and to identify new risk factors that develop during the course of chronic diseases. We think that our study will contribute to the literature in this sense.

There is no conflict of interest between authors.

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Katılma Nöbeti ile Takip Edilen Çocukların Annelerinde Aile Rol Perfomansının Değerlendirilmesi

The Evaluation of Family Role Performance in The Mothers Who Have Children With Breath-Holding Spells

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Öz

Amaç: Çalışmamızda birincil amaç anne ebeveyn rolüne ilişkin kendilik algısı ile çocuktaki katılma nöbetlerinin ilişkisini araştırmak, ikincil amaç ise katılma nöbeti ile anne eğitim düzeyi, aile gelir düzeyi ilişkisinin araştırılmasıdır.

Gereç ve Yöntem: Bu çalışmada 01.11.2019-01.11.2021 arasında, İzmir Tepecik Eğitim ve Araştırma Hastanesi çocuk sağlığı ve hastalıkları polikliniği veya çocuk nöroloji polikliniklerine başvuran katılma nöbeti tanılı 6 ay-6 yaş arasındaki 46 hastanın annesine Ebeveyn Rolüne İlişkin Kendilik Algısı Ölçeği doldurtuldu. Benzer yaş ve cinsiyette 44 sağlıklı çocuk olgunun annelerine de aynı form verildi. Her iki gruptan olan olguların hastane kayıtları üzerinden hemogram, demir paneli ve ekokardiyografi sonuçları kaydedildi.

Bulgular: Çalışmaya alınan hasta grubundaki çocuklara ait yaş ortalaması 22,43±14,71 ay iken kontrol gurubunda 28,57±20,70 ay idi. Her iki grupta cinsiyet dağılımı açısından anlamlı bir fark yoktu. Katılma nöbeti tanılı olguların ilk atak başlangıç yaşı 7,93±6,93 ay, ayda geçirdiği nöbet sıklığı ise 5,96 saptandı. Her iki grupta hemoglobin, demir parametreleri ve ekokardiyografi bulguları arasında fark saptanmadı. Ebeveyn Rolüne İlişkin Kendilik Algısı ölçeği skorları karşılaştırıldığında rol doyumu alt boyutu, katılma nöbetli çocuk sahibi olan annelerde düşük saptandı.

Sonuç: Çalışmamızın katılma nöbeti olan çocuk sahibi annelerin rol doyumu skorları düşük saptandı. Bu bulgu bu annelerin çocuklarını yeterince benimseyemediği anlamına gelmektedir. Özellikle bu alt boyutun düşüklüğü anne-bebek arasındaki bağlanma ile ilgili diğer komponentlerin de sorunlu olabileceğini akla getirmiştir.

Anahtar Kelimeler: Katılma nöbeti, demir eksikliği anemisi, rol doyumu

Abstract

Aim: In our study, the primary aim was to investigate the relationship between self-perception of the mother-parent role and the breath-holding spell in the child, and the secondary aim was to examine the relationship between the breath holding spell of the child and mother education level and family household income.

Materials and Methods: In this study, the Parent Role-Related Self-Perception Scale was asked of the mothers of 46 patients between the ages of 6 months and 6 years who were diagnosed with a breath-holding spell, who applied to the pediatric internal medicine and pediatric neurology outpatient clinics of İzmir Tepecik Training and Research Hospital between 01.11.2019 and 01.11.2021. The same form was given to the mothers of 44 healthy children of similar age and gender. Hemograms, iron panels, and echocardiography results of the patients from both groups were recorded from the hospital records.

Results: While the mean age of the children in the patient group included in the study was 22.43±14.71 months, it was 28.57±20.70 months in the control group. There was no significant difference in terms of gender distribution in both groups. The age of onset of the first attack was 7.93±6.93 months, and the frequency of seizures per month was 5.96 in the cases diagnosed with a seizure attack. Both groups had no difference between hemoglobin, iron parameters, and echocardiography findings. When the Parent Role-Related Self-Perception Scale scores were compared, the role satisfaction sub-dimension was low in mothers with children with a breath-holding spell.

Conclusion: In our study, the role satisfaction scores of mothers who had children with a breath-holding spell were found to be lower. This finding means that these mothers could not adopt their children sufficiently. In particular, the low level of this sub-dimension suggested that other components related to mother-infant attachment might also be problematic. Other problems, such as attachment problems of children with breath holding spells and mothers, may be the subject of future studies.

Keywords: Breath holding spell, iron deficiency anemia, role satisfaction

Giriş

Katılma nöbeti (KN) ağlama, acı çekme ve hayal kırıklığı gibi provokasyonla başlayan, ağlama ve sonrasında renk değişikliği ile kendini gösteren paroksismal non-epileptik olaydır (1). Genellikle 6-18 ay arasında görülür, nadiren yenidoğan döneminden vakalar bildirilmiştir (2). Çocuk olguların %5'inde görülür ve yaş ilerledikçe sıklığı azalır (3).

Etiyolojisi tam olarak bilinmemektedir. Olguların %20-35'inde aile öyküsü olması ile otozomal dominant genetik geçiş olduğu düşünülse de parasempatik-sempatik sinir sistemi arasındaki dengesizlik, demir ve çinko eksikliği, kardiyak ritim bozukluğu gibi organik nedenlerin yanında, sosyoekonomik durum, anne-baba eğitim durumu ve annenin psikolojik durumu (anksiyete, depresyon) gibi psiko-sosyal nedenler de sorumlu tutulmaktadır (1,3-5). Ebeveynlerin, özellikle annelerin psikolojik durumunun çocuklardaki KN'ye etkisini gösteren çalışmaların yanında, annelere verilen psikolojik desteklerin çocuklardaki KN'yi azalttığını gösteren çalışmalar da mevcuttur (1).

Etiyolojisinin net olmaması birçok farklı tedavi yönteminin denenmesine sebep olmuş, ancak uygulanan tedavi yöntemlerinin tüm hastalarda etkili ve yeterli olduğu gösterilememiştir (3). Bu tedavilerden en yaygın olanı demir eksikliği anemisi (DEA) olan çocuklardaki demir tedavisidir. Literatürde ayrıca annenin psikolojik durumunun çocuklarda KN'yi tetikleyebileceği ve ebeveynlerle özellikle annelerle yapılan uygun psikiyatri konsültasyonu ile bu nöbetlerin büyük ölçüde önlenebileceği tartışılmaktadır (3,6). Kuhle ve arkadaşları psikolojik tedavinin KN'yi sonlandırdığına dair vaka bildirmiş ve bu tartışmalardan yola çıkararak anne psiko-eğitiminin, annenin kaygısını azaltarak nöbetleri hafifletebileceği öngörülmüştür (6).

Kendilik algısı, ebeveynlerde yapılan çalışmaların temelini oluşturmaktadır. Kendilik algısı ebeveynlerin benlik duygusunu ve ruh sağlığını etkilemekte, ebeveyn rolünü ve çocuk yetiştirme faaliyetlerini şekillendirmektedir. Ebeveynlerin Ebeveyn Rolüne İlişkin Kendilik Algısı Ölçeği (ERKA) çocuk gelişiminde dolaylı ya da doğrudan etkisi olan kendilik algısını değerlendirmek için düzenlenmiştir (7).

Bu çalışmada annenin ebeveyn rolüne ilişkin kendilik algısı ile çocuktaki KN'nin ilişkisinin araştırıldı. Ayrıca KN ile anne eğitim düzeyi, aile gelir düzeyi ve annenin çalışma durumu ile ilişkisi değerlendirildi.

Gereç ve Yöntem

Çalışma tasarımı kesitsel olgu-kontrol şeklindedir. Hastanemiz çocuk sağlığı ve hastalıkları polikliniği veya çocuk nöroloji polikliniklerine 01.11.2019-01.11.2021 tarihleri arasında KN ile başvuran, 6 ay-6 yaş arasındaki çocukların annelerine çalışmacılar tarafından oluşturulan sosyodemografik veri formu ve ERKA ölçeği uygulaması yapıldı. Aynı yaş grubunda benzer sayı ve yaşta sağlıklı çocuk olguların anneleri (solunum yolu enfeksiyonu nedeniyle tedavi almış ve ardından genel pediatri polikliniğine kontrole gelmiş olguların anneleri) kontrol gurubuna dahil edildi. Çalışmaya lokal etik kuruldan izin alınarak başlandı (12.10.2020, karar no: 2020/12-16). Onam vermeyi kabul etmeyen, Türkçe bilmeyen ve eksik verileri olan olgular çalışma dışı bırakıldı.

Çalışmada annelerin yaşı, eğitim durumu, çalışma durumu, çocukların yaşı, KN geçiren olguların ilk atak yaşı ve ayda geçirdikleri nöbet sayısı sorgulandı. Son 3 ay içerisinde istenmiş, hemogram, demir, ferritin düzeyi, EKO raporları kaydedildi ve hasta grubu ile kontrol grubu karşılaştırıldı.

Ebeveyn Rolüne İlişkin Kendilik Algısı Ölçeği ebeveyn bilişlerini konu alan çalışmalarda en fazla kullanılan ölçek olduğu için çalışmada bu ölçeği kullanmayı uygun olarak değerlendirdik. Annelerin psikolojik durumunun, yaşam şartlarının KN'yi tetiklemesi ve oluşumundaki katkısını araştırılan bu çalışmada olgulardan tetkik istenmeyerek ERKA ölçeğinin doldurulması istendi.

Ebeveyn Rolüne İlişkin Kendilik Algısı Ölçeği (Self Perception of Parental Role- SPPR)**:** Bireylerin davranışlarını, düşüncelerini ve duygularını yönlendiren kendilik (benlik) kavramı, bireyin kendi özelliklerinin, fikirlerinin ve ideallerinin bilincinde olup, kendisini nasıl tanımladığını ve değerlendirdiğini gösterir (8). Mead (1934) bu kavramın sosyal yaşantılar sonucunda toplum tarafından bireye kazandırıldığını belirtmiştir (9).

MacPhee ve arkadaşları (1986) tarafından annelerle, ebeveynliğe yönelik kendilik algısı ile ilişkili çalışma yapmış ve sonucunda anneliğe yönelik kendilik algısını belirleyen işlevleri tanımlamışlardır (8). Bu çerçevede Ebeveynlerin kendilik algısını değerlendirmek için 16 maddeden oluşan ERKA ölçeği düzenlenmiştir. Bu maddeler rol doyumu, yatırım, yeterlilik ve rol dengeleme şeklinde 4 alt boyut değerlendirilmektedir (8). Bu ölçek Güler ve Yetim tarafından 2008 yılında Türkçe kültürüne uyarlanmıştır.

Rol doyumu: Hem ebeveynin ebeveyn olmaktan ne kadar memnun olduğunu hem de ebeveynin çocuğu ile arasındaki ilişkiden ne kadar memnun olduğunu gösterir (10). Sonuç olarak bir kadın annelik rolünden ne kadar tatmin olursa bir o kadar bu rolün getirdiği sorumluluklara, isteğe ve duyarlılığa sahip olacaktır. Neticede çocuğu ile olan anne-çocuk ilişkisi daha kaliteli olacaktır (11).

Yatırım: Ebeveynin çocuklara katılımını ve bağlılığını gösterir ve çocuk yetiştirme konusundaki yeterliliği algısını değerlendirir. Çocuğun fiziksel etkinliklere katılması, çocuk bakımında ebeveyn sorumlulukları, çocuk ile geçirilen zamandan zevk alma, iyi bir sağlık bakımının olması, yeterli beslenmesinin sağlanması, çocuğun duygularına özen göstermek yatırımlara verilebilecek örnekler arasındadır.

Yeterlilik: Yeterlilik, bir şeyi başarmak için veya etkili ve yeterli olarak yapmak için gerekli olan yetenek olarak tanımlanmaktadır. Algılanan ebeveyn yeterliliği ise, ebeveynlerin çocukların ihtiyaçlarını karşılamak için gerekli olan beceriyi nasıl algıladıklarını ifade eder (12)

Rol dengeleme: Rol dengeleme, bireyin sahip olduğu rolleri yani ebeveyn, çalışan, eş kimliklerini dengeli bir şekilde yürütülmesidir (13). Literatürde, genel kanın aksine çoklu role sahip kadınların kendine güveninin yüksek olduğu, düşük depresyon seviyesine sahip oldukları ve neticede daha iyi bir psikolojik ve fizik sağlığına sahip olduğu belirtilmiştir.

Veriler *SPSS* 21.0 istatistik programına (SPSS Inc., Chicago, IL) kaydedildi. Kolmogorov-Smirnov testi ile normal dağılım varlığı araştırıldı. Kategorik değişkenler ki-kare testi uygulanarak analiz edildi. Gruplar arasındaki karşılaştırmalar Student-t testi veya Mann Whitney-U ve ki-kare testleri kullanılarak yapıldı. Veriler parametrik ve non-parametrik analizlerine göre, ortalama ± SD değerleri sunuldu. P değerinin 0,05'den az olması istatiksel olarak anlamlı kabul edildi.

Bulgular

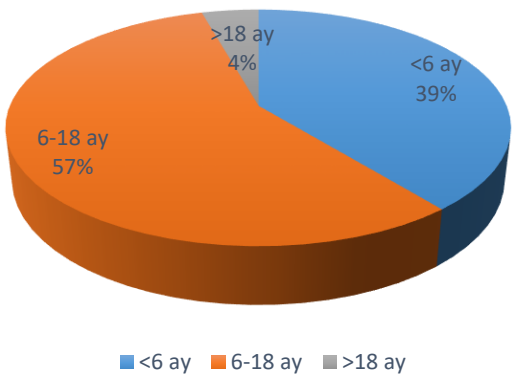
Çalışmaya çocuğunda KN tanısı olan 72 anneden 58'i katılmaya gönüllü oldu. Ancak bu annelerden 12 kişinin okur-yazarlığı yoktu veya ana dili Türkçe değildi. Sonuçta 46 KN'li çocuğun annesi çalışmaya dahil edildi. Kontrol grubu olarak da solunum yolu enfeksiyonu kontrolü için başvuran çocukların 62'sinin ebeveyni çalışmaya dahil edildi. Bunlardan 44 kişi çalışmaya katılmayı kabul etti.

Çalışmaya katılan hasta ve kontrol grubundaki annelerin yaş dağılımları benzerdi. Hasta grubunda annelerin %13,1'inin eğitiminin olmadığı, kontrol grubunda ise eğitim almayan anne olmadığı görüldü. Hasta grubundaki annelerin %15,2'sinin, kontrol grubundaki annelerin ise %36,4'ünün çalıştığı ve aralarındaki farkın istatistiksel olarak anlamlı olduğu görüldü. Ailelerin aylık geliri sorgulandığında hasta grubunda 27 anne, kontrol grubunda da 31 anne, aylık gelirini 3000-9000 TL arasında belirtti (Tablo 1).

Tablo 1. Annelerin ve çocukların sosyoekonomik ve demografik özellikleri

	Hasta grubu (n=46)	Kontrol grubu (n=44)	*p*
Annenin yaşı (n, %)			0,829
<20 yaş	0	0	
20-29 yaş	19 (41,3)	20 (45,5)	
30-39 yaş	25 (54,3)	19 (43,2)	
≥ 40 yaş	2 (4,4)	5 (11,3)	
Annenin eğitim durumu (n, %)			0,132
Eğitimi yok	6 (13,1)	0	
İlköğretim birinci kademe	6 (13,1)	6 (13,6)	
İlköğretim ikinci kademe	10 (21,7)	12 (27,3)	
Lise	14 (30,4)	14 (31,8)	
Üniversite/Yükseköğretim	10 (21,7)	12 (27,3)	
Annenin çalışma durumu (n, %)			**0,021**
Çalışıyor	7 (15,2)	16 (36,4)	
Çalışmıyor	39 (84,8)	28 (63,6)	
Ailenin gelir durumu (TL/ay)			0,05
0-3000 TL	9 (18,6)	0	
3-6000 TL	18 (39,1)	20 (45,5)	
6-9000 TL	15 (32,6)	11 (25,0)	
≥ 10000 TL	4 (8,7)	13 (29,5)	
Cinsiyet (n, %)			0,993
Kız	22 (52,2)	21 (47,7)	
Erkek	24 (47,8)	23 (52,3)	
Yaş (ay, ort±SD)	22,43±14,71	28,57±20,70	0,111

Çalışmaya alınan hasta grubundaki çocuklara ait yaş ortalaması 22,43±14,71 ay iken, kontrol grubunda 28,57±20,70 ay idi. Her iki grupta cinsiyet dağılımı açısından anlamlı bir fark yoktu (p=0,993). KN tanılı olguların ilk atak başlangıç yaşı 7,93±6,93 ay, en sık başlangıç aylarının ise 6-18 ay arasında olduğu görüldü (Şekil 1). Ayda geçirdiği nöbet sıklığı ise ortalama 5,96 KN/ay olarak saptandı.



Şekil 1. Katılma nöbeti başlangıç yaş aralıkları

Olguların tıbbi kayıtları incelendiğinde tam kan sayımı hasta grubunun %71'inde (n=33), kontrol grubunun %66'sında (n=29), demir parametreleri ise hasta grubunun %56'sında (n=26), kontrol grubunun %39'unda (n=17) bakılmıştı. Her iki grupta hemoglobin, demir ve ferritin düzeyleri karşılaştırıldığında anlamlı fark bulunmadı. EKO yapılan 27 hasta grubunda beş olguda patoloji saptanırken, EKO yapılan altı kontrol hastasının ikisinde patoloji saptandığı görüldü (Tablo 2).

Tablo 2. Olguların hemoglobin, demir, ferritin ve EKO sonuçları

	Hasta grubu	Kontrol grubu	*p*
Hemoglobin değeri (g/dL)	11,27±1,27	11,77±1,52	0,161
Demir düzeyi (ng/dL)	55,57±39,88	36,47±26,34	0,090
Ferritin düzeyi (ng/L)	24,97±31,76	38,12±34,17	0,209
EKO (n, %)			
Yapılmadı	19 (41,3)	38 (86,4)	
Normal	22 (47,8)	4 (9,1)	
Patent foramen ovale	4 (8,7)	2 (4,5)	
Aort kapak anomalisi	1 (2,2)	0	

Annelerin ERKA ölçek puanları değerlendirildiğinde, rol doyum alt boyut puanı istatistiksel olarak anlamlı düzeyde kontrol grubunda daha yüksek saptandı (Tablo 3).

Tablo 3. Annelerin Ebeveyn Rolüne İlişkin Kendilik Algısı Ölçeği alt boyut puanları

	Hasta grubu (n=46)	Kontrol grubu (n=44)	*p*
Rol doyumu alt boyutu	14,9±3,5	16,9±3,6	**0,026**
Yeterlilik alt boyutu	17,3±4,9	16,2±5,8	0,335
Yatırım alt boyutu	11,9±3,0	11,8±4,5	0,886
Rol dengeleme alt boyutu	16,6±4,0	16,3±4,0	0,713

Tartışma

Çalışma sonucunda bulgular bize KN'li çocuk sahibi annelerin ebeveyn rolüne ilişkin kendilik algısının rol doyumu alt boyutunun anlamlı derecede olumsuz olduğunu gösterdi. Diğer alt boyutlarda ise farklılık saptanmadı. Hemoglobin, demir, ferritin ve kardiyak patolojiler gibi medikal faktörlerin karşılaştırılmasında ise yine iki grup arasında farklılık gözlenmedi.

Çalışmada ilk KN'nin görülme zamanı yaklaşık sekiz ay saptandı ve cinsiyetler arasında farklılık yoktu. KN nadiren de olsa yenidoğan döneminde görülmesine rağmen genellikle 6 ay ila 18 ay arası çocuklarda görülen ve bu çocukların yalnız %5'ini etkileyen non-epileptik paroksismal bir reflekstir (1). Yapılan çalışmaların genelinde kız erkek oranı KN'de yakın bulunmuştur (3,5,14,15). Bu çalışmada KN tanılı olgular ile kontrol grubu arasında demir eksikliği anemisi veya diğer hematolojik parametreler için anlamlı bir fark bulunmadı. Literatürde farklı sebepler ön görülerek, KN'nin mekanizmasını ve nedenini araştırmak için birçok çalışma yapılmıştır. Ama bugüne değin kesin bir neden bulunamamıştır. Daha önce yapılan çalışmalarda demir eksiliği anemisi, otonom disfonksiyon, kardiyak nedenler arasında ilişki bildirilmiş ama bu çalışma sonuçları ile çelişen başka raporlar da gösterilmiştir (16-18).

Literatürde KN tanılı çocuklarda, annenin stres ve yüksek depresyon düzeylerinin, bebeğin duygu ve otonomik düzenlenmesi üzerinde olumsuz etkileri olduğunu ve bu durumun KN'nin oluşumuna katkıda bulunduğu gösteren çalışmalar mevcuttur (3,5). 1992'de Di Mario ve ark. tarafından yapılan çalışmada KN tanılı çocukların davranış profili kontrol grubuyla karşılaştırılmış ve anlamlı bir farklılık bulunamamıştır (5). 2008'de Hindistan'da yapılan bir başka çalışmada ise KN olanların kontrol grubuna göre daha kızgın mizaçlı olduğu gösterilmiştir (19).

Otonom sinir sistemi, strese karşı yanıt ile beraber duygusal durumların da otonom, somatik yönlerini düzenlemekten sorumludur. Yani annenin emosyonel disregülasyonuna cevap olarak bebekte oluşan otonomik disregülasyon KN oluşmasına veya şiddetinin artmasına neden olur. Bu teoriye dayalı yapılan yeni bir çalışma sonuçlarına göre annenin stres ve yüksek depresyon düzeylerinin, bebeğin duygu ve otonomik düzenlenmesi üzerinde olumsuz etkileri olduğunu ve bu durumun KN'nin oluşumuna katkıda bulunduğu gösterilmiş, annelere uygulanan psikoterapi sonrasında ise anne emosyonel stabilitesini sağlamakla olguların KN'nin tamamen kesilmesi veya şiddetinin azalması ile sonuçlanmıştır. Psikoterapinin anneler üzerindeki iki etkisi daha ön planda saptanmıştır. Bunlar annenin kaygısı azaltılarak bebeğin olumsuz duygularını düzenleyebilmesi ve stresle başa çıkmasıdır. Çünkü endişeli ve kaygılı bir anne kendi anksiyete semptomlarına odaklandığı için ebeveyn olarak bebeğini tatmin edemeyebilir. Diğer taraftan KN, annenin kaygı ve depresyon düzeyini etkilediği ve bu iki durumun birbirini çift yönde etkilediği bildirilmiştir (1). Veriler olmasına rağmen KN tanılı olgularda otonom düzensizlik ve duygusal düzensizlik arasındaki ilişkiyi değerlendirmek için gelecekteki çalışmalara ihtiyaç vardır. Bir bebek kendini annenin yüzünden görür. Gebelik döneminden başlayan, anne-bebek arasındaki duygusal bağlılık doğum sonrası da devam ederek bebeğin yeni ortama uyum sağlamasına katkıda bulur. O yüzden bir annenin içinde bulunduğu bu rolü ne kadar kabullendiği, anne olarak kendisini ne derece yeterli gördüğü annenin ruh durumuna yansımaktadır. Ebeveynin kendilik değerlendirmeleri, çocuk yetiştirme faaliyetlerini etkilemekte olup çocuk gelişiminde dolaylı ya da doğrudan rol oynamaktadır (8,20). Anneliğe ilişkin kendilik algısını belirleyen işlevleri; kendisini ne derece yeterli gördüğü, rolüne yatırımı, rolünden aldığı doyum ve diğer rolleri ile arasında ne derecede denge kurduğunu ölçmek amacıyla en uygun ölçek olan ERKA ölçeğini kullandık.

Çalışmaya katılması için kontrol grubu olabilecek annelere 'çalışmamıza katılır mısınız' şeklinde sorduğumuzda 62 anneden 44'ü bir maddi kazancı olmamasına rağmen zaman harcayıp ankete katıldı. Bu annelerin sosyoekonomik ve eğitim bilgilerine baktığımızda genellikle hasta grubuna göre daha yüksek sosyoekonomik düzeye sahipti ve çalışır-okur annelerdi. Bu nedenle kontrol grubundaki annelerin sosyoekonomik düzeyinin yüksekliği yazarlarca bu nedene bağlandı.

İngiliz çocuk doktoru ve psikanalist olan Winnicott, "Annesiz bebek olmaz" demiştir. Yani bir bebeğin psikolojik durumunu tartışmadan önce annenin psikolojik durumu değerlendirilmelidir (21). Benzer şekilde KN'de de çocuk hastaların izlem ve tedavisinin yanında, annelerin de psiko-sosyal yönden değerlendirilmesi ve hangi desteklerin önerileceğine yönelik çalışmalar düzenlenmelidir.

Çalışmamızın ana hipotezi olan ebeveyn kendilik algısının katılma nöbetli çocuk annelerinde daha zayıf olması sadece alt boyutlardan rol doyumu için gösterildi. Bu annelerin çocuklarını yeterince benimseyemediği anlamına gelmektedir. Özellikle bu alt boyutun düşüklüğü anne-bebek arasındaki bağlanma ile ilgili diğer komponentlerin de sorunlu olabileceğini düşündürmüştür. KN'li çocukların ve annelerin bağlanma problemleri gelecekteki çalışmaların konusu olabilir.

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KLİNİK ÇALIŞMA / CLINICAL TRIAL
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İmplante Edilebilir Kardiyak Defibrilatör Takılan Hastalarda ACEF Risk Skoru ile Uygun Kardiyak Şoklama Arasındaki İlişki

The Relationship Between ACEF Risk Score and Appropriate Cardiac Shock in Patients with Implantable Cardiac Defibrillator

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Öz

Amaç: On yıldan fazla bir süre önce, ICD' lerin (implante edilebilir kardiyak defibrilatör) ani kardiyak ölüm riski altındaki hastalarda sağkalımı iyileştirdiği gösterilmiştir. ICD implantasyonu en çok iskemik kalp hastalığı nedeniyle olmak üzere, diğer yapısal kalp hastalıkları için de yapılabilmektedir. Çok merkezli otomatik defibrilatör implantasyonu çalışması (MADIT) II, birincil ICD tedavisinin, önceden MI geçirmiş ve ileri evre sol ventrikül disfonksiyonu olan hastalarda sağkalımı iyileştirdiğini göstermiştir. MADIT-ICD adı verilen bir skor geliştirilerek öncelikle birincil korunma hastalarında kullanıldı ve tüm nedenlere bağlı ölüm ile ilişkisi araştırıldı. Ranucci ve arkadaşları elektif kalp cerrahisi geçiren hastalarda mortaliteyi tahmin etmek için basit, üç değişkenli bir model olan yaş, kreatinin ve ejeksiyon fraksiyonu (ACEF) skorunu tanıttı. ACEF risk skoru, sadece kısa ve uzun vadeli mortalite açısından değil, aynı zamanda majör istenmeyen vasküler olayları da tahmin edici prediktif değerler ile ilişkilidir. Bu çalışmadaki amacımız hastanemizde primer veya sekonder koruma nedeniyle ICD takılmış hastalarda ACEF risk skoru ile uygun kardiyak şoklama arasındaki ilişkiyi saptamaktır.

Yöntem: Çalışmaya hastanemizde 2019 Ocak – 2022 Ağustos tarihleri arasında ICD implantasyonu yapılan 104 hasta ardışık olarak alındı. Hastalar rutin vizitlerdeki kontrollerde yapılan pil ölçümlerinde uygun kardiyak şoklama alanlar (n=25) ve uygun kardiyak şoklama almayanlar (n=79) olarak 2 gruba ayrılarak incelendi. ACEF risk skoru şu formül ile hesaplandı: yaş / sol ventrikül ejeksiyon fraksiyonu (EF) (kreatinin>2.0 ise +1 puan eklendi). Çalışmamız retrospektif, gözlemsel bir araştırmadır.

Bulgular: Çalışmamızdaki ICD implantasyonu yapılmış 104 hastanın, grup 1 (ortalama yaş 68.36±9.66 yıl, %96 erkek) ve grup 2 (ortalama yaş 62.58±11.01 yıl, %81 erkek)' den oluşmaktaydı. Grup 1' deki hastaların sol ventrikül EF ortalama değerleri istatistiksel olarak anlamlı düşüktü (Grup 1: %26.04±5.53 ve Grup 2: %30.77±10.55, p=0.03). Grup 1' deki hastaların kreatinin değerleri ortalaması Grup 2' den anlamlı oranda yüksekti (Grup 1: 1.25±0.44 ve Grup 2: 1.06±0.27, p=0.01). ACEF risk skoru grup 1 lehine anlamlı yüksekti (Grup 1: 2.84±0.81 ve Grup 2: 2.21±0.69, p<0.001). ACEF risk skoru>2.49 değerinde %68 duyarlılık ve %69 özgüllük ile ICD implantasyonu yapılan hastalarda uygun kardiyak şoklama için bir öngördürücü olarak saptandı (eğri altındaki ROC alanı: 0.726, %95 CI: 0.611-0.840, p=0.001).

Sonuç: ICD implantasyonu yapılan hastalarda basit şekilde hesaplanabilen ACEF risk skorunun yüksekliği uygun kardiyak şoklamanın öngördürücüsüdür ve ICD implantasyonu sonrası takiplerde bu skorun kullanılması hangi hastaların uygun kardiyak şok almaya daha yatkın olduğunu anlamamıza fayda sağlayabilir.

Anahtar Kelimeler: ICD takılması, kardiyak şoklama, ACEF risk skoru.

Abstract

Aim: More than a decade ago, ICDs (implantable cardiac defibrillators) were shown to improve survival in patients at risk of sudden cardiac death. ICD implantation can be performed mostly for ischemic heart disease, but also for other structural heart diseases. The multicenter automated defibrillator implantation trial (MADIT) II has shown that primary ICD therapy improves survival in patients with prior MI and advanced left ventricular dysfunction. A score called MADIT-ICD was developed and used primarily in primary prevention patients and its relationship with all-cause mortality was investigated. However, endpoints other than all-cause mortality, such as the need for generator replacement and receiving appropriate shock, have not yet been studied in secondary prevention patients. Ranucci et al introduced the age, creatinine, and ejection fraction (ACEF) score, a simple, trivariate model for predicting mortality in patients undergoing elective cardiac surgery. The ACEF risk score is associated with predictive values not only for short- and long-term mortality, but also for major adverse vascular events. Our aim in this study is to determine the relationship between ACEF risk score and appropriate cardiac shock in patients who had an ICD for primary or secondary protection in our hospital.

Material and method: 104 consecutive patients who underwent ICD implantation between January 2019 and August 2022 in our hospital were included in the study. The patients were divided into 2 groups as those who received appropriate cardiac shock (n=25) and those who did not receive appropriate cardiac shock (n=79) in the pacemaker measurements made at the controls at routine visits. The ACEF risk score was calculated with the following formula: age / left ventricular ejection fraction (EF) (+1 point added if creatinine >2.0). Our study is a retrospective, observational study.

Results: Group 1 (mean age 68.36±9.66 years, 96% men) and group 2 (mean age 62.58±11.01 years, 81% men) of 104 patients who underwent ICD implantation in our study. The left ventricular EF mean values of the patients in Group 1 were statistically significantly lower (Group 1: 26.04±5.53% and Group 2: 30.77±10.55, p=0.03). The mean creatinine values of the patients in Group 1 were significantly higher than Group 2 (Group 1: 1.25±0.44 and Group 2: 1.06±0.27, p=0.01). The ACEF risk score was significantly higher in favor of group 1 (Group 1: 2.84±0.81 and Group 2: 2.21±0.69, p<0.001). The ACEF risk score >2.49 was found to be a predictor of appropriate cardiac shock in patients with ICD implantation with 68% sensitivity and 69% specificity (ROC area under the curve: 0.726, 95% CI: 0.611-0.840, p=0.001).

Conclusion: The high ACEF risk score, which can be easily calculated in patients with ICD implantation, is a predictor of appropriate cardiac shock, and the use of this score in the follow-ups after ICD implantation may help us to understand which patients are more likely to receive appropriate cardiac shock.

Keywords: ICD implantation, cardiac shock, ACEF risk score,

Giriş

On yıldan fazla bir süre önce, ICD' lerin (implante edilebilir kardiyak defibrilatör) ani kardiyak ölüm riski altındaki hastalarda sağkalımı iyileştirdiği gösterilmiştir. ICD implantasyonu en çok iskemik kalp hastalığı nedeniyle olmak üzere, diğer yapısal kalp hastalıkları için de yapılabilmektedir (1). Kardiyomiyopatiler (idiopatik, hipertrofik obstruktif kardiyomiyopati, aritmojenik sağ ventrikül displazisi, konjenital uzun QT sendromu, dilate kardiyomiyopati) ve ventrikül kaynaklı aritmiler ICD implantasyonuna ihtiyaç duyulan diğer kardiyak patolojilerdir. ICD implantasyonu primer ve sekonder koruma ile toplam ölüm oranında yaklaşık %20 azalma sağlarken, MI (miyokard infarktüsü) sonrası ölümü yaklaşık %50 azaltır (2,3). Hastalarda semptomatik düzelmeye tam bir fayda olmasa da aritmi nedenli ölümleri engellemektedir.

Çok merkezli otomatik defibrilatör implantasyonu çalışması (MADIT) II, birincil ICD tedavisinin, önceden MI geçirmiş ve ileri evre sol ventrikül disfonksiyonu olan hastalarda sağkalımı iyileştirdiğini göstermiştir (4). MADIT-ICD adı verilen bir skor geliştirilerek öncelikle birincil korunma hastalarında kullanıldı ve tüm nedenlere bağlı ölüm ile ilişkisi araştırıldı. Fakat sekonder koruma hastalarında jeneratör replasman gereksinimi ve uygun şok alma gibi tüm nedenlere bağlı ölümler dışındaki sonlanım noktaları henüz çalışılmamıştır.

Ranucci ve arkadaşları elektif kalp cerrahisi geçiren hastalarda mortaliteyi tahmin etmek için basit, üç değişkenli bir model olan yaş, kreatinin ve ejeksiyon fraksiyonu (ACEF) skorunu tanıttı (5). Daha da önemlisi, ACEF skorunun prediktif değeri, perkütan koroner girişimler (PCI) ve transkateter aort kapak implantasyonu (TAVI) uygulanan farklı hasta alt gruplarında doğrulanmıştır (6-10). ACEF risk skoru, sadece kısa ve uzun vadeli mortalite açısından değil, aynı zamanda majör istenmeyen vasküler olayları da tahmin edici prediktif değerler ile ilişkilidir (7,8,10,11). Ek olarak ACEF risk skorunun uzun süreli takipte tüm tedavi stratejileri ST elevasyonlu olmayan miyokard enfarktüslü hastalarda MACE' yi (majör advers kardiyovasküler olay) diğer risk skorlarından (GRACE, SYNTAXs) daha anlamlı bir şekilde öngördüğü belirtilmiştir (12). Bu çalışmadaki amacımız hastanemizde primer veya sekonder koruma nedeniyle ICD takılmış hastalarda ACEF risk skoru ile uygun kardiyak şoklama arasındaki ilişkiyi saptamaktır.

Gereç ve yöntem

Çalışma popülasyonu

Çalışmamıza 2019 Ocak – 2022 Ağustos tarihleri arasında hastanemizde ICD veya CRT-D (kardiyak resenkronizasyon tedavisi- defibrilatör) implantasyonu yapılmış 104 hasta ardışık olarak dahil edildi. Bu hastalar poliklinik koşullarında rutin pil kontrolleri yapılan ve kontrol sonuçları ilgili pil firması tarafından dökümante edilenlerden oluşmaktaydı. Çalışmaya 18 yaşından büyük, bazal ekg (elektrokardiogram)' si, rutin kan tetkikleri (içerisinde böbrek fonksiyon testleri) ve transtorasik ekokardiyografi kayıtları bulunanlar dahil edildi.

Çalışmadan orta-ciddi kapak hastalığı, aktif enfeksiyonu bulunan, ciddi karaciğer ve böbrek fonksiyon bozukluğu bulunan, 18 yaşından küçük ve şoklama özelliği olmayan pil takılmış hastalar dışlandı. Hastanemizde yapılan rutin vizitlerde hastaların demografik verileri (yaş, cinsiyet), klinik özellikleri (komorbid hastalık öyküsü ve risk faktörleri), transtorasik ekokardiyografide modifiye simpson yöntemi ile ölçülen sol ventrikül ejeksiyon fraksiyonları (EF), hematolojik ve biyokimyasal kan sonuçları ve mevcut kullandıkları ilaçları hastane bilgi yönetim sisteminden not edildi. Hastaların klinik özelliklerinden hipertansiyon için kan basıncı >140/90 mmHg veya en az bir antihipertansif ilaç kullanmaları, diyabetes mellitus için açlık kan şekeri >126 mg/dl olması veya antidiyabetik tedavi kullanımı (oral antidiyabetik veya insülin) kabul edildi.

Mevcut çalışmada geriye dönük inceleme ile ICD implantasyonu sonrası uygun kardiyak şoklama alan ve almayan olarak 2 grupta inceleme yapılmıştır. Grup 1 hastaları uygun kardiyak şoklama alan (25 hasta) iken, grup 2 hastaları (79 hasta) uygun kardiyak şoklama almayanlardan oluşmaktaydı.

Tüm hastalar için ACEF risk skoru şu formülle hesaplandı: Yaş / Sol ventrikül EF (kreatinin>2.0 ise skora +1 olarak eklendi).

Hastaların tümünden yazılı onamları tek tek alındı. Bakırçay Üniversitesi girişimsel olmayan klinik etik kurulundan çalışma için onay alındı (Karar no:2022/709). Çalışmamız etik koşulları dünya sağlık örgütünün helsinki deklarasyonuna uygun olarak tasarlanmıştır.

İstatistiksel analiz

Spss Windows sürüm 24.0 kullanılarak istatistiksel analiz yapıldı. Sürekli değişkenlerin dağılımı normalliği Kolmogorov-Smirnov testi kullanılarak kontrol edildi. Sürekli değişkenler için student t testi kullanılarak ortalama ± standart sapma (SD), kategorik değişkenler ise ki-kare testi kullanılarak sayı ve sıklık olarak rapor edildi. ICD implantasyonu yapılan hastalarda uygun kardiyak şoklamayı tahmin etmek için ROC (receiving operating characteristics) eğrisi analizi ile optimum cut-off değerleri belirlendi. Tüm hipotezler için 0.05 altındaki değerler istatistiksel olarak anlamlı kabul edildi.

Bulgular

Çalışmamızda ICD takılmış 104 hastanın, grup 1 (ortalama yaş 68.36±9.66 yıl, %96 erkek) ve grup 2 (ortalama yaş 62.58±11.01 yıl, %81 erkek) verileri incelendi. İki grup arasında yaş açısından grup 1 lehine anlamlı yükseklik vardı. Mevcut çalışmadaki hastaların; %50' sinde hipertansiyon (n=53), %29' unda diyabetes mellitus (n=31), %69' unda koroner arter hastalığı (n=72) vardı. Grup 1' deki hastaların sol ventrikül EF değerleri istatistiksel olarak anlamlı düşüktü (Grup 1: %26.04±5.53 ve Grup 2: % 30.77±10.55, p=0.03). ACEF risk skoru için grup 1' de anlamlı yüksekti (Grup 1: 2.84±0.81 ve Grup 2: 2.21±0.69, p<0.001). Hastaların Tablo 1' de demografik verileri, komorbid hastalıkları, sol ventrikül EF değeri, ACEF risk skoru ve kan sonuçları ayrıntılı olarak gösterilmiştir.

Tablo 1. Klinik özellikler, komorbid hastalıklar ve demografik veriler

Veriler	Grup 1 (n=25)	Grup 2 (n=79)	p değeri
Yaş (Ortalama±SS)	68.36±9.66	62.58±11.01	**0.02**
Erkek cinsiyet, n(%)	24 (96)	64 (81)	0.07
Hipertansiyon, n(%)	12 (50)	41 (51)	0.87
Diabetes mellitus, n(%)	5 (20)	26 (32)	0.21
KMP, n(%)			
İskemik	18 (72)	54 (68)	0.73
Non-iskemik	6 (24)	24 (30)	
Diğer (HKMP, Non-Komp, ARVD)	1 (4)	5 (6)	
PAH, n(%)	2 (8)	5 (6)	0.77
Stroke (inme) öyküsü, n(%)	1 (4)	5 (6)	0.66
Beyaz küre sayısı,x10^3/L	8.95±2.63	8.59±3.15	0.60
Hemoglobin, gr/dl	13.35±1.99	12.92±2.18	0.40
Trombosit sayısı, x10^3/L	218.87±86.19	221.87±68.74	0.86
Glukoz, mg/dl	118.24±40.76	118.73±36.37	0.95
Üre, mg/dl	54.48±44.15	41.50±18.24	**0.03**
Kreatinin, mg/dl	1.25±0.44	1.06±0.27	**0.01**
Sodyum, mEq/L	136.92±5.15	138.75±4.20	0.07
Potasyum, mEq/L	4.23±0.67	4.43±0.54	0.14
Magnezyum, mEq/L	2.07±0.29	1.92±0.30	0.05
Sol ventrikül EF, (%)	26.04±5.53	30.77±10.55	**0.03**
ACEF skoru	2.84±0.81	2.21±0.69	<**0.001**

p<0.05 olan değerler koyu renkle gösterilmiştir.
n: hasta sayısı, SS: standart sapma, KMP: kardiyomiyopati, EF: ejeksiyon fraksiyonu, ACEF: age creatinin ejection fraction, Grup 1: uygun kardiyak şoklama olanlar , Grup 2: uygun kardiyak şoklama olmayanlar .

Tablo 2. ICD implantasyonu ve takibiyle ilgili, bazal elektrokardiogram verileri

Veriler, (Ortalama±SS)	Grup 1 (n=25)	Grup 2 (n=79)	p değeri
ICD implantasyonu endikasyonu, n(%)			
Primer koruma	16 (64)	63 (79)	0.1
Sekonder koruma	9 (36)	16 (20)	
ICD implantasyon zamanı, yıl	1.54±1.03	1.58±1.80	0.91
ICD tipi, n(%)			
VVI	19 (76)	52 (65)	0.42
DDD	4 (16)	12 (15)	
CRT-D	2 (8)	15 (18)	
Pil empedans, Ω	541.32±121.88	630.31±217.57	0.05
Pil eşik ölçümü, Volt	0.80±0.13	0.85±0.54	0.61
ICD implantasyon sonrası şok alma zamanı, ay	17.56±12.12	5.36±8.48	<**0.001**
ICD implantasyon sonrası olay, n(%)			
Ventriküler Taşikardi	12 (48)	-	<**0.001**
Ventriküler Fibrilasyon	7 (28)	-	
Atrial Fibrilasyon	3 (12)	10 (12)	
Supraventriküler Taşikardi	-	26 (32)	
Uygunsuz şok, n(%)	4 (16)	28 (35)	0.06
İstirahat nabız, /dk	74.40±12.84	74.13±14.15	0.93
Hastanın bazal ritmi, n(%)			
Atrial Fibrilasyon	6 (24)	12 (15)	0.31
Sinüs	19 (76)	67 (84)	

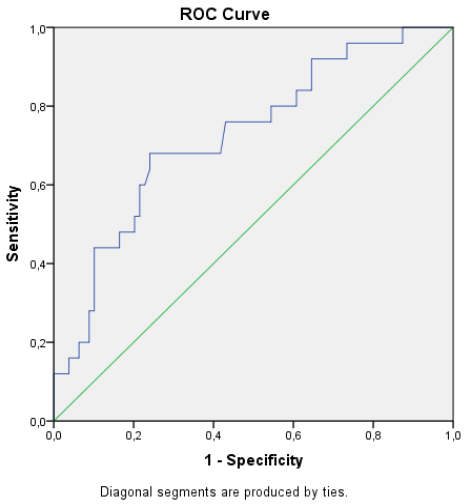
p<0.05 olan değerler koyu renkle gösterilmiştir. n: hasta sayısı, SS: standart sapma, ICD: implante edilebilir kardiyak defibrilatör, VVI: tek odacıklı, DDD: çift odacıklı, CRT: kardiyak resenkronizasyon tedavisi, Grup 1: uygun kardiyak şoklama alanlar , Grup 2: uygun kardiyak şoklama almayanlar.

Tablo 3. İlaçlar

Kullanılan ilaçlar, n(%)	Grup 1 (n=25)	Grup 2 (n=79)	p değeri
Betabloker	21 (84)	73 (92)	0.13
RAS bloker	7 (28)	17 (21)	0.12
Diüretikler	22 (88)	58 (73)	0.15
Amiodaron	11 (44)	12 (15)	**0.003**
Oral antidiyabetik	4 (16)	21 (26)	0.12
İnsülin	1 (4)	5 (6)	0.65
Antiplatelet	19 (76)	62 (78)	0.71
Oral antikoagülan	7 (28)	17 (21)	0.52

RAS: renin anjiotensin sistemi, n: hasta sayısı, Grup 1: uygun kardiyak şoklama alanlar, Grup 2: uygun kardiyak şoklama almayanlar.

ROC (receiving operating characteristicting) eğrisi analizi ACEF risk skoru>2.49 değerinin %68 duyarlılık ve %69 özgüllük ile uygun kardiyak şoklamayı öngördüğünü ortaya çıkardı (Eğri altındaki alan [EAA] 0.726, %95 CI: 0.611-0.840, p=0.001) (Resim-1).



Resim-1: ROC eğrisi ACEF risk skoru dağılımının optimal cut-off değerlerinin analizi.

Tartışma

Bu çalışmada ACEF risk skorunun ICD implante edilen hastalarda uygun kardiyak şoklamanın öngördürücüsü olduğu gösterildi. ICD implantasyonu sonrası meydana gelen kardiyak şoklamanın uygunluğunu kolay ve hızlı ulaşılabilir bir skorlama ile tahmin etmenin olay insidansı açısından kritik hastaları tespit etmede faydalı olduğu düşünülmektedir. Bu basit puanlama yöntemi (yaş, kreatinin ve EF), KABG veya PCI (perkütan koroner girişim) uygulanan hastalarda test edilmiş ve sonucu tahmin etmede değerli olduğu kanıtlanmıştır. Ek olarak, ACEF skorunun PCI sonrası akut böbrek zedelenmesinin iyi bir tahmin edicisi olduğu bildirilmiştir (13). ACEF skoru operatif mortalite riskini değerlendirdikten sonra farklı amaçlarda kullanılmaya başlanmıştır. LEADERS çalışmasında (14), 1208 perkütan koroner girişim (PCI) geçiren hasta için ACEF puanı hesaplanmış ve 1 yıllık takipteki ACEF skorları derecelendirilmiştir. Yüksek ACEF skoru olan hastalarda miyokard infarktüsü, ölüm, muhtemel ve muhtemel yüksek riskte stent trombozu oranı daha yüksek bulunmuştur.

Kore' de yapılan retrospektif kayıt üzerinden ICD implante edilen hastalarda uygunsuz kardiyak şokların uzun vadeli klinik sonuçlar üzerinde tahmin edici etkisi çalışmasında (15) yaşı küçük hasta grubunda sinüs taşikardisi ve anormal ritm algılama nedenli uygunsuz şok daha fazla iken, bizim çalışmamızda uygun kardiyak şok alan hasta grubunun yaşı istatistiksel olarak daha büyüktü (p=0.02)

Uslu ve ark (16) ICD implante edilmiş 146 hastada, daha önce çok merkezli otomatik defibrilatör implantasyon (MADIT trial) çalışmasında belirlenen MADIT skoru ile ICD' li hastalarda uzun dönem takiplerde ortaya çıkan istenmeyen kardiyovasküler olay arasındaki ilişki incelenmiştir. Beş klinik parametre olarak değerlendirilen MADIT ICD skoru (kan üre azotu>26 mg/dl, fonksiyonel kapasite>2, AF varlığı, yaş>70, QRS>120 msn) her bir parametreye 1 puan verilerek belirlenmiştir. Hastalar düşük-orta-yüksek skor puanlarına göre üçe ayrılıp analiz edilmiş, yüksek MADIT ICD skoru ile istenmeyen kardiyak olaylar arasında pozitif korelasyon bulunmuş, ancak uygun kardiyak şoklama ile anlamlı ilişki bulunmamıştır. MADIT-ICD skoru ile yapılan analizde, mevcut çalışmamızda saptandığı gibi sol ventrikül ejeksiyon fraksiyonu ve yaş uygun kardiyak şok için bağımsız öngördürücü olarak bulunmuştur. Yine benzer şekilde bizim çalışmamız ile korele olarak majör kardiyak istenmeyen olay yaşanan grupta, böbrek fonksiyon testleri anlamlı daha yüksekti. Yakın zamanda Naksuk ve ark. (17), MADIT' inkine benzer daha sınırlı bir popülasyonda, MADIT-ICD skorlarının tüm nedenlere bağlı mortaliteyi öngörmede yararlı olduğunu belirtti; bununla birlikte, bu puanlamanın uygun şok için öngördürücü bir değeri olmadığını öne sürmüşlerdir. Mevcut çalışmamızda ise ACEF risk skoru yüksekliğinin uygun kardiyak şoklamanın bir öngördürücüsü olduğu bulunmuştur.ACEF risk skoru bileşenlerinden biri olan sol ventrikül EF; DEFINITE (Significance of follow-up left ventricular ejection fraction measurements in the Defibrillators in Non-Ischemic Cardiomyopathy Treatment Evaluation trial) çalışmasında (18) göstermiştir ki sol ventrikül iyileşmesi olan grupta mortalite azalma eğiliminde ve aritmik olay yaşama ihtimali azalmaktadır. Bu nedenle iskemik veya non-iskemik kalp yetmezliği hastalarında sol ventrikül EF değeri azaldıkça ventriküler kaynaklı aritmi sıklığında artış beklenmekte ve bu kantitatif değer ile hesaplanan ACEF risk skoru daha yüksek saptanmaktadır.

Çalışma kısıtlılıkları

Çalışmamızın tek merkezli ve retrospektif oluşu yanı sıra, küçük çaplı uygun kardiyak şoklama alan (25 hasta) bir hasta grubunu içermesi gibi kısıtlılıkları bulunmaktaydı. Çalışmamızın daha fazla hasta grubunda yapılarak desteklenmeye ihtiyacı vardır.

Sonuç

ICD implantasyonu yapılan hastalarda basit şekilde hesaplanabilen ACEF risk skorunun yüksekliği uygun kardiyak şoklamanın öngördürücüsüdür ve ICD implantasyonu sonrası takiplerde bu skorun kullanılması hangi hastaların uygun kardiyak şok almaya daha yatkın olduğunu anlamamıza fayda sağlayabilir.

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Level of Response to COVID-19 Vaccine in Hemodialysis Patients and Factors Affecting This Level

Hemodiyaliz Hastalarında COVID-19 Aşısına Yanıt Düzeyi ve Bu Düzeyi Etkileyen Faktörler

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Abstract

Objectives: In this study, it was aimed to determine the antibody responses of hemodialysis patients to two doses of inactivated SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) vaccine(Coronavac)

Methods: The patients were divided into two groups as 14-20(Group 1) and 8-13(Group2) weeks over two doses of SARS-CoV-2 vaccine. In addition, patients were divided according to anti-spike IgG response as inadequate < 0.2 µg/mL and adequate response ≥ 0.2 µg/mL. The patients' age, hemodialysis data, presence of diabetes mellitus and Kt/V factors that may affect the response to the SARS-CoV-2 vaccine were compared and analysed(significant p value was taken as <0.05).

Results: 30 of 67 patients were excluded according to exclusion criteria. Adequate antibody response was found in 52.7% of Group 1 and 33.3% of Group 2. In group 2, the age of those without antibody response was 65.0±10.4 years, while those with a response were 50.5±11.0 years (p=0.015, 95% CI). In addition, a patient in Group 1 who received 4 doses of 40 µgr recombinant hepatitis B vaccine did not respond to both SARS-CoV-2 vaccine and HBV vaccine (anti-HBs <10 IU/mL). Antibody responses to SARS-CoV-2 vaccine were not different in both groups in terms of other characteristics of the patients (p>0.05).

Conclusions: The second dose of SARS-CoV-2 vaccine responses in HD patients was analyzed and the positive effect of being relatively younger was determined 8-13 weeks after second dose.

Keywords: Inactivated SARS-CoV-2 vaccine, Antibody responses to SARS-CoV-2, Hemodialysis, Anti-SARS-CoV-2 IgG, COVID-19

Öz

Amaç: Bu çalışmada hemodiyaliz hastalarının iki doz inaktif SARS-CoV- 2 (severe acute respiratory syndrome coronavirus 2) aşısına antikor yanıtlarının belirlenmesi amaçlandı.

Yöntem: Hastalar iki doz SARS-CoV-2 aşısı üzerinden 14-20(Gurup 1) ve 8-13(Gurup2) hafta süre geçenler olarak ikiye bölündü. Ayrıca hastalar anti-spike IgG yanıtına göre yetersiz < 0,2 µg/mL ve yeterli yanıt ≥ 0,2 µg/mL olarak ikiye bölündü. SARS-CoV-2 aşısına yanıtı etkileyebilecek hastaların yaşı, hemodiyaliz verileri, diabetes mellitus varlığı ve Kt/V gibi faktörler ile karşılaştırılarak analiz edildi (anlamlı p değeri<0.05 olarak alındı).

Bulgular: 67 hastanın 30'u dışlama kriterlerine göre çıkarıldı. Grup 1'in %52,7'si Grup 2'nin %33,3'ü yeterli antikor yanıtı oluşturdu. Grup 2'de antikor yanıtı olmayanların yaşı 65,0±10,4 iken, yanıtı olanlarda 50,5±11,0 idi (p=0,015, %95 GA).

Ayrıca Grup1 de bulunan ve 4 doz 40 µgr rekombinant hepatit B aşısı uygulanan bir hastamızda hem SARS-CoV-2 aşısına hem de HBV aşısına yanıt alınmadı (anti-HBs <10 IU/mL). SARS-CoV-2 aşısına karşı antikor yanıtları her iki grupta da hastaların diğer özellikleri açısından farklı değildi (p>0,05).

Sonuç: HD hastalarında ikinci doz SARS-CoV-2 aşısı yanıtları analiz edildi ve ikinci dozdan 8-13 hafta sonra nispeten daha genç olmanın olumlu etkisi belirlendi.

Anahtar Kelimeler:Inaktif SARS-CoV-2 aşısı, SARS-CoV-2 Antikor yanıtları, Hemodiyaliz, Anti-SARS-CoV-2 IgG, COVID-19

Introduction

A hemodialysis (HD) patient may become infected with COVID-19 through close contact with a patient or healthcare provider with possible COVID-19.The HD patient will likely be more susceptible to COVID-19 due to having diseases such as hypertension or diabetes mellitus. In HD patients, the weakening of innate and adaptive immune systems functions due to the decrease in both skewed Th1/Th2 T-cell ratios and dendritic and T-cell cells increases the tendency to infections [1].Therefore, end-stage renal disease (ESRD) is a risk factor for COVID-19 disease, which may result in death, and mortality is high in those who continue HD treatment [2]. In previous studies, it has been shown that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection poses high mortality risk compared to the healthy population [3]. Although isolating COVID-19 patients by taking precautions such as face mask and regular SARS-CoV-2 testing is beneficial in reducing the risk in HD patients, the mortality risk is still high in these patients.

At the same time as the start of the COVID-19 vaccination process worldwide, HD patients began to be vaccinated rapidly. With this process, it has been started to investigate how much the antibody levels obtained by vaccination in healthy or all patient groups are and how long they are in the serum. In a previous study, it was shown that T and B cell responses decreased by 17.1% four months after two doses of SARS-CoV-2 vaccine in HD patients [4].Since SARS-CoV-2-specific IgG titer can be detected, patients can be monitored to evaluate whether additional vaccine doses are required or the selection of the vaccine effective against the common variant in that country [5].However, the response levels to the COVID-19 vaccine in HD patients and the answer to the question of how many months this response can remain after the vaccine will become clear as the data of the studies are published. Due to the immunosuppressive nature of HD patients, it seems that response levels to the COVID-19 vaccine should be monitored at certain periods.

In this study, it was tried to determine the level of antibody responses after two doses of inactivated SARS-CoV-2 vaccine in HD patients and whether there is any factor associated with these levels.

Material and Methods

This cross-sectional study was carried out with 67 patients in Kars State Hospital hemodialysis center. The data of the study had been obtained by analysing the demographic, clinical, laboratory and serological records of patients who underwent HD treatment for 4 hours 3 times a week in the centres between 1may- 1august 2021.

The information of COVID-19 vaccine:

This study to evaluate of antibody response after COVID-19 Vaccine [(Vero cell), Inactivated (CZ02 strain), each syringe contains 0.5 mL with 600SU of inactivated SARS-CoV-2 antigen]. This vaccine was developed by Sinovac Life Sciences (Beijing, China), and received authorization for emergency use in Turkey in January 2021.

Vaccination protocol:

Vaccination was carried out following the national health authorities' instructions. According to this, the first vaccination is for those 65 years and older, after that it was offered to those under 65. Therefore, while some patients completed the two-dose vaccination protocol in March 2021, others were able to complete it in april and may. The vaccine was administered to the patients by intramuscular injection into the deltoid region of the upper arm.The first and second dose interval recommended by the manufacturer of 14-28 days for the COVID-19 vaccine.

Exclusion criteria:

Those infected with SARS-CoV-2 in the three months prior to vaccination and currently (n:16), those who were in close contact with someone who had SARS-CoV-2 infection in the last 10 days and did not have a PCR test(n:2), those who were infected with SARS-CoV-2 after the first dose (n:6), those who were infected with SARS-CoV-2 after the second dose (n:3), those who have active malignancy (n:1), those who have pregnancy (n:0), those who was received any kind of immunosuppressive treatments in the previous 12 months (n:1), those who have any active infections other than COVID-19(n:1).37 of the 67 patients who participated in the study were exluded in accordance with the exclusion criteria. Finally, 37 dialysis patients were included in the study, 12 women and 25 men.

After "The scientific research support" was provided by the University of Kafkas , in Turkey. Serum samples were taken to determine the levels of SARS-CoV-2-specific IgG on august 1, 2021. Patients were divided into two different groups according to their completion of the second dose of COVID-19 vaccine.

Group 1: Blood sample collection date: August 1, 2021, the number of weeks after second dose of COVID-19 vaccine: 14-20.

Group2: Blood sample collection date: August 1, 2021, the number of weeks after second dose of COVID-19 vaccine: 8-13.

Serological assessment:

The analysis was carried out by Human anti-SARS-CoV-2 (S) IgG ELISA kit (Catalogue No: EH4981, Wuhan Fine Biotech, Wuhan, China) which is a indirect enzyme-linked immune-sorbent assay (ELISA) that measures IgG antibodies to the spike protein of SARS-CoV-2. The serums were diluted by 1/50 values below 0.2µg/mL could not be determined and were considered negative [6].

Inadequate response: anti-SARS-CoV-2 (S) IgG< 0.2 µg /mL

Adequate response: anti-SARS-CoV-2 (S) IgG≥ 0.2 µg /mL

Processing of blood samples foranti-SARS-CoV-2 (S) IgG:

Samples were centrifuged on a Hettich Rotanta 460r centrifuge at 3000rpm for 10 minutes, aliquoted and anonymized. They were then stored at -70° C and thawed prior to testing.

The serume samples that for variables of study were obtained pre-hemodialysis and post-hemodialysis after the blood pump was reduced to 100 ml/min for 15 seconds, before saline administration, according to the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (NKF-K/DOQI) recommendations [7]. The formulation of Daugirdas was used to determine Kt/V [Single-pool(sp) Kt/V= -Ln (R – 0.008×t) + (4- 3.5×R) × UF / W] [8]. R = post-hemodialysis / pre-hemodialysis blood urea nitrogen, t (hours)= The time on HD, UF = ultrafiltration in liters and W= The post-hemodialysis body weight in kilograms.For the urea reduction rate: URR=100×(1-postdialysis blood urea nitrogen (BUN)/predialysis BUN was used. BUN= blood urea nitrogen [9].

Statistical analysis:

For statistical evaluation SPSS Statistics of Windows v.21,0 (SPSS; IBM Corporation, New York, USA) was used. Continuous parametric data were presented as average ± standard deviation and Student-t test was used for comparisons. Mann–Whitney U test was used for data that showed non-normal distribution. We applied the Chi square and Fisher's exact test in the analysis of the countable data. Results were evaluated according to a p-value of < 0.05 and confidence internal of 95%.

Ethical approval: The study protocol was approved by the Ethics Committee for Clinical Research, Faculty of Medicine, Kafkas University, Kars, Turkey. The study was conducted according to the declaration of Helsinki. Informed consent was obtained from all individual participants included in the study (Meeting decision number and date: 80576354-050-99/89 and 26.05.2021 respectively).

The scientific research support was provided by the University of Kafkas (project date and code : 04.06.2021 and 2021-TS-58 respectively)

Results

The number of patients in the HD center was 67, and when the exclusion criteria were applied, the number of patients included in the study was 37.

The number of patients identified as anti-spike IgG Antibodie 14-20 weeks after the second dose of inactivated COVID-19 vaccine is 19, the female/male ratio is 7/12, the rate of patients with an antibody response is 52.7%,antibody response in women 42.8%, the antibody response in men was 58.3%.

When Table 1 was followed, no statistically significant difference was found between the antibody response 14-20 weeks after the second dose of COVID-19 vaccine and the parameters such as biodemographic, biochemical, hormonal, diabetes mellitus presence and dialysis adequacy of the patients. For all independent variables: p>0.05 was found.

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Table 1: Effect of independent variables on responses of inactivated SARS-CoV-2 vaccine after 14-20 weeks the second dose.

Independent variables		**Dependent variable (anti-spike IgG Antibodies)**		P
		Not detectable <0.2(µg /mL)	**detectable ≥0.2** (µg /mL)	
		n(%) 9(47.3)	**n(%) 10(52.7)**	
Age	Years	9.5(mean rank) Age Min-Max:66-75	10,4(mean rank) Age Min-Max:62-81	0.712 [a]
Gender	Female	n:4	n:3	0.430[b]
	Male	n:5	n:7	
Dialysis vintage	Months	63±33 (min-max:6-120)	67±80 (min-max:12-204)	0.850[c]
BMI	kg/m^2	10.6(mean rank) (min-max:22-38)	9,4 (mean rank) (min-max:23-31)	0.624[a]
Serum albumin	gr/dL	3.7±0.3	3.8±0.4	0.333[c]
Hemoglobin	gr/dL	11.4±1.2	11.4±0.9	0.941[c]
CRP	range:0-5 mg/L	15.1±12.0	18.5±17.7	0.632[c]
Ferritin level	mg/dL	581±494	813±514	0.332[c]
Parathormone	pg/mL	476±252	446±304	0.818[c]
Vitamin D treatments[k]	Yes/No	4/5	4/6	1.000[b]
Erithropoetin used	Yes/No	7/2	8/2	1.000[b]
Vasculer Access	AVF/CVC	6/3	7/3	1.000[b]
KT/V	Daugirdas formula	1.58±0.30	1.49±0.20	0.454[c]
URR	%	73±7	72±5	0.598[c]
Diabetes Mellitus	Yes/No	2/7(n)	2/8(n)	1.000[b]
Anti-HCVPositive[d]	Yes/No	0/9(n)	0/10(n)	-
HBsAg Positive[d]	Yes/No	0/9(n)	0/10(n)	-
Anti-HBstiter	<10 IU/mL ≥10 lU/mL	1(n) 8(n)	1(n) 9(n)	1.000[b]

n=number, , a=with Mann-Whitney Test, b=with Fisher's Exact Test, c= with Student's t-test, BMI=Body Mass Index, CRP=C-reactive protein, URR Urea reduction rate, AVF Arteriovenous fistulae, CVC=Central Venous Catheter(cuffed),d= statistical analysis was not performed as all patients were negative

The number of patients who were determined to have anti-spike IgG antibodies 8-13 weeks after the second dose of COVID-19 vaccine was 18,female/male ratio 5/13, The rate of patients with adequate antibody response after the second dose of COVID-19 vaccine was 33.3%,While the antibody response was 20% in women, it was 38.4% in men.

In addition one of our two patients in the first group who were negative for HBsAg and Anti-HBs and who received Four doses of 40 µgr recombinant hepatitis B vaccine and did not get anti-HBs antibody response was also unresponsive to the second dose of COVID-19 vaccine (anti-HBs <10 IU/mL).

When Table 2 was followed, a statistically significant difference was found between the antibody response and the age of the patients 8-13 weeks after the second dose of COVID-19 vaccine. While the mean age of those who did not form an antibody response was 65.0±10.4, the mean age of responders was 50.5±11.0 (p=0.015, 95% CI) .On the other hand, no statistically significant difference was found between the parameters such as biodemographic, biochemical, hormonal, diabetes mellitus and dialysis adequacy of the patients and the Inactivated COVID-19 vaccine response (p>0.05).

Table 2: Effect of independent variables on responses of inactivated SARS-CoV-2 vaccine after 8-13 weeks the second dose.

Independent variables		Dependent variable (anti-spikeIgG Antibodies)		p
		Not detectable <0.2 (µg /mL)	detectable ≥0.2 (µg /mL)	
		n(%) 12(66.6)	n(%) 6(33.3)	
Age	Years	65.0±10.4	50.5±11.0	**0.015**[c]
Gender	Female	n:4	n:1	0,615[b]
	Male	n:8	n:5	
Dialysis vintage	months	8,25 (mean rank) min-max: 6-84	12,00 (mean rank) min-max: 12-168	0.156[a]
BMI	kg/m^2	27,3±6,2	22,9±5,6	0.164[c]
Serum albumin	gr/dL	3.9±0.4	4.0±0.2	0.433[c]
Hemoglobin	gr/dL	12,1±0,9	11,1±1,9	0,123[c]
CRP	range:0-5 mg/L	12,2±13,4	6,7±7,2	0,366[c]
Ferritin level	mg/dL	573±304	816±422	0,179[c]
Parathormone	pg/mL	506±468	471±425	0.879[c]
Vitamin D treatments[k]	Yes/No	7/5	2/4	0.620[b]
Erithropoetin used	Yes/No	8/4(n)	4/2(n)	1,000[b]
Vasculer Access[c]	AVF/CVC/(Greft)[d]	9/3/0 (n)	5/0/1 (n)	0,515[b]
KT/V	Daugirdas formula	1,56±0,24	1,63±026	0,562[c]
URR	(%)	72,7±5,4	74,2±7,2	0,631[c]
Diabetes Mellitus	Yes/No	6/6(n)	2/4(n)	0,638[b]
Anti-HCVPositive[e]	Yes/No	0/12(n)	0/6(n)	-
HBsAg Positive[e]	Yes/No	0/12(n)	0/6(n)	-
Anti-HBstiter[f]	<10 IU/mL ≥10 IU/mL	0(n) 12(n)	0(n) 6(n)	-

n=number, , a=with Mann-Whitney Test, b=with Fisher's Exact Test, c= with Student's t-test, BMI=Body Mass Index, CRP=C-reactive protein, k=Active Vitamin D or analog or calcimimetic, URR Urea reduction rate, AVF Arteriovenous fistulae, CVC=Central Venous Catheter(cuffed),d=not tested as there is only one person with a graft, k=Active Vitamin D or analog or calcimimetic, e=statistical analysis was not performed as all patients were negative, f= statistical analysis was not performed as all patients were Anti-HBs titer ≥10 IU/mL.

In Table 3, SARS-CoV-2 vaccine responses are presented according to the etiological causes of both groups. Statistical comparison was not performed due to the small number of cases. In two patients with Hypertension and Coronary artery disease, antibodies were tested 14-20 weeks after the second dose of SARS-CoV-2 vaccine and no antibody response was found.In addition, two patients with renal cell carcinoma had hypertension or diabetes mellitus and they had no response 8-13 weeks after the second dose of SARS-CoV-2 vaccine.

Table 3: End-stage renal disease etiologies and SARS-CoV-2 vaccine responses of patients.

End-stage renal disease etiologies	Female/ Male(n) (Total)	Level of anti-spikeIgG			
		Patients with antibodies tested that 14-20 weeks after the second dose vaccine		Patients with antibodies tested that 8-13 weeks after the second dose vaccine	
		<0.2 μg /mL (n)	**≥0.2 μg /mL (n)**	**<0.2 μg /mL (n)**	**≥0.2 μg /mL (n)**
DM	5/6(11)	2	2	5	2
HT	1/7(8)	2	3	2	1
HT+Hypothyroidism	1/0(1)	-	1	-	-
HT+CAD	0/2(2)	2	-	-	-
Urolithiasis	1/3(4)	1	1	2	-
Polycystic renal disease	1/2(3)	1	1	1	-
Renal cell carcinoma	0/2(2)	1	1		
Renal cell carcinoma+HT	1/0(1)			1	
Renal cell carcinoma+DM	0/1(1)			1	
Chronic pyelonephritis	1/0(1)	-	1	-	-
SLE	0/1(1)	-	-	-	1
Unknown	1/1(2)	-	-	-	2
Totale(n)	**12/25(37)**	**9**	**10**	**12**	**6**

DM =Diabetes mellitus, HT=Hypertension, CAD=Coronary artery disease, SLE=Systemic Lupus Erythematosus

Discussion

Previous studies have shown that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections have higher risk in HD patients compared to the general population. Especially since it was shown that antibody levels after natural COVID-19 infection seem to decline in HD patients over time. It has been started to investigate how much the antibody levels obtained by vaccinationCOVID-19 in healthy or all patient groups are and how long they are in the serum. In HD patients, the weakening of innate and adaptive immune systems functions due to the decrease in both skewed Th1/Th2 T-cell ratios and dendritic and T-cell cells increase the tendency to infections. Therefore, it is important to determine the periodic intervals of additional doses by determining the antibody levels of these patients during the ongoing pandemic process [3,10,11].In recent studies in HD patients, the antibody level was 80% after two doses of SARS-CoV-2 inactivated vaccine, while the Serologic response in HD patients with mRNA vaccine was approximate90% [12,13].These results are one month after the second dose of vaccine. Presumably, these levels may decrease as the antibody levels are checked again in the following weeks.

In one study, antibody levels were highest three months after two doses of inactivated SARS cov-2 vaccines, and decreased at six months. Therefore, we are in the process of administering additional doses of SARS-CoV-2 vaccine under pandemic conditions, regardless of the antibody levels of the patients [14].

The inactivated vaccine CoronaVac was found effective in a Phase 3 trial on a group of volunteers aged 18–59 years old [15]. However, in some previous studies, antibody responses after the second dose of both inactivated SARS-CoV-2 and mRNA BNT162b2 vaccine were found to be lower in kidney transplant recipients and HD patients [16,17]. In recent studies, it has been shown that seroresponse rates increase after the third dose of SARS-CoV-2 mRNA vaccinein HD patients [18].

In our study, these levels were found to be lower both in the group in which antibodies were tested 2-3 months after the second dose and that of in the group after 4-5 months. Due to the gradual decreasing in the number of healthy people who are not infected with COVID-19 as a result of the rapid spread of the pandemic, only the antibody results of HD patients were examined in our study. In our study of humoral response to two doses of SARS-CoV-2 inactivated vaccine, we observed a low seroconversion rate of 52.7% and 33.3% in the results of two different groups after 16-20 and 8-13 week using the manufacturers' recommended. To our knowledge, this is one of the first studies on the effectiveness of inactivated SARS-CoV-2 vaccine in HD patients of northeast Turkey.

In the study, besides the biodemographic characteristics of the patients, some biochemical, hormonal, Kt/V and URR values and antibody levels for hepatitis B and C were also evaluated. HD patients are known to generate reduced immunity to the vaccines, hepatitis B vaccine being the most widely studied.

All patients in our study were negative for HBsAg and anti-HCV. Anti-HBs levels were insufficient in two patients (2/37) among all patients [19]. While one of these patients had anti-spike protein antibodies, the other did not, who is 14-20 weeks after the second dose of SARS-CoV-2 inactivated vaccine. This patient, with anti-HBs titration <10 IU/mL, was a 72-year-old male. He was diabetic and also had heart failure,and his Kt/V and URR values were 1.85% and 81% respectively.That is, he was a patient who received adequate HD(9).This patient received four doses of 40 µgr recombinant hepatitis B vaccine and the last HBV vaccine dose was on April 30, 2021. The second dose of the SARS-cov-2 vaccine was administered on April 4, 2021. This poor response to the HBV vaccine has been emphasized in previous studies as a potential indicator of the response to the SARS-CoV-2 vaccine [20].

As a result, it was determined that 8-13 weeks after the second dose of SARS-CoV-2 vaccine, those who responded to the vaccine were relatively younger than those who did not respond. The results of this study require cautious interpretation, since the number of patients evaluated was small. However, our study can contribute to meta-analysis studies.

Limitations: Small sample size is one of the limitations of the study. Additionally, our test system only tested humoral, but no cellular immune response. The cellular part of the adaptive immune system probably plays a role in protection from COVID-19. Another limitation is SARS-CoV-2 antibodies were not screened at baseline for all patients to exclude possible asymptomatic infections.

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KLİNİK ÇALIŞMA / CLINICAL TRIAL
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Does The Reimplantation Of Nasal Cartilage in Nasal Septum Surgery Affect Complications Such As Septal Hematoma Or Septal Perforation?

Nazal Septum Cerrahisinde Nazal Kıkırdağın Geri Yerine Yerleştirilmesi Septal Hematom Veya Septal Perforasyon Gibi Komplikasyonları Etkiler Mi?

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Abstract

Objective: Nasal septum surgery is a common surgical procedure to relieve nasal obstruction. The aim of this study is to evaluate the frequency of complications in patients who underwent nasal septal surgery such as closed or open technical septoplasty and septorhinoplasty performed in our clinic. In addition, it is to evaluate whether shaping and reimplanting the cartilage removed during septum surgery increases the risk in terms of septal hematoma or whether not reimplanting the cartilage increases the risk in terms of septum perforation. Also, the difference between preoperative and postoperative routine hemogram parameters was also investigated.

Materials and Methods: 98 surgical operations of 94 patients who underwent septoplasty with Cottle technique, external septoplasty or external septorhinoplasty in our hospital were included. Complication rates were evaluated. Preoperative and postoperative hemogram results of the patients were compared.

Results: Septal hematoma was observed in 3 of 25 surgeries in which the deviated septal cartilage was reshaped to correct the curvature and reimplanted back, and septal perforation was not observed in them. Septal perforation was observed in 2 of 73 surgeries in which the removed deviated septal cartilage was not reshaped and reimplanted, and septal hematoma was not observed in them. The risk of septal hematoma was found to be statistically increased by reimplanting the deviated septal cartilage. There was no statistically significant difference in terms of septum perforation between the techniques in which the deviated cartilage septum was reimplanted back in its place and not placed. Hemogram values of 31 patients with postoperative 3rd-12th mounth control were compared with their preoperative values. Statistically significant decrease was observed in hemoglobin and erythrocyte count. There was no statistical difference in mean platelet volume.

Conclusion: Correcting and reimplanting of the deviated septum cartilage removed in nasal septum surgery may increase the development of septal hematoma or decrease the possibility of septal perforation. The risks should be evaluated and decided according to the patient and the situation.

Keywords: Nasal septal perforation, hematoma, nasal septum, hemoglobin

Öz

Amaç: Nazal septum ameliyatı, burun tıkanıklığını gidermek için yaygın bir cerrahi prosedürdür. Bu çalışmanın amacı kliniğimizde kapalı veya açık teknik septoplasti ve septorinoplasti gibi nazal septal cerrahi uygulanan hastalarda komplikasyon sıklığını değerlendirmektir.

Ayrıca septum cerrahisi sırasında çıkarılan kıkırdaklara şekil verip yerine koymanın septal hematom açısından riski artırıp artırmadığı veya kıkırdağın değiştirilmemesinin septum perforasyonu açısından riski artırıp artırmadığının değerlendirilmesidir. Ayrıca preoperatif ve postoperatif rutin hemogram parametreleri arasındaki fark da araştırıldı.

Gereç Ve Yöntemler: Hastanemizde Cottle tekniğinde septoplasti, eksternal septoplasti ve eksternal septorinoplasti operasyonu yapılan 94 hastanın 98 cerrahi operasyonu dahil edildi. Komplikasyon oranları değerlendirildi. Hastaların preoperatif ve postoperatif hemogram sonuçları karşılaştırıldı.

Bulgular: Çıkarılan deviye septal kartilajdaki eğriliğin giderilecek şekilde yeniden şekillendirildiği ve geri yerine yerleştirildiği 25 cerrahinin 3'ünde septal hematom görüldü, septum perforasyonu görülmedi. Çıkarılan deviye septal kartilajın şekillendirilerek geri yerine yerleştirilmediği 73 cerrahinin 2 tanesinde septum perforasyonu görüldü, septal hematom görülmedi. Deviye septal kartilajın şekillendirilerek geri yerine yerleştirilmesi ile istatistiksel olarak septal hematom riski artmış görüldü. Deviye kartilaj septumun düzleştirilerek geri yerine yerleştirildiği ve yerleştirilmediği teknikler arasında septum perforasyonu açısından istatistiksel anlamlı fark bulunmadı. Postoperatif 3. - 12. aylarda hemogram kontrolü olan 31 hastanın hemogram değerleri preoperatif değerleri ile karşılaştırıldı. Preopratif ve postoperatif 3. - 12. aylardaki hemoglobin ve eritrosit sayılarında istatistiksel olarak anlamlı azalma görüldü. Ortalama trombosit hacminde istatistiksel fark görülmedi.

Sonuç: Nazal septum cerrahisinde çıkarılan deviye septum kartilajının düzleştirilerek geri yerine yerleştirilmesi septal hematom gelişimini artırıyor veya septum perforasyonu oluşması ihtimalini azaltıyor olabilir. Hastaya ve duruma göre riskler değerlendirilip karar verilmelidir.

Anahtar Kelimeler: Nazal septal perforasyon, hematom, nazal septum, hemoglobin

Introduction

Nasal septum surgery is a common surgical procedure performed to relieve nasal obstruction due to deviation in the cartilage and bone septum of the nose (1). Nasal septum deviation is a common pathology that can be seen at a rate of 75-80% in anatomical studies performed on cadavers (2). Various reasons such as ethnic factors, birth traumas, developmental deformities, septum trauma have been suggested in its etiology. It can cause a variety of symptoms beside nasal obstruction such as sinusitis, facial pain, epistaxis. Medical and surgical treatment can be done and its surgical treatment is nasal septum surgery (3).

Nasal septum surgery can be performed as open and closed technical septoplasty or septorhinoplasty. It can also be performed with procedures such as lower turbinoplasty and/or endoscopic sinus surgery (3). Nasal septum surgery is often a safe surgery, but major and minor complications may develop peroperatively and postoperatively.

Various complications such as postoperative epistaxis, septal hematoma, septal abscess, edema, synechiae in the nasal cavity, cartilage dislocation, septum perforation, CSF rhinorrhea, infection (toxic shock syndrome, meningitis, wound infection, etc.), dental anesthesia, anosmia, aesthetic deformities can be seen (4,5).

Nasal septum deviation causes chronic upper airway obstruction. The severity of nasal obstruction may cause varying degrees of alveolar hypoventilation, and developing hypoxia may result in secondary polycythemia (6). The aim of this study is to evaluate the frequency of complications in patients who underwent nasal septal surgery such as closed or open technical septoplasty and septorhinoplasty performed in our clinic. In addition, it is to evaluate whether shaping and reimplanting the cartilage removed during septum surgery increases the risk in terms of septal hematoma or whether not reimplanting the cartilage increases the risk in terms of septum perforation. It is necessary to ensure that the cartilage to be reimplanted is sufficiently flattened. Otherwise, the risk of septal hematoma increases. In the group in which the cartilage is not reimplanted, the risk of perforation increases. Especially in cases with bilateral mucosal damage, cartilage reimplantation reduces the risk of perforation. A septal hematoma may develop, especially with the reimplantation of a poorly formed cartilage when it is not necessary. Unnecessary surgeries can be applied for hematoma intervention. On the other hand, especially in patients with mucosal damage, septum perforation may develop because the cartilage is not reimplanted. Additional surgery may be needed due to complaints such as crusting, bleeding, nasal congestion due to perforation. The surgeon should consider the risks according to the patient and make a decision. Also, the difference between preoperative and postoperative routine hemogram parameters was also investigated.

Material and Method

The approval of the Karadeniz Technical University Ethics Committee with protocol number 2021/0394 was obtained for the study. Between June 2019 and September 2021, those who applied to the otorhinolaryngology and head and neck surgery department of Şebinkarahisar State Hospital for reasons such as nasal obstruction, snoring and sleep disturbance, and nasal deformity or functional symptoms such as sinusitis, nasal polyp, had undergone septoplasty with the Cottle technique, external septoplasty or septorhinoplasty. 98 patients who underwent septoplasty with the Cottle technique together with endoscopic sinus surgery were included. Informed consent was obtained from all patients. The rates of surgical complications such as bleeding, septal hematoma, CSF rhinorrhea, synechia, septal perforation, and anosmia were evaluated after surgery.

Preoperative routine hematological values of the patients were compared with the postoperative results in order to evaluate the postoperative increased oxygenation as a result of surgical correction of nasal septum deviation. It was evaluated whether shaping and reimplanting the deviated cartilage, which was removed during surgery, is associated with the risk of septal hematoma. It was evaluated whether the risk of septum perforation increased with not reimplanting the removed cartilage.

Surgical technique:

In the study, all patients underwent septorhinoplasty, external septoplasty, or septoplasty with the Cottle technique by the same surgeon. External septorhinoplasty was performed in patients with external deformity, axial deviation, or cusp and low type. External septoplasty was performed in patients who had septal luxation or vertical fracture in the anterior aspect of the columella and no deformity of the nasal bridge or middle roof. In patients with deviations of the isolated bony nasal septum, septoplasty was performed using the Cottle technique. All surgical procedures were performed under general anaesthesia. In patients who underwent septoplasty according to Cottle, a hemitransfixation incision was made. In patients who underwent external septoplasty or septorhinoplasty, a Goodman incision was made. Mucoperichondrial and mucoperiosteal flaps were elevated bilaterally. Deviated nasal septum was removed. At least one centimetre of cartilage support was left on the dorsum and anterior part to support the structure. It was used various grafts such as cartilage spreaders, struts, Alar-Butten grafts in patients who underwent external septoplasty and septorhinoplasty. Spreader graft was applied to patients with vertical fractures of the cartilage dorsum or axis deviation. A strut graft was used to increase augmentation in the nose type. The Alar-Butten graft was used in patients with nasal valve insufficiency or deformity of the lateral crus of the alar cartilage. If there was cartilage that could be reused, it was shaped and reimplanted. In patients who underwent Cottle septoplasty and might have aesthetic concerns later, the cartilage was straightened and reimplanted. A transseptal suture and an intranasal silicone splint were placed in each patient. Nasal splint tampons were removed after an average of 5 days. All patients received routine antibiotics, analgesics, and saline irrigation postoperatively.

Statistical Analysis:

The distribution of interval data was evaluated by Kolmogrov-Smirnov or Shapiro-Wilk test. Independent groups with parametric distribution were evaluated with the Student t test and those with nonparametric distribution with the Mann Whitney U test. Paired-samples t test and Wilcoxon analysis were used to evaluate dependent groups. The chi-square test was used to evaluate ordinal data. Statistical analyzes were performed using IBM SPSS Statistics for Windows version 20.0 (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, version 20.0. Armonk, NY: IBM Corp.). $p < 0.05$ was considered statistically significant.

Results

A total of 98 surgical procedures in 94 patients, 59 men and 35 women, between June 2019 and September 2021 were included in the study. The overall mean age was 25.78 years (Table 1). Cottle septoplasty was performed in 34 of 98 surgical operations, external septoplasty in 24, and septorhinoplasty in 40 patients (Table 1).

Table 1: Gender Distribution of 94 Patients and Distribution of 98 Surgical procedures

	Patient number	Cottle Septoplasty	External Septoplasty	Septorhinoplasty
Male	59	26	13	22
Female	35	8	11	18
Total	94	34	24	40

In 24 operations, additional surgical procedures were performed together with nasal septum surgery. The most common additional surgical application was lower turbinoplasty (Table 2).

Table 2: Distribution of Surgical Procedure Applied in Addition to Nasal Septum Surgery

Surgery	n
Inferior concha turbinoplasty	13
Functional endoscopic sinus surgery	4
Concha bullosa resection	3
Nasal valve surgery	3
Revision due to Septal Hematoma	2
Adenoidectomy	2

The preoperative deviation types of patients were classified as right, right fort, left, left fort, and bilateral deviation (Table 3). The proportion of right and left septal deviations was approximately equal.

Table 3: Preoperative Deviation Rates

	n	%
Right Deviation	34	34,69
Right Severe Deviation	10	10,2
Bilateral Deviation	7	7,14
Left Deviation	28	28,57
Left Severe Deviation	19	19,39
Total	98	100

Deviation due to vertical or oblique fracture lines in the cartilaginous septum was noted peroperatively in 47 patients. In 44 of 47 patients, a spreader graft was used to straighten the fracture lines (Table 4).

Table 4: Distribution of Peroperative Spreader Graft Application

	n	%
Right	23	23,47
Left	9	9,18
Bilateral	12	12,24
None	54	55,1
Total	98	100

No complications occurred in 80 of 98 operations. Various perioperative and postoperative complications occurred in 18 cases (Table 5).

Table 5: Postoperative Early and Late Complication Rates

	n	%
Postoperative Epistaxis	4	4,08
Postoperative Residual Axis Deviation	4	4,08
Postoperative Residual Septal Deviation	2	2,04
Hematoma	3	3,06
Septal Perforation	2	2,04
Hyposmia/Anosmia	1	1,02
None	82	83,67
Total	98	100

Thirty patients had preoperative axis deviation (24 patients had axis deviation to the right, 6 patients had axis deviation to the left). Septorhinoplasty was performed in 21 patients, external septoplasty in 8 patients, and Cottle septoplasty in 1 patient. Postoperative axis deviation was corrected in 26 of 30 patients. Limited correction of postoperative axis deviation was achieved in 4 patients. In 1 of these patients, revision surgery was performed and the axis deviation was completely corrected. In addition, 2 patients were observed to have residual postoperative deviation in the nasal septum that did not narrow the airway. One of these 2 patients underwent revision surgery with a Cottle septoplasty.

Postoperative septal hematoma was observed in 3 patients, although silicone splint packing was used and transseptal sutures were placed in the anterior portion of the septum in all patients. In 2 of these patients, the procedure was performed under general anesthesia. In these patients, the deviated septal cartilage was straightened and repositioned. However, it was observed that the septal cartilage was again curved after straightening with the scalpel. It was suspected that the curved cartilage would cause a potential gap between the bilateral mucopericonium and mucoperiosteal flaps. The cartilage was removed and the clots were aspirated and sutured transseptally. In the third patient with postoperative septal hematoma, the septal mucosa was slightly bulging. A mild hematoma was drained through an incision in the mucosa. Bilateral nasal packing was applied. No permanent symptoms occurred after treatment in these 3 patients. In 25 patients who underwent nasal septal surgery, the septal cartilage was straightened and reimplanted. In 71 patients, the septal cartilage was not reimplanted. In 2 patients, the cartilage inserted in revision surgery was removed. Thus, the cartilage was not reimplanted in 73 patients.

Postoperative epistaxis requiring intervention occurred in 4 patients. Epistaxis requiring cauterization from the edge of the mucosal tear in the septal mucosa after removal of the silicone pads occurred in only one patient. The cauterization procedure was performed under local anesthesia in the clinic. In the other 3 patients, mild epistaxis was observed in the early postoperative period, and bleeding was controlled with anterior nasal packing. In patients who had bilateral mucosal tear during the procedure, transseptal sutures were used to approximate the mucosal edges, and cartilage was placed between them.

Postoperative septal perforation of less than 1 cm was noticed in 2 patients. However, these patients did not have bilateral mucosal tears during surgery. In these two patients, the septal cartilage was not reimplanted. Revision surgery was not performed because it was smaller than 1 cm and no additional symptoms occurred. Follow-up is recommended.

Of all the patients included in the study, revision surgery was required in only 4 patients. In two of these patients, revision surgery was performed under general anesthesia because of a septal hematoma. The hematoma was drained, and the cartilage septum inserted during the previous surgery was removed. In one of the other two revision patients, a Cottle septoplasty was performed because of a remaining deviated septum, and the deviation of the cartilage septum was corrected. In the other patient, external septoplasty was performed because of residual axial deviation, and the axial deviation was corrected. There was no significant difference between pre- and postoperative hemoglobin levels when patients were divided into severe deviated and non- severe deviated groups (p=0.842) (t-test in independent groups).

While hematoma developed in 3 (12%) of the 25 patients whose cartilage was reimplanted, it was observed that hematoma did not develop in any of the 73 (0%) patients whose cartilage was not reimplanted, which was statistically significant (p=0.016, chi-square). No significant difference was found when the patients were divided into reimplanted and non-reimplanted cartilage, while the perforation rate increased from 0% in the reimplanted to 2.98% in the non- reimplanted patients (p=0.537).

It was noted that 31 patients evaluated in our study referred to different departments of our hospital for non-infectious reasons after surgery and hemogram test was investigated. Infection, drug use for any reason were excluded. These results were retrospectively scanned and categorized according to the month of the postoperative period. Patients' preoperative hemogram results were compared with postoperative hemogram results 1-4 months, 4-8 months, 8-12 months, and 12 months after operation. When these results were analyzed separately, no significant difference was found between them (p=0.570) (repeated measures analysis of variance).

When we considered the arithmetical mean of blood count results at the postoperative 2nd and 14th months as the averaged postoperative values, and compared these values with the preoperative values, a significant difference was found in hemoglobin (HGB) values (preoperative: 14.58±1.56 and postoperative: 14.2±1. 57), p=0.021 paired samples t-test). When comparing the erythrocyte values (preoperative: 5.12±0.54 and postoperative: 4.99±0.52, p=0.019), a significant difference was found. When comparing mean platelet volume (MPV) preoperatively (9.46±1.91) and postoperatively (9.18±1.53), no significant difference was found (paired samples t-test p=0.434).

Discussion

Nasal congestion is a very common symptom due to decreased airflow from the nasal cavity. There can be several reasons for this. Nasal congestion is usually a symptom that the patient describes subjectively. Medical and surgical treatments are often used to relieve the symptoms (7). Nasal septum surgery is one of the most commonly performed surgeries by ENT physicians worldwide (2).

The most important airway area is the nasal vestibule and the area of the internal nasal valve, which is responsible for 50% of airway resistance. Functionally, it is very important to correct the caudal part of the nasal septum (2).

Nasal septum surgery is often a safe procedure, but major and minor complications can occur per- and postoperatively. Various complications such as postoperative epistaxis, septal hematomas, septal abscesses, edema, synechiae in the nasal cavity, cartilage displacement, septal perforation, cerebrospinal fluid rhinorrhea, infections (toxic shock syndrome, meningitis, wound infections, etc.), dental anaesthesia, anosmia, and aesthetic deformities may occur (4,5).

Postoperative residual nasal obstruction is a common complication due to incomplete repair of deviations that require more aggressive correction (8). In our study, residual deviation was observed in 2 patients, and nasal septum surgery was performed in one patient due to residual deviation. In addition, there may be axis deviations in the external appearance of the nose due to broken lines in the cartilage at the dorsum of the septum. In 1 patient, the axis deviation could not be corrected due to the fracture line in the dorsum of the cartilage septum, and a spreader graft was used with revision surgery. Successful results were obtained after revision surgery in both patients.

Perforation of the septum can result from the reciprocal of mucoperichondrial and mucoperiosteal mucosal tears that form during elevation and are not repaired. In addition, vascular malnutrition of the mucosa may occur due to postoperative hematoma or abscess formation. As a result, septal perforations may be seen (8). During septal surgery, removal of the cartilaginous and bony septum creates a dead space between the mucoperichondrial and mucoperiosteal flaps. Blood can accumulate in this dead space, and a septal hematoma can develop. This can lead to pathologies such as ischemia due to the hematoma, septal perforation due to vascular malnutrition, septal cartilage necrosis and decreased septal support, and septal abscess (9). Placement of cartilage by straightening may prevent postoperative septal perforation. In our study, cartilage was straightened and reimplanted in 25 patients. In 73 patients, septal cartilage was not reimplanted for various reasons such as the use of cartilage as a graft, deformed cartilage that cannot be straightened to a sufficient size, or the low probability of revision surgery due to the patient's age. Septal hematoma developed in 3 of 25 patients in whom the septal cartilage was straightened and reimplanted, and septal perforation was not observed in any of them. Also, no hematoma occurred in any of the 73 patients in whom the cartilage was not reimplanted. However, septal perforation of less than 1 cm occurred in 2 patients. Insertion of the septal cartilage by straightening may prevent the development of septal perforation. However, reimplantation of the cartilage may increase the risk of hematoma. In our study, a statistically significant septal hematoma developed in the nasal surgery group in which the cartilage was reimplanted.

Similarly, when the groups with and without cartilage reimplantation were compared, no statistically significant difference was found with respect to septal perforation. However, postoperative septal perforation was observed in 2 patients in the group in which cartilage was not reimplanted, whereas no septal perforation occurred in the group in which cartilage was reimplanted, suggesting that evaluation in a larger group of patients is necessary.

Tham et al. reported that postoperative septal perforation developed in 3 (2.91%) patients in a retrospective study of 103 patients. This rate was similar to our study. No septal hematomas were seen in the study, which reported excessive nosebleeds in 2 patients (10).

In another retrospective study by Shin ch et al., complication rates were investigated in 1506 patients who underwent septoplasty surgery. Similar to our study, hematoma was the third most common complication in 55 (3.7%) patients. In the same study, septal perforation was seen in 9 (0.6%) patients and it was less common than our study (11). In the literature, studies on septoplasty complications could not find any research on the cause of septal hematoma or septal perforation complications. We think that the complication of septal hematoma or septum perforation is related to the reimplantation of the cartilage removed during surgery.

Epistaxis is one of the most common complications after nasal septum surgery. Before surgery, all patients should be informed that there may be a slight discharge of blood for 1-2 days after surgery. However, bleeding requiring intervention after nasal septum surgery has been reported in 6% to 13.4% of cases, sometimes requiring hospitalization (9). In our study, epistaxis requiring postoperative intervention was observed in 4 patients (4.08%). Three patients were treated with anterior nasal packing. Bipolar cauterization was performed in only one patient in the outpatient clinic.

In a study conducted by Biden et al, excessive nosebleeds were the most common complication of septoplasty, with a rate of 3.3%. This was followed by transient hyposmia/anosmia at 3.1%, infection at 3.1%, and septal perforation at 2.3% (2). In our study, epistaxis and septal perforation were observed at similar rates, whereas hyposmia/anosmia were observed at a lower rate. In our study, no signs of severe postoperative infection were observed in any of the patients.

Dental pain and hypoesthesia may occur after septoplasty, but these are usually transient and resolve within a few weeks (8). The probability of occurrence of postoperative infection is 0.48% to 2.5%. This is an important complication that should be avoided. Postoperative septoplasty infections are usually limited to the nasal septum and nasal cavity, but can occur in more dangerous forms, such as meningitis, cerebritis, subdural empyema, brain abscess, and cavernous sinus thrombosis, which can occur rarely (9). Serious complications such as cerebrospinal fluid leakage, unilateral blindness, and death are extremely rare (8).

Postoperative infections did not occur in any patients in our study. No life-threatening situations such as CSF rhinorrhea, meningitis, brain abscess, etc. were observed.

Synechiae is a common complication after septoplasty or sinus surgery and causes postoperative nasal obstruction. It is an adhesion between the nasal mucosa. It is a common symptom occurring in approximately 7% of patients after septoplasty (9). We used silicone tampons in all patients and got the tampons back after an average of 5 days. In our study, nasal synechiae was not observed in any of the patients.

Nasal septal deviation is one of the main causes of chronic upper airway obstruction. As long as there are no symptoms, nasal septal deviation does not require surgical correction. However, depending on the severity of the nasal septal obstruction, alveolar hypoventilation may occur to a greater or lesser degree, and the resulting hypoxia. This event may lead to secondary polycythemia (6). To compare this effect of nasal septal deviation, Karataş et al. compared pre- and postoperative third-month erythropoietin (EPO) and hemoglobin (HGB) levels and found no statistical difference between pre- and postoperative EPO and HGB levels (6). In our study, it was found that postoperative hemograms were controlled in 31 patients. When comparing the mean hemoglobin values of these patients, which ranged from 1-14 months postoperatively, with the preoperative value, a statistically significant decrease in hemoglobin value was found (p=0.021). There was also a statistically significant difference in the erythrocyte value (p=0.019). In the study of Karataş et al. the follow-up period was 3 months, but in our study the follow-up period was longer. The reason for this statistical difference might be the follow-up time. Correction of septal deviation and chronic upper airway obstruction by rhinoplasty may improve oxygenation. In this way, there might have been a statistically significant decrease in erythrocyte levels. In addition, it is known that long-term changes in coagulation, platelet count, and platelet function may occur as a result of hypoxia. Mean platelet volume (MPV), which is related to platelet function and activation, increases as a result of hypoxia. It is considered an indicator of larger, more reactive platelets resulting from increased platelet turnover. This may be a risk factor for all-cause vascular mortality, including myocardial infarction. Poorey et al found that MPV increased in chronic nasal obstruction due to deviated septum, and this increase was consistent with the severity of the deviation (12). However, in our study, there was no statistically significant difference between the preoperative and postoperative MPV mean values (p=0.434).

The small number of patients and the fact that it was a single-center study are the limitations of the study. Studies in larger groups including multiple centers are needed.

Conclusion

Our study focused on evaluating the results of nasal septum surgery performed in our clinic. It was found that flattening and reimplanting the deviated septal cartilage statistically significantly increased the risk of septal hematoma. If the cartilage was not reimplanted, the risk of postoperative septal perforation did not increase statistically significantly. However, it was considered to be important that postoperative septal perforations were observed in the group in which the cartilage was not reimplanted. A septal hematoma may develop, especially with the reimplantation of a poorly formed cartilage when it is not necessary. Unnecessary surgeries can be applied for hematoma intervention. On the other hand, especially in patients with mucosal damage, septum perforation may develop because the cartilage is not reimplanted. Additional surgery may be needed due to complaints such as crusting, bleeding, nasal congestion due to perforation.

The surgeon should consider the risks according to the patient and make a decision In addition, a statistically significant difference was observed in preoperative and postoperative hemoglobin and erythrocyte values althogh there was no statistically significant difference in MPV values. In conclusion, whether to reimplant the deviated septum cartilage, which was removed in nasal septum surgery, should be decided according to the patient and the situation, taking into account the results.

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Antioxidant Efficacy Of Astaxanthin On Amiodarone Induced Toxicity in Rat

Amiodaron'un Neden Olduğu Sıçan Doku Toksisitesinde Astaksantin'in Antioksidan Etkinliği

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Abstract

Aim: We aimed to evaluate the effect of astaxanthin on amiodarone induced kidney tissue damage.

Methods: 3 groups were formed using 30 Wistar albino rats. In group 1 (control group) (n=10), neither any drugs were given nor anything was performed. In group 2 (amiodarone group) (n=10), 100 mg/kg amiodarone was given for 7 days. In group 3 (amiodarone+astaxanthin group) (n=10), 100 mg/kg amiodarone and 25 mg/kg astaxanthin were given for 7 days. Right kidneys were surgically extirpated in all groups. Blood malondialdehyde (MDA) levels and activities of catalase (CAT) and superoxide dismutase (SOD) were measured. Also, toxicity markers such as vascular congestion, hemorrhage, tubule degeneration and glomerular damage were assessed by examining the slides prepared from kidney tissue with microscopy.

Results: The MDA levels were significantly higher and the activities of SOD, and CAT were lower in group 2 than group 3 ($p<0.05$). Tissue damage was significantly higher in group 2 than group 3 ($p<0.05$).

Conclusion: According to our short term findings, astaxanthin reversed the toxicity of amiodarone on kidney tissue.

Keywords: Amiodarone, astaxanthin, rat, kidney, toxicity

Öz

Amaç: Astaksantin'in amiodaronun neden olduğu böbrek dokusu hasarı üzerindeki etkisini değerlendirmeyi amaçladık.

Yöntemler: 30 adet Wistar albino rat kullanılarak 3 grup oluşturuldu. Grup 1'de (kontrol grubu) (n=10) herhangi bir ilaç verilmedi ve herhangi bir işlem yapılmadı. Grup 2'ye (amiodaron grubu) (n=10) 100 mg/kg amiodaron 7 gün verildi. Grup 3'e (amiodaron+astaksantin grubu) (n=10) 100 mg/kg amiodaron ve 25 mg/kg astaksantin 7 gün verildi. Tüm gruplarda sağ böbrekler cerrahi olarak çıkarıldı. Kan malondialdehit (MDA) seviyeleri ve katalaz (CAT) ve süperoksit dismutaz (SOD) aktiviteleri ölçüldü. Ayrıca böbrek dokusundan hazırlanan lamlar mikroskopi ile incelenerek damar tıkanıklığı, kanama, tübül dejenerasyonu ve glomerüler hasar gibi toksisite belirteçleri değerlendirildi.

Bulgular: Grup 2'de MDA düzeyleri grup 3'e göre anlamlı olarak daha yüksek, SOD ve CAT aktiviteleri daha düşüktü ($p<0.05$). Doku hasarı grup 2'de grup 3'e göre anlamlı olarak yüksekti ($p<0,05$).

Sonuç: Kısa vadeli bulgularımıza göre astaksantin, amiodaronun böbrek dokusu üzerindeki toksisitesini tersine çevirmiştir.

Anahtar Kelimeler: Amiodaron, astaksantin, sıçan, böbrek, toksisite

Introduction

Amiodarone, an iodine-rich benzofuranic derivative, is currently used as an antiarrhythmic agent in the treatment of arrhythmias such as ventricular arrhythmias, paroxysmal supraventricular tachycardia, and atrial fibrillation (1). Amiodarone causes a number of histological changes, including intertubular leukocyte infiltration, degeneration of the renal tubules, and glomerular atrophy (2). The inhibition of the liposomal phospholipase enzyme by amiodarone results in an increase in phospholipid and free radical levels and cell death occurs (3). The high iodine content of amiodarone limits its use because it causes adverse effects on the thyroid and other tissues (4).

Astaxanthin is an important carotenoid pigment found in microalgae, mushrooms, seafood, flamingos and quails used in the food, cosmetics and feed industries (5). In addition to the very strong antioxidant properties of astaxanthin; it is thought to have many properties that are protective against ultraviolet (UV) light photo-oxidation, anti-inflammatory, anticancer, antidiabetic, anti-ulcer due to Helicobacter pylori, immunomodulatory, aging and age-related diseases, or healing on liver, heart, eye, joint and prostate (6, 7). Astaxanthin exhibits strong antioxidant effect due to its oxygen content. In a study in which a diabetic retinopathy model was created, astaxanthin increased the level of oxygenase 1 enzyme and restored homeostasis in the cell (8). It is known that astaxanthin has been used successfully in the treatment of many pathologies such as Alzheimer's disease, Parkinson's disease, Huntington's disease, Amyotrophic Lateral Sclerosis, especially neurological disorders (9, 10). Therefore, we aimed to reverse the kidney damage in rats given amiodarone with astaxanthin.

Material and Methods

In this study, it was investigated whether astaxanthin was effective in kidney damage due to amiodarone in Wistar Albino rats. The amiodarone and astaxanthin used in the study were obtained from a local pharmacy. A total of 24 Wistar albino rats were included in the study. Animals were obtained from Erciyes University Animal Experiments Department. The study was carried out in Erciyes University Faculty of Medicine, Department of Histology and Embryology. Ethical approval of the study was obtained from Erciyes University Animal Experiments Local Ethics Committee. Rats were fed ad libitum feeding method with free access to water and food, and were exposed to a temperature of 20-22 C and a 12-hour light/dark period.

A total of 3 groups were created. The groups and given drugs are shown in **Table 1.**

Table 1. Experimental groups and given drugs

Number of the groups	Groups	Number of the patients	Amount of the substance
1	Control group	10	None
2	Amiodarone group	10	amiodarone (100 mg/kg/day) 7 days
3	Amiodarone+astaxanthin group	10	amiodarone (100 mg/kg/gün 7 days+ astaxanthin 25 mg/kg/day (350 µl dissolved in olive oil, oral) 7 day

Ketamine hydrochloride (50 mg/kg, Ketalar, Eczacıbaşı, İstanbul, Turkey) and xylazine hydrochloride (5 mg/kg, Rompun, Bayer, Leverkusen, Germany) were administered intraperitoneally for anesthesia. Blood was collected from rats by cardiac puncture. Then, the right kidney tissues were surgically removed and the animals were sacrificed by cervical dislocation.

Tissues were fixed in formaldehyde solution and then embedded in paraffin. Sections of 5 µm in diameter were taken. Sections were stained with hematoxylin-eosin stain. In addition, staining with pax 2 was performed immunohistochemically. Samples were examined with a light microscope (Olympus® Co. CX41 Tokyo, Japan). Damage to kidney tissue was evaluated using the modified scoring system. Histopathological scoring was made according to the highest area. By semi-quantitative analysis; four categories were determined (0: Absent 1: Minimal 2: Mild 3: Moderate 4: Severe) and parameters were scored accordingly.

To determine the extent of tubular damage, glomerular damage and interstitial damage, ''tubular dilatation, proteinous material accumulation in tubule, tubular epithelial cell change, glomerular damage (fibrosis/atrophy/thrombosis), interstitial fibrosis, interstitial congestion/hemorrhage, interstitial habilitate mononuclear cell infiltration'' ' parameters were used. Pax 2 expression levels were graded using the 0-3+ range. (pax 2; 0: no staining, 1: less than 10% nuclear staining of renal tubule epithelial cells, 2: nuclear staining of 10-30% of renal tubule epithelial cells, 3: nuclear staining of more than 30% of renal tubule epithelial cells staining) (11).

Malondialdehyde (MDA) levels and superoxide dismutase (SOD) and catalase (CAT) activities were measured by calculating absorbance in a spectrophotometer (Shimadzu UV 1800, Kyoto, Japan). The thiobarbituric acid test was used to calculate MDA levels (12). SOD enzyme activity was determined by Marklund et al. It was calculated according to the method reported by (13). CAT activity was measured as stated by Aebi et al. (14).

Statistical Package for the Social Sciences (22.00 SPSS Inc., Chicago, IL) was used for statistical analysis. Power analysis was used and the sample size was calculated as at least 8 for each group with 80% accuracy. Chi-square for categorical variables and independent t-test for numerical values were used. P value < 0.05 was considered statistically significant.

Results

Blood MDA levels and SOD and CAT enzyme activity levels are shown in **Table 2.** MDA levels in the amiodarone group were significantly higher than those in the amiodarone + astaxanthin group ($p < 0.05$). SOD and CAT enzyme activities were compared, the values in the amiodarone group were lower than the amiodarone + astaxanthin group, the difference was statistically significant ($p < 0.05$).

Table 2. Distribution of blood malondialdehyde (MDA), superoxide dismutase (SOD) and catalase (CAT) levels according to groups.

Gruplar (n = 8)	MDA (nmol/mg)	SOD (U/mg)	CAT (U/mg)
Control group	8.32 ± 1.65	60.5 ± 9.61	108.4 ± 19.7
Amiodarone group	20.12 ± 4.38*	25.12 ± 5.71*	56.75 ±13.22*
Amiodarone+astaxanthin group	11.23 ± 2.27*	43.87 ± 8.54*	87.59 ± 15.23*

MDA: malondialdehyde, SOD: superoxide dismutase, CAT: catalase

Data were expressed as ± standard deviation

* Significant difference between groups 2 and 3 ($p < 0.05$)

There was no difference between the groups in terms of the macroscopic appearance of the tissues. When the damage to the kidney tissue was scored, the histopathological damage in the amiodarone group was significantly higher than the amiodarone + astaxanthin group ($p < 0.05$). Damage levels in tissues are shown in **Table 3.**

Table 3. Distribution of histopathological findings according to groups

Groups (n = 10)	Hemorrhage	Fibrosis	Glomerular atrophy	Edema	Inflammatory cell infiltration
Control group	0	0	0	0	0
Amiodarone group	2*	2*	2*	2*	3*
Amiodarone+astaxanthin group	1*	1*	1*	1*	1*

* Significant difference between groups 2 and 3 ($p < 0.05$).

The highest area was determined and histopathological scoring was performed. Four categories (0: Absent 1: Minimal 2: Mild 3: Moderate 4: Severe) were determined by semi-quantitative analysis and the parameters were scored accordingly.

In the control group, the parenchyma structure in the kidney tissue appeared normal and the cellular architecture was intact **(Figure 1A).** Glomerular atrophy, inflammatory cell infiltration and interstitial fibrosis were observed in the amiodarone group **(Figure 1B).** Minimal parenchymal damage and tubular cell damage were observed in the amiodarone + astaxanthin group **(Figure 1C).**

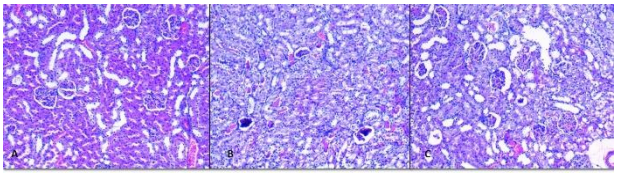

Figure 1. Evaluation of the kidney with light microscopy. (A) Renal parenchyma view of rats in the control group (H&E, x200). (B) Renal parenchyma view of rats in the amiodarone group. Significant hemorrhage, mononuclear inflammatory cell infiltration and glomerular atrophy were observed (H&E, x200). (C) Renal parenchyma view of rats in the amiodarone+astaxanthin group. Local mononuclear inflammatory cell infiltration and hemorrhage were observed (H&E, x200).

When the Pax 2 stained preparations were examined, it was determined that the parenchymal destruction caused by amiodarone was reversed with astaxanthin **(Figure 2A, B, C).**

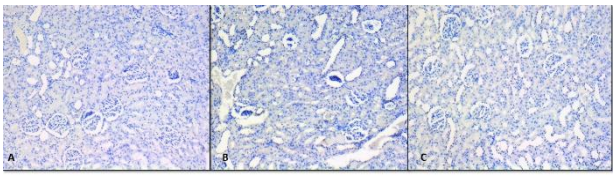

Figure 2. Evaluation of kidney with pax 2 immunostain. (A) Renal parenchyma view of rats in the control group (x200). (B) Renal parenchyma view of rats in the amiodarone group. (x200). (C) Renal parenchyma view of rats in the amiodarone+astaxanthin group. (x200**).**

Discussion

In this randomized controlled experimental study, the effect of astaxanthin on the renal toxicity of amiodarone was investigated. To our current knowledge, this is the first study to investigate the protective effect of astaxanthin against amiodarone-induced nephrotoxicity. Short-term findings show that MDA levels in the amiodarone group were significantly higher than those in the amiodarone + astaxanthin group, while SOD and CAT enzyme activities were significantly lower ($p < 0.05$).

In addition, it was observed that tissue damage, which was more pronounced in the amiodarone group, regressed with the administration of astaxanthin. Our results were consistent with the thesis that kidney damage and structural changes secondary to amiodarone could be reduced by administering an antioxidant.

Amiodarone, which is a class 3 derivative antiarrhythmic, has many side effects such as acute liver failure, nephrotoxicity, cardiac arrest, adult respiratory distress syndrome and hypotension (15). Robin et al. stated that recurrent hypotension attacks play a role in amiodarone-induced kidney damage (16). Serviddio et al. suggested that amiodarone increases mitochondrial hydrogen peroxide synthesis, resulting in increased lipid peroxidation and kidney damage (17). Other theories regarding the pathogenesis of amiodarone-induced nephrotoxicity include oxidative stress, free radical increase, phospholipase inhibition, and membrane destabilization (18).

Since oxidative stress plays an important role in the pathogenesis of amiodarone toxicity, antioxidants can be used to reduce these side effects. Astaxanthin, which is a pigment in many plants, is a natural component that contains antioxidant, antiproliferative, anti-inflammatory properties and is also called carotenoid (19). Astaxanthin, which is also obtained from algae such as Haematococcus pluvialis or fungi such as Phaffia rhodozyma and is in red, has been touted as a unique antioxidant that prevents cell and tissue damage caused by oxidative stress (10). Therefore, we thought that the astaxanthin molecule, which has strong antioxidant properties, may be effective in preventing amiodarone-induced nephrotoxicity.

Pax 2 is is localized in the long arm of 10th chromosome. Pax 2 protects the cell from cell death during cellular stress. Pax 2 gene expression has been shown to increase during oxidative stress. With this increase, the ability of the cell to be protected from cell death increases (20). We demonstrated that the parenchymal destruction caused by amiodarone was reversed with astaxanthin by using pax 2 immunohistochemical stain.

In this study, subsequent addition of astaxanthin to rats given amiodarone resulted in a decrease in MDA levels and an increase in SOD and CAT enzyme activities. The protective effect of the astaxanthin molecule has also been confirmed histopathologically. When the parameters indicating damage were scored, the score in the amiodarone+astaxanthin group was found to be lower than that in the amiodarone group. Limitations of the study are the difficulty in adapting the findings in rats to humans and the relatively small sample size.

Conclusion

As a result, astaxanthin was found to be effective in preventing amiodarone-induced kidney damage.

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KLİNİK ÇALIŞMA / CLINICAL TRIAL
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Hipertrigliseridemi İlişkili Akut Pankreatitte Psödohiponatreminin Kötü Prognostik Bir Değeri Var mıdır?

Does Pseudohyponatremia Have a Poor Prognostic Value in Hypertriglyceridemia-Induced Acute Pancreatitis ?

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Öz

Amaç: Hipertrigliseridemi ilişkili pankreatit, akut pankreatitin en sık 3. nedenidir. Psödohiponatremi (sodyum ≤ 130 mEq/dl) bu hasta grubunda görülebilmektedir. Çalışmamızda hipertrigliseridemi ilişkili akut pankreatitte psödohiponatreminin kötü prognostik bir değeri olup olmadığı amaçlanmıştır.

Yöntem: 2016-2022 yılları arasında hipertrigliseridemi ilişkili akut pankreatit tanısı alan 31 hasta çalışmaya retrospektif olarak alınmıştır. Bu hasta grubunun demografik, laboratuvar verileri, Ranson skorları, Atlanta sınıflaması düzeyleri ve yatış süreleri kaydedildi.

Bulgular: Hastalarımızın yaş ortalaması 43±8.5 idi. Hastaların 21 (%67.7)'i erkekti. 19 (%61.3) hastada diyabetes melitus var iken 14 (%45.2) hastada da alkol kullanımı mevcuttu. Hastaların ortalama serum sodyum düzeyleri 128.8±6.2 mEq/dl idi. 17 (%54.8) hastada serum sodyum düzeyi ≤130 mEq/dl iken 14 (%45.2) hastada serum sodyum düzeyi > 130 mEq/dl idi. Serum sodyum düzeyi ≤130 mEq/dl olanlar ile >130mEq/dl olanlar karşılaştırıldığında Ranson skoru (3.3±0.8 vs 1.9±1.2, *p*=0.004), CRP 48. saat düzeyi (173.5±69.1 mg/dl vs 115±97.4 mg/dl, *p*=0.015), trigliserit düzeyi (3730±1572 mg/dl vs 2277±1195 mg/dl, *p*=0.019), Atlanta sınıflaması düzeyi orta-şiddetli olanlar (11(%73.3) vs 4(%26.7), *p*=0.049) ve yatış süresi (9.3±3.5 gün vs 6.2±2.9 gün, *p*=0.014) açısından anlamlı farklılıklar mevcuttu.

Sonuç: Hipertrigliseridemi ilişkili akut pankreatit tanısı ile başvuruda başlangıç serum sodyum düzeyi tedavi yönetimi, risk değerlendirmesi ve prognoz açısından kötü prognostik bir parametre olabilir.

Anahtar Kelimeler: Hipertrigliseridemi ilişkili akut pankreatit, psödohiponatremi, Ranson skoru

Abstract

Objective: Hypertriglyceridemia-induced pancreatitis is the third most common cause of acute pancreatitis. Pseudohyponatremia (sodium ≤ 130 mEq/dl) can be seen in this patient group. In our study, we aimed to determine whether pseudohyponatremia has a poor prognostic value in hypertriglyceridemia-induced acute pancreatitis.

Methods: Thirty-one patients diagnosed with hypertriglyceridemia-induced acute pancreatitis between 2016-2022 were included in the study retrospectively. Demographic, laboratory data, Ranson scores, Atlanta classification levels and length of stay of this patient group were recorded.

Results: The mean age of our patients was 43±8.5. 21(67.7%) of the patients were male. While 19 (61.3%) patients had diabetes mellitus, 14 (45.2%) patients also had alcohol use. The mean serum sodium levels of the patients were 128.8±6.2 mEq/dl. While the serum sodium level was ≤130 mEq/dl in 17 (54.8%) patients, the serum sodium level was >130 mEq/dl in 14 (45.2%) patients.

Comparing those with serum sodium level ≤130 mEq/dl and those with >130 mEq/dl Ranson score (3.3±0.8 vs 1.9±1.2, *p*=0.004), CRP 48th hour level (173.5±69.1 mg/dl vs 115±97.4 mg/dl, *p*=0.015), triglyceride level (3730±1572 mg/dl vs 2277±1195 mg/dl, *p*=0.019), Atlanta classification level moderate-severe (11(%73.3) vs 4(%26.7), *p*=0.049) and length of stay (9.3±3.5 days vs 6.2±2.9 days, *p*=0.014), there were significiant differences.

Conclusion: İnitial serum sodium level may be a poor prognostic parameter in terms of treatment management, risk assesment and prognosis at admission with the diagnosis of hypertriglyceridemia-induced acute pancreatitis.

Keywords: Hypertriglyceridemia-induced acute pancreatitis, pseudohyponatremia, Ranson score

Giriş

Hipertrigliseridemi ilişkili akut pankreatit (HTG-AP) tüm akut pankreatit nedenlerinin %1-14' ünü oluşturmaktadır. Akut pankreatitin en sık karşılaşılan iki nedeni olan biliyer sistem taşları ve alkol kullanımından sonra en sık neden olarak karşımıza çıkmaktadır (1). HTG-AP, diğer akut pankreatit nedenlerine göre daha yüksek oranda nekrotizan pankreatit, multiorgan yetmezlik ve mortalite ile ilişkilidir (2). Daha fazla mortalite ve morbidite nedeni olması nedeni ile, HTG-AP tanısı ve erken dönemde tedavisi önem arz etmektedir. HTG-AP tanısı trigliserit düzeyinin ≥ 1000 mg /dl olması ile birlikte tipik epigastrik ağrı, serum amilaz-lipaz düzeyi yüksekliği ve pankreatit ile uyumlu görüntüleme tetkiklerinin olması ile konulur. Tedavisi intravenöz yeterli sıvı, analjezik ve trigliserit düşürücü uygulamalar (ilaç/lipit aferezi) şeklindedir (3).

Şiddetli trigliserit yüksekliği plazma su içeriğini azaltarak, serum ozmolalitesini değiştirmeden serum sodyum düzeyinin düşük ölçülmesine (psödohiponatremi) neden olabilir (4). Daha önce yapılmış çalışmalarda trigliserit yüksekliği ile pankreatit şiddeti orantılı şekilde tespit edilmiştir (5-7). Trigliserit düzeyindeki artış ile ortaya çıkan psödohiponatremi de prognoz ile ilişkilendirilebilir. Bu nedenlerle HTG-AP'de psödohiponatremi prognozu belirlemede kullanılabilecek parametrelerden biri olabilir.

Biz bu çalışmada HTG-AP tanısı almış olan hastalarda psödohiponatreminin kötü prognostik bir değerinin olup olmadığını belirlemeyi amaçladık.

Gereç ve Yöntemler

Ocak 2016-Ocak 2022 tarihleri arasında 3.basamak bir hastaneye trigliserit yüksekliğine bağlı akut pankreatit tanısı ile yatmış olan hastalar retrospektif olarak çalışmaya alındı. Hastaların yaş, cinsiyet, laboratuvar değerleri (hastaneye başvuru anı hemogram-biyokimya, lipaz ve 48.saat CRP ölçümleri), komorbid durumları, Ranson skorları, akut pankreatit Atlanta sınıflaması düzeyleri ve yatış süreleri hasta dosyalarından taranarak kaydedildi. Trigliserit ≥ 1000 mg /dl ve 3 kriterden (tipik pankreatit ağrısı, serum lipaz düzeyinin 3 kat ve üzeri artması, abdominal tomografi) en az ikisinin olması ile HTG-AP tanısı konuldu (8). Akut pankreatit derecelendirmesi revize Atlanta sınıflamasına göre yapıldı (8). Psödohiponatremi, sodyum sınır değeri 130 mEq/dl ve altı olacak şekilde tanımlandı (9).

< 18 yaş hastalar, gebelik durumu ve dosyada eksik veri olması dışlama kriteri olarak belirlendi.

Bu çalışma 3.basamak bir hastanede Helsinki Deklerasyonu Prensipleri'ne uygun, etik kurul onayı alınarak yapılmıştır (karar:12, protokol no: 2022/86).

İstatistiksel Analiz

İstatistik analizleri SPSS 26.0 (SPSS Inc., Chicago, IL, USA) programı kullanılarak yapıldı.. Tanımlayıcı analizler normal dağılan değişkenler için ortalama±standart sapma verilerek yapıldı. Normal dağılmayan değişkenler için ortanca ve çeyrekler arası kullanılarak verildi. Sodyum ve pankreartit şiddeti ki-kare ya da Fisher testleri ile değerlendirildi. P değerinin 0.05'in altında olduğu durumlarda istatiksel olarak anlamlı sonuçlar şeklinde değerlendirildi.

Bulgular

HTG-AP tanısı alan 31 hasta çalışmaya alındı. Hastaların ortalama yaşı 43±8.5 idi. 21 (%67.7) hasta erkekti. Hastaların 19(%61.3)'unda diyabet öyküsü var iken 14(%45.2)'ünde alkol kullanımı mevcuttu. Ortalama trigliserit düzeyi 3074±1574 mg/dl, sodyum düzeyi 128.8±6.2 mEq/dl olarak tespit edildi (Tablo-1).

Tablo 1: HTG-AP hastalarının demografik, laboratuvar ve klinik özellikleri

Yaş, ortalama	43±8.5
Cinsiyet	
Kadın, n (%)	10 (32.3)
Erkek, n (%)	21 (67.7)
Diabetes mellitus, n (%)	19 (61.3)
Alkol, n (%)	14 (45.2)
Lipaz U/L, ortanca	255 (25-2675)
Sodyum mEq/dL	128.8±6.2
Trigliserit mg/dL	3074±1574
CRP 48. saat mg/dl	147±86.8
Ranson skoru	2.6±1.2
Atlanta Düzeyi	
Hafif, n (%)	16 (51.6)
Orta-Şiddetli, n (%)	15 (48.4)
Yatış süresi, gün	7.9±3.6

***HTG-AP: Hipertrigliseridemi ilişkili akut pankreatit , *CRP: C-reaktif protein**

Hastalar sodyum sınır değeri 130 mEq/dl alınarak 2 gruba ayrıldı. Serum sodyum düzeyi ≤130 mEq/dl olanlar ile >130mEq/dl olanlar karşılaştırıldığında Ranson skoru (3.3±0.8 vs 1.9±1.2, *p*=0.004), CRP 48. saat düzeyi (173.5±69.1 mg/dl vs 115±97.4 mg/dl, *p*=0.015), trigliserit düzeyi (3730±1572 mg/dl vs 2277±1195 mg/dl, *p*=0.019), Atlanta sınıflaması düzeyi orta-şiddetli olanlar (11(%73.3) vs 4(%26.7), *p*=0.049) ve yatış süresi (9.3±3.5 gün vs 6.2±2.9 gün, *p*=0.014) açısından anlamlı farklılıklar mevcuttu. (Tablo-2). Sodyum düzeyi > 130 meq/dl olan hastaların (n:14) 10'unda pankreatit hafif seyirli iken 4 'ünde orta şidette idi, şiddetli pankreatiti olan hasta yoktu. Sodyum düzeyi ≤130 mEq/dl olan hastalarda (n:17) 6 hastada pankreatit hafif iken, 10 hastada orta şiddette, 1 hastada ise şiddetli pankreatit bulguları mevcuttu.

Tablo 2: Sodyum düzeyine göre hastaların klinik özellikleri

Değişkenler	Sodyum>130m Eq/dL (n=14)	Sodyum≤130m Eq/dL (n=17)	*P*
CRP 48.saat mg/dl	115±97.4	173.5±69.1	0.015
Trigliserit mg/dl	2277±1195	3730±1572	0.019
Ranson skoru	1.9±1.2	3.3±0.8	0.004
Atlanta düzeyi (orta-şiddetli), n (%)	4 (26.7)	11 (73.3)	0.049
Yatış süresi, gün	6.2±2.9	9.3±3.5	0.014

***CRP: C-reaktif protein**

Tartışma

HTG-AP akut pankreatitin önemli nedenlerinden biridir. Diğer akut pankreatit nedenlerine göre daha fazla morbidite ve mortalite oranlarına sahiptir. Bu nedenle bu hasta grubunun tanısı ve erken dönemde tedavisi önemlidir (10). Trigliserit düzeyinin ≥ 1000 mg/dl olması ve akut pankreatit tanı kriterleri birlikteliğinde tanı konmaktadır. HTG-AP tedavisi, akut pankreatit tedavisi yanında trigliserit düşürücü tedavi birlikteliğini kapsamaktadır. Trigliserit düşürücü tedaviler insülin infüzyonu, lipit aferezi ve hastanın orali açılır açılmaz oral farmakolojik tedavileri (fibratlar) içermektedir (11).

Akut pankreatitin daha sık nedenleri safra yolu taşı ve alkol kullanımıdır. Bu sebeple akut pankreatit tanısı ile acil servislere başvuruda trigliserit yüksekliğine bağlı akut pankreatit akılda olması gereken tanılar arasında olmayabilmektedir. Aynı zamanda çoğu 2.basamak hastane acil servislerinde lipit paneli çalışılamamaktadır. Bu nedenlerle HTG-AP tanısında gecikmeler yaşanabilmektedir. Bu hasta grubunda sodyum düşüklüğü, trigliserit yüksekliğine bağlı azalmış plazma su içeriğine bağlı olarak serum sodyum düzeyinin düşük (psödohiponatremi) ölçülmesine yol açabilmektedir. Bu nedenle serum sodyum düzeyi düşük olan akut pankreatit hasta grubunda HTG-AP tanısı ilk akılda olması gereken durumdur.

Hiponatreminin kötü prognoz ile birlikteliği daha önceleri farklı klinik çalışmalarda gösterilmiştir (12-13). Akut pankreatit, kalp yetmezliği, son dönem böbrek yetmezliği ile ilgili çalışmalarda hiponatremi kötü prognostik belirteç olarak bulunmuştur (9,14,15). Bizim çalışmamızda hiponatremisi olan HTG-AP hastalarında 48.saat CRP düzeyi, trigliserit düzeyi, Ranson skoru, Atlanta sınıflaması düzeyi (orta-şiddetli olan hastalar) ve yatış süresi anlamlı olarak daha yüksek bulunmuştur. Wang ve ark. (9) yaptığı çalışmada hiponatremisi olan HTG-AP hastalarında Ranson skoru, böbrek yetmezliği seviyesi ve BISAP (yatak başı pankreatit skoru) skoru anlamlı şekilde yüksek bulunmuştur. Çalışmamız literatür ile benzer sonuçlar içermekteydi.

Sodyum düzeyinin düşük olması trigliserit düzeyi yüksekliği ile paralellik gösterir. Bizim çalışmamızda da sodyumu düşük olan grubun trigiserit düzey ortalaması anlamlı şekilde daha yüksek idi. İndirekt olarak şöyle de yorumlanabilir; trigliserit düzeyi artan hastalarda prognoz daha kötü olabilir. HTG-AP patofizyolojisinde fazla miktardaki trigliserit pankreatik lipaz ile hidrolizi sonucunda yüksek konsantrasyonda serbest yağ asitleri ortaya çıkarır. Serbest yağ asitleri toksiktir ve asiner hücreleri ve kapiller endoteli yıkar. Aynı zamanda artmış şilomikron konsantrasyonu damarın viskozitesini arttırır, pankreastaki kan akımının bozulması pankreas içinde iskemi ve asidoza sebep olur. Asidozdaki yağ asitleri tripsinojeni aktifleştirir ve akut ödemi ve nekrotizan pankreatiti başlatır (16). Serum sodyum düzeyi düşük olan hastaların daha yüksek trigliserit düzeyi olması kliniği kötüleştiren tetikleyici unsurlardan biri olarak düşünülmüştür. Diğer unsurlar olarak çalışmamızda demografik veri olarak değinilen fakat ayrıntılı irdelenmemiş olan serum glukoz düzeyi yüksekliği (diabetes mellitus) ve alkol kullanımı olabilir.

Çalışmamızın bazı kısıtlılıkları mevcuttu. Bunlardan ilki çalışmanın retrospektif dizayn edilmiş olması, diğeri ise hasta sayısının kısıtlı olmasıydı. Çok merkezli ve hasta sayısının yüksek olduğu çalışmalar ile veriler daha değerli hale getirilebilir.

Sonuçlar

Sonuç olarak, hiponatremisi olan HTG-AP hastalarında daha önce pankreatitte tanımlanmış prognostik göstergeler (Ranson skoru, CRP-48.saat) anlamlı olarak daha yüksek saptandı. Bu nedenle HTG-AP tanısı ile başvuruda başlangıç serum sodyum düzeyi tedavi yönetimi, risk değerlendirmesi ve kötü prognoz açısından prognostik bir parametre olabilir.

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Investigation of the Profile and Results of Intoxication Cases Admitted to the Tertiary Level Intensive Care Unit

Üçüncü Düzey Yoğun Bakım Ünitesine Kabul Edilen İntoksikasyon Olgularının Profili ve Sonuçlarının İncelenmesi

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Abstract

Introduction : All over the world, many cases of accidental or suicidal poisoning apply to hospitals. Various factors affect the incidence of morbidity and mortality of acute poisoning.

Methods: We analyzed data from 126 patients admitted to ICU with acute poisoning. Data regarding demorgraphic data, type of poisoning, time of presentation, psychiatric disease history, reason for ICU admission, ICU course and outcome were obtained.

Results: 126 patients treated in the intensive care unit . Six (4.76%) of them died. 68 (54%) of the patients were female and 58 (46%) were male. The mean age of all cases was 34.32±15.25. SOFA score of all our patients was 2.33±1.079, APACHE II score was 10.03±5.28, Glasgow Coma Scale was 13.44±2.93. Acute poisoning was most common in the spring (27.8%) and summer (27.8%). 28 (22.2%) patients had a psychiatric disorder. Most common cause was antidepressants (13.49%), antipsychotics (11.9%) and benzodiazepines (10.31%). It was determined that 98 (77.8%) patients had suicidal intoxication.

Discussion and Conclusion : Analgesics and antidepressant-antipsychotic drugs are the most common causes of poisoning because they are easily accessible. A low Glascow Coma Scale at admission is associated with a poor prognosis.

Keywords: Poisoning, intoxication, organophosphate, toxicology, intensive care

Öz

Giriş : Tüm dünyada birçok kaza sonucu veya intihar amaçlı zehirlenme vakası hastanelere başvurmaktadır. Akut zehirlenmenin morbidite ve mortalite insidansını çeşitli faktörler etkilemektedir.

Yöntem ve gereç: Yoğun bakıma akut zehirlenme ile başvuran 126 hastanın verilerini analiz ettik. Demografik veriler, zehirlenme şekli, başvuru zamanı, psikiyatrik hastalık öyküsü, yoğun bakıma yatış nedeni, yoğun bakım seyri ve sonucuna ilişkin veriler elde edildi.

Bulgular: Yoğun bakımda 126 hasta zehirlenme nedeniyle tedavi yatırıldı. Bunlardan altısı (%4,76) öldü. Hastaların 68'i (%54) kadın, 58'i (%46) erkekti. Tüm olguların yaş ortalaması 34,32±15,25 idi. Tüm hastalarımızın SOFA skoru 2,33±1,079, APACHE II skoru 10,03±5,28, Glasgow Koma Skalası 13,44±2,93 idi. Akut zehirlenme en çok ilkbahar (%27,8) ve yaz aylarında (%27,8) görüldü. 28 (%22,2) hastada psikiyatrik bozukluk vardı. En sık zehirlenme nedeni antidepresanlar (%13,49), antipsikotikler (%11,9) ve benzodiazepinler (%10,31) idi. 98 (%77,8) hasta da suicid amaçlı intoksikasyon olduğu belirlendi.

Tartışma ve Sonuç : Analjezikler ve antidepresan-antipsikotik ilaçlar kolay ulaşılabilir oldukları için en sık zehirlenme nedenleridir. Başvuruda düşük bir Glaskow Koma Skalası, kötü prognoz ile ilişkilidir.

Anahtar Kelimeler: Zehirlenme, intoksikasyon, organofosfat, toksikoloji, yoğun bakım

Introduction

All over the world, many cases of accidental or suicidal poisoning apply to hospitals. Poisonings needs close follow-up treatment due to morbidity and mortality are admitted to intensive care units (ICU). Overall in-hospital mortality for poisoning patients is 0.2 – 1.1%. The death rate in poisonings, which represents approximately 3%-6% of all intensive care hospitalizations, is approximately four times that of cases treated in other in-hospital units.(1)

Poisoning can occur as a result of taking drugs or substances for suicidal purposes, using high doses of drugs, or adverse drug reactions. The general characteristics of patients with a diagnosis of poisoning do not depend only on socioeconomic, religious and cultural status. The clinical course is related to the agent exposed, dose, pre-existing comorbidities, time from exposure to a healthcare provider to presentation, and healthcare team experience. Mortality is lower in drug-induced poisonings. Mortality increases with pesticides taken for suicide. According to the World Health Organization, it is estimated that 300 thousand people die every year due to the intake of various poisonous substances. The most common cause of acute poisoning in developed countries is the abuse of commercially available drugs, the most common cause in developing countries is insecticides(2, 3).

Various factors affect the incidence of morbidity and mortality of acute poisoning. Timely recognition and appropriate management of critically poisoned patients is an important component. A systematic assessment allows early identification and hospitalization of high-risk and critically poisoned patients based on the clinical features of poisoning. While toxic substances and their health effects are numerous, specific, effective measures against the causative agent can be used to treat only a small minority of patients. The aim of this study is to reveal the reasons for admission to the intensive care unit of acute poisoning patients, the main factors affecting the course and outcomes of the patients, and the clinical approaches applied.

Materials and Method

The study includes patients who were treated in the 61-bed intensive care unit of our tertiary hospital between 01.06.2017- 31.10.2022. Data were collected retrospectively from medical records

Demographic data of the patients (gender, age), type of substance causing poisoning (medicinal drugs, pesticides, poisonous gas, methyl alcohol and others), psychiatric disease history, type of poisoning (accidental, suicide) and exposure to poisoning were collected. In addition, the patient's length of stay in the intensive care unit, mechanical ventilation requirements, neurological status at admission, Glasgow Coma Score (GCS) assessment, Sequential Organ Failure Assessment (SOFA) score, and Acute Physiology and Chronic Health Assessment II (APACHE II) score were recorded at admission to the ICU.

Data were collected by determining the clinical outcomes of the patients regarding discharge to their home, transfer to another service, need for renal replacement therapy, or death. Patients were admitted to the ICU according to the ICU admission policy for toxicology patients based on international recommendations. Patients were intubated to secure the airway or when otherwise indicated. Similarly, other medical practices and patterns of weaning from mechanical ventilation were according to standard ICU protocols.

Ethical approval was obtained for the study from the local ethics committee (16.11.2022 Decision no: 2022/129). This study was carried out in accordance with the Declaration of Helsinki Principles.

Statistical analysis was performed using Statistical Package for the social Sciences 20.0 (Statistical Package for the Social Sciences version 20, IBM Corp., Armonk, New York, IL, USA) software.Whether the variables fit the normal distribution or not was evaluated with the Kolmogorov - Smirnov test. Student -t test was used for the comparisons between groups of normally distributed continuous data. Parametric data with normal distribution were shown as mean ± standard deviation (SD). Values with $p < 0.05$ were considered statistically significant. categorical variables are presented as frequency and percentages

Results

A total of 5817 patients were admitted in intensive care units during the study period. 126 (2.16%) were hospitalized and treated in the intensive care unit due to acute intoxication. (4.76%) of 126 patients died. 68 (54%) of the patients were female and 58 (46%) were male. The mean age of all cases was 34.32±15.25 (min: 16 – max: 91), while the mean age of male patients was 35.81±15.9 years, and the mean age of female patients was 32.57±14.28 years. When we divided the ages according to the groups, it was determined that the patients under the age of 30 (n=55, 43.6%) years were admitted to the intensive care unit the most, followed by the 30-39 age group (n=35, 27.7%)(Table-1).

Table 1. Demographic and clinical characteristics of the patients

	Male n=68	Female n=58	Total n=126(%)	p	Non-survived n=6(%)
Age(mean)	35.81±15.9	32.57±14.28	34.32±15.25		48.0±10.01
• <29	26	29	55(43.7)		-
• 30-39	21	14	35(27.8)		2
• 40-49	8	5	13(10.3)		-
• 50-59	6	8	14(11.1)		4
• 60-69	4	1	5(4.0)		-
• 70>	4	-	4(3.2)		-
Intent					
• Suicide	47	51	98(77.7)		4
• Accident	21	7	28(22.3)		2
Psychiatric illness					
• Yes	14	14	28(22.2)		0
• No	54	44	98(77.8)		6
Route of exposure					
• Oral	62	53	105(83.3)		4
• İnhalation or dermal	6	5	11(16.7)		2
Season				0.591	
• Winter	22	11	33(26.2)		1
• Spring	11	12	23(18.3)		3
• Summer	17	18	35(27.8)		2
• Autumn	18	17	35(27.8)		1
Length of stay(days)	4.26±8.16	2.43±3.05	3,42±6,38	0.236	10.33±15.9
SOFA(mean)	2.57±1.25	2.04±0.73	2,33±1,079	<0.05	3.67±2.06
APACHE II(mean)	11.35±5.9	8.4±3.7	10,03±5,28	<0.05	18.33±9.13
GCS(mean)	13.02±3.24	13.94±2.4	13,44±2,93	0.07	9.83±4.2
Spesific treatment	9	3	12(9.52)		1
Invasive ventlilation	8	4	12(9.52)		6
Renal replacement therapy	6	4	10(7.93)		-

Abbreviations: SOFA, Sequential Organ Failure Assessment; APACHE II, Acute Physiology and Chronic Health Assessment II; GCS, Glasgow Coma Score

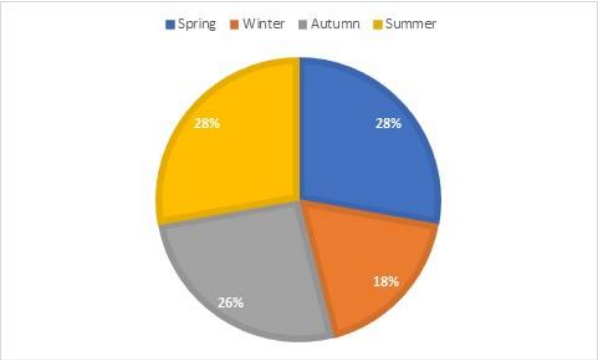

Figure 1 : Seasonal distribution of poisonings

When we look at the seasonal distribution of poisonings, it was seen that acute poisoning was most common in the spring (27.8%) and summer (27.8%) periods (Figure-1).

The mean length of hospital stay for all patients was 3.42±6.38 (min:1- max: 52), and the mean length of hospital stay for six patients who died was 10.33±15.9 (min:1 -max: 42)(p=0.31). The number of patients staying in intensive care for more than two days was 40. While the mean SOFA score of all our patients was 2.33±1.079 (min:1-max:7), the mean SOFA score of six patients who died was 3.67±2.06 (min:1-max:7) (p=0.15). The mean APACHE II score was calculated as 10.03±5.28(min:3-max:28) in the intensive care unit admission of the patients, the mean APACHE II score was 18.33±9.13(min:7-max:28) for the patients who died. Glasgow Coma Scale (GCS) of 126 patients was 13.44±2.93(min:3 – max:15) at the time of admission, GCS of patients who died was 9.83±4.26(min:5 – max:15)' and it was statistically significantly lower (p<0.05).

15(11.9%) of the patients needed intubation during hospitalization. While specific treatment was applied to the poisoned substance in 12 (9.52%) patients, symptomatic treatment was applied to the other 114 patients. Renal replacement therapy was applied to ten patients. 28 (22.2%) patients had a psychiatric disorder for which they had been treated before. Two of the patients who were admitted in the ICU due to intoxication were pregnant. It was determined that 98 (77.8%) of the acute poisoning cases were exposed to a toxic substance as a result of suicide and 28 (22.2%) of them were accidental.

89% of the patients were drug-induced poisoning. 34 (26.8%) patients were hospitalized due to multiple drug poisoning. When the toxic substances causing acute toxication were examined, it was seen that the most common antidepressants (13.49%), antipsychotics (11.9%) and benzodiazepines (10.31%) were respectively. Other commonly used drugs are shown in Table 2. Nine patients used pregabalin or drugs together with ethyl alcohol. Eight of our patients had organophosphate intoxication with a high mortality rate and two patients died.

Five of the patients who died were male and one was female. None of them had a previously diagnosed psychiatric condition and none of them needed renal replacement therapy. Only one patient received specific treatment for the poisoned substance. Two patients died due to organophosphate poisoning, two patients due to methyl alcohol poisoning, and one patient died due to carbon monoxide intoxication. The cause of poisoning in one patient was unknown. It was only known that he was addicted to drugs. All data of deceased patients are summarized in Table-2.

Table-2: The most common poisoning drugs and other substances

	n	**%**
Antidepressant	17	13,49206
Antipsychotic	15	11,90476
Benzodiazepine	13	10,31746
Paracetamol	12	9,52381
Nsaiid	12	9,52381
Antiepileptic	11	8,730159
Cardiac Drug	10	7,936508
Ethanol With Other Drugs	9	7,142857
Organophosphate	8	6,349206
Drugs	6	4,761905
Carbon Monoxide	5	3,968254
Pesticide	5	3,968254
Pregabalin	5	3,968254
Drug Name Unknown	5	3,968254
Methyl Alcohol	4	3,174603
Rat Poison	2	1,587302
Mushroom	2	1,587302

Discussion

The proportion of poisoning patients admitted to intensive care units shows significant local differences between regions(4). Acute poisoning may occur due to drug-related or non-drug-related causes. While drug-related poisonings are more common in Turkey, alcohol and drug use are the most common non-drug poisonings in Western countries(5).

Poisonings are most common in patients under 30 years of age in the literature (6, 7). In our study, poisoning cases were seen most frequently in the group below the age of 30 (43.6%). 68 (54%) of the patients were female. Tüfekçi et al(7). found the rate of female patients in posioning cases to be %73, Satar et al(8) % 65.4 and Göksu et al(9) %64.3. In a study, they had a similar number of female patients with our study (53%)(10). In our study, the rate of female patients was higher, albeit slightly.

77.8% of poisoning cases were for suicidal purposes. In studies conducted in different countries and cities of Turkey in the literature, cases of suicidal poisoning were found to be high at a rate of 78.3-94%, which is consistent with our study.(3, 6, 11-13). When we look at the seasonal distribution of poisoning cases, the first most common incidence varies, but it is most frequently seen in the spring and summer seasons. Mete at al(14). and Yaylacı et al.(13) found that it is most commonly seen in the summer months after the spring. On the other hand, Aydın et al(15) and Arıcı et al(16) found that it is most common in summer, then spring. In our study, it was observed that acute intoxication was most common in the spring (27.8%) and summer (27.8%) periods, as compared to the literature. The mean number of hospitalization days for all patients was 3.42±6.38 days. This period was found to be 1.55-4.6 days in studies conducted in different regions of our country. (5, 17). In a study conducted in India it was 3.9 days(11). In our study, drug-related poisoning occurred in 89% of the patients. 26.8% of the patients had taken more than one drug. In different studies conducted in Turkey, the rate of poisoning with more than one drug was found to be 28.6%-48.3%.(13, 18). The reason for the low percentage of those who used more than one drug compared to other studies in the literature may be due to the unreliability of the anamnesis obtained from the cases as well as regional and sociocultural differences.

In some studies on acute intoxication, antidepressants and psychoactive drugs are the most common causes of poisoning, while in some studies analgesics and benzodiazepines are the most common causes of poisoning(5, 17). When all our poisoning cases were evaluated, it was observed that the most common poisoning was with antidepressants, antipsychotics and benzodiazepines . These drugs were followed by paracetamol and NSAIDs . In studies conducted in different centers in Turkey, in accordance with our study, analgesic-anti-inflammatory and antidepressant-antipsychotic drugs were ranked first in drug poisoning in poisoning cases(19, 20). Analgesic-anti-inflammatory agents and antidepressants are more easily accessible as a result of over-the-counter and widespread use. Moreover; The fact that patients use antipsychotic or antidepressant drugs due to their psychiatric problems makes it possible to use these drugs for suicide attempt. In the studies, it was determined that 9.2-51% of the patients had a previous psychiatric diagnosis(13, 17, 19). In our data, 28 (22.2%) patients had psychiatric disorders for which they had been treated before.

While the Glasgow coma scale (GCS) was 13.44 on average in all our patients, the GCS of the patients who died was 9.83. In the study of Liisanantti et al(10), the mean GCS was 9.7. Forsberg et al(21). reported that approximately 30% of hospitalized poisonings had significant CNS depression at presentation. The death rate in poisoning cases presenting with deeper coma (GCS score 3 – 6) is approximately seven times higher than the general hospital mortality rate from acute poisoning(21).

In a study GCS <8 was found to be associated with morbidity and mortality(22) Another study argued that tracheal intubation criteria are available for trauma when GCS is ≤8, but it is not a criterion for patients receiving drug overdose (23).

Liisanantti et al(10) found the mean APACHE II score of the patients to be 14.4, APACHE II score of the non-survived patients to be 27.2, Mc Mahon et al(24) in all patients 14 and 34 in non-survived patients, Aydın et al(15) as 6 and 24, respectively. APACHE II score was 10.03 in all patients and 18.3 in patients who died. Our results were higher in patients who died, consistent with the literature.

Fifteen (11.9%) of the patients needed intubation during hospitalization. Intubation rate has been reported between 3.3-25.9% in different studies in Turkey (9, 13, 15). Nagashima et al (23) revealed that the use of anticonvulsants and antipsychotics was associated with an increased risk of tracheal intubation in patients taking drug overdose.

Koylu et al(6) found the need for renal replacement therapy as 2.1% in their study on 623 patients. This rate was found to differ between regions such as 15% in the study conducted in India, 14% in Ireland, and 2% in Finland.(3, 10, 24). Liisinantti et al (10). reported that kidney failure were associated with maintenance hospitalization and mortality. In our study, renal replacement therapy was applied to ten patients (7.93%) during their stay in the intensive care unit.

Different mortality rates have been reported for acute poisoning cases in our country and in the world. While the mortality rate is lower in developed countries, mortality in developing countries such as India varies between 15-30%.(11). Mortality was around 9%, while rates ranging from 0.92-4.9% were reported in Turkey. (17, 25). Our mortality rate was 4.76%. In the studies, the level of intensive care and the clinical condition of the patients are also effective on mortality. Our intensive care unit serves as the upper center following the patients in the most critical condition in the region as the 3rd level intensive care unit.

Conclusion

Intoxication cases are one of the important reasons for intensive care hospitalization. It shows some differences between regional and hospitals. Analgesics and antidepressant-antipsychotic drugs are the most common causes because they are easily accessible and patients with a history of psychiatric illness are more prone to intoxication. A low GCS at admission is associated with a poor prognosis.

The main limitations of the study were that it was a single-center, retrospective study, the drug doses were not clearly determined, and we could not reach the results of the psychiatric evaluation.

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Akut Pankreatit Geçirmiş Hastaların Biyokimyasal Parametreleri İle Abdominal Bilgisayarlı Tomografi Sonuçlarının Bir Yıllık Takip Sonrası Komplikasyon Gelişimi Açısından Değerlendirilmesi

Evaluation of Biochemical Parameters and Abdominal Computerized Tomography Results of Patients with Acute Pancreatitis in terms of Complication Development After One-Year Follow-up

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Öz

Giriş: Akut pankreatit geçirdiği abdominal bilgisayarlı tomografi (BT) ile belirlenen hastaların bir yıl sonrasındaki biyokimyasal parametrelerini, vücut ölçümlerini incelemek, komplikasyon gelişimini değerlendirmek; hepatosteatoz ve pankreatik steatoz tablosunun komplikasyon gelişimine olan etkisini incelemek bu çalışmada amaçlanmıştır.

Gereç ve Yöntem: Kesitsel, retrospektif olarak planlanan çalışmamıza İç Hastalıkları kliniğine 01/01/2016-01/01/2017 tarihleri arasında başvuran abdominal BT çekilen 18-94 yaş aralığında toplamda 182 hasta dahil edilmiştir.

Bulgular: Akut pankreatit geçirmiş hastaların akut pankreatit geçirmemiş hastalara göre aspartat aminotransferaz (AST), alanin aminotransferaz (ALT), gama glutamil transferaz (GGT), alkalen fosfataz (ALP), laktat dehidrogenaz (LDH), amilaz, lipaz, glukoz, C-reaktif protein (CRP), beyaz kan hücresi (WBC), HbA1c ve sedimantasyon değerlerinin istatiksel olarak anlamlı şekilde yüksek olduğu belirlendi. Bir yıl sonraki veriler incelendiğinde akut pankreatit geçirmiş hastalarda HbA1c ve trigliserid değerlerinin akut pankreatit geçirmemiş hastalara göre daha yüksek olduğu izlendi. Tekrardan akut pankreatit atağı geçirme oranının akut pankreatit geçirmiş hastalarda istatistiksel olarak anlamlı şekilde yüksek olduğu belirlendi.

Sonuç: Akut pankreatit mevcut olan kötü beslenme alışkanlıkları, alkol kullanımı, genetik sebepler ve çevre koşulları gibi nedenlerle oluşan hipertrigliseridemi, obezite, kan şekeri yüksekliği nedeniyle toplumda oldukça sık izlenmekte ve izlenmeye devam edeceği düşünülmektedir. Bu koşullar sonucunda oluşan hepatosteatoz ve pankreatik steatoz zaman geçtikçe daha çok gündemde olacaktır. Bu sebeple hepatosteatoz ve pankreatik steatoz konusunda hem patofizyoloji hem tedavi açısından daha çok araştırma yapılması gerekmektedir. Bizim çalışmamız da hepatosteatoz ve pankreatik steatoz konusunda eksikliklere katkı sağlayacağı ve diğer çalışmalara yardımcı olacağı düşünülmüştür.

Anahtar Kelimeler: Akut pankreatit, Hepatosteatoz, Pankreatik steatoz

Abstract

Introduction: In this study, it was aimed to examine the biochemical parameters, body measurements, complication development, and the effect of hepatosteatosis and pancreatic steatosis one year after patients diagnosed with acute pancreatitis through a computerized scan (CT).

Materials and Method: A total of 182 patients between the ages of 18-94 who applied to the Internal Medicine clinic between 01/01/2016 and 01/01/2017 and underwent abdominal CT were included in our cross-sectional and retrospective study.

Results: Compared to patients without acute pancreatitis, AST, ALT, GGT, ALP, LDH, amylase, lipase, glucose, CRP, WBC, HbA1c and sedimentation values were found to be statistically significantly higher in patients with acute pancreatitis. When the data after one year were analyzed, it was observed that HbA1c and triglyceride values were higher in patients who had been diagnosed with acute pancreatitis than in patients who had not been diagnosed with acute pancreatitis. In addition, it was determined that the acute pancreatitis relapse rate was statistically significantly higher in patients who had experienced acute pancreatitis earlier.

Conclusion: Acute pancreatitis is observed quite frequently and will continue to be observed in society due to hypertriglyceridemia, obesity, and high blood sugar, which are caused by poor eating habits, alcohol use, genetic reasons, and environmental conditions. Hepatosteatosis and pancreatic steatosis resulting from these conditions will be on the agenda more and more as time goes on. Therefore, more research is needed on hepatosteatosis and pancreatic steatosis in terms of both pathophysiology and treatment. It is thought that our study will also contribute to the deficiencies in this regard.

Keywords: Acute pancreatitis, Hepatosteatosis, Pancreatic steatosis

Giriş

Akut pankreatit, pankreas bezinin inflamasyonu ile karakterize bir hastalıktır. Hastalığın klinik seyri hafiften şiddetli tabloya kadar geniş bir aralıktadır. Bu sebeple prognoz oldukça değişken izlenmektedir (1). Safra taşları ve alkol en sık sebepler olup; hipertrigliseridemi, hiperkalsemi, infeksiyon, travma ve otoimmun hastalıklar da etiyolojide yer almaktadır (2).

Özellikle obezite ile ilişkili olan yağ dokusu infiltrasyonu, karaciğer, pankreas, kalp, böbrek gibi birçok organda izlenebilmektedir. Yağ infiltrasyonu oksidatif stres oluşmasına neden olup, sonrasında organ disfonksiyonuna sebep olmaktadır. Bu infiltrasyonun klinik olarak en iyi bilinen örneği karaciğerde meydana gelmektedir ve hepatosteatoz olarak isimlendirilmektedir (3). Klinik olarak önemi net olarak ortaya konulmasa da son yıllarda pankreas dokusunda yağ infiltrasyonu konusu dikkat çekmektedir.

Pankreas dokusunda yağ birikimi, asiner hücrelerin ölümü sonrasında yerine adiposit hücrelerin geçmesiyle gerçekleşir (4). Pankreatik steatoz oluşumunda ön planda obezite ve insülin direnci dikkat çekmektedir. Tanısında kullanılabilecek spesifik bir biyokimyasal belirteç bulunmamakta olup, görüntüleme yöntemleri sıklıkla kullanılmaktadır. Kesin tanısı biyopsi sonucuyla histopatolojik yöntemlerle konulmaktadır (5).

Çalışmamızda, abdominal bilgisayarlı tomografi (BT) sonuçları ile akut pankreatit geçirdiği belirlenen hastaların bir yıl sonrasındaki biyokimyasal parametrelerini, vücut ölçümlerini incelemek, komplikasyon gelişimini değerlendirmek; hepatosteatoz ve pankreatik steatoz tablosunun komplikasyon gelişimine olan etkisini incelemek amaçlanmıştır.

Gereç Ve Yöntem

Araştırmamız için S.B.Ü. Haseki Eğitim ve Araştırma Hastanesi Klinik Araştırmalar Etik Kurulu'ndan 23.12.2020 tarihinde 2020-237 numaralı etik kurul onayı alındı. Bu çalışma kesitsel, retrospektif bir çalışmadır. İç Hastalıkları kliniğine 01/01/2016-01/01/2017 tarihleri arasında başvuran abdominal BT çekilen 18-94 yaş aralığında toplamda 192 hasta çalışmamıza dahil edildi. 84 akut pankreatit geçiren hasta karşılığında, aynı dönemde herhangi bir sebeple abdominal BT çekilen 108 kontrol grubu hastası belirlendi. Karın ağrısı, pankreas enzim yüksekliği ve görüntüleme yöntemlerinde akut pankreatit lehine bulgu olması kriterlerinden en az ikisini bulunduran hastalar akut pankreatit geçiren hasta grubuna dahil edildi. Akut pankreatit geçirmeyen hasta grubuna ise kriterlerden bir veya daha azını bulunduranlar dahil edildi. Karaciğer sirozu, son dönem böbrek yetmezliği, sepsis, akut batın tablosu, nöropsikiyatrik hastalığı olan hastalar, gebe ve emzirme dönemindeki kadınlar çalışmamıza dahil edilmedi. Öncesinde akut pankreatit geçirmiş hastalar da çalışmamıza alınmadı. Hastalarda biyokimyasal veri olarak aspartat aminotransferaz (AST), alanin aminotransferaz (ALT), gama glutamil transferaz (GGT), alkalen fosfataz (ALP), laktat dehidrogenaz (LDH), amilaz, lipaz, glukoz, HbA1c, C-reaktif protein (CRP), üre, kreatinin, total protein, albumin, total kolestrol, trigliserid, yüksek yoğunluklu lipoprotein (HDL), düşük yoğunluklu lipoprotein (LDL), beyaz kan hücresi (WBC), trombosit sayısı (Plt), hemoglobin sayısı (Hgb), sedimantasyon, kalsiyum (Ca), potasyum (K) ve sodyum (Na) değerleri incelendi.

Pankreatik steatoz ve hepatosteatoz değerlendirilmesinde abdominal BT verileri kullanıldı. Abdominal BT çekimlerinde karaciğer, dalak ve pankreasın yağlı infiltrasyonu (steatosis) HU (Hounsfield Unit) ile ölçülen atenüasyon değeri ile belirlendi. Karaciğer-dalak atenüasyon farkının 10 HU ve daha fazla olması durumunda hepatosteatoz var olarak kabul edildi. Pankreatik steatoz varlığı ise dalak referans alınarak pankreas-dalak atenüasyon farkının negatif HU değerlerinde olmasına göre belirlendi. Hepatosteatoz tanısı koymak için bir cut-off değeri çalışmamızda kontrol grubunun pankreas-dalak atenüasyon farkı HU medyan değerine göre hesaplandı (Medyan:-7.00 HU). Pankreatik steatoz olarak <–7 HU kabul edildi.

Bir yıl sonrasında hastaların biyokimyasal verileri hastane bilgi sisteminden alınıp tekrardan değerlendirildi.

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Biyokimyasal verilere ek olarak hastaların bel çevresi ve vücut kitle indeksi (VKİ) de değerlendirmeye alındı. Kardiyovasküler olay, mortalite, malignite, tip 2 diyabet ve tekrardan akut pankreatit gelişimi komplikasyon olarak değerlendirilip, akut pankreatit geçirmiş ve geçirmemiş gruplar arasında karşılaştırıldı. Ek olarak pankreatik steatoz ve hepatosteatoz varlığına göre hastalar alt gruplara ayrılarak komplikasyon gelişimi açısından değerlendirildi.

İstatistiksel Analiz

İstatistiksel analiz için SPSS 16.0 for Windows programı kullanıldı. Tanımlayıcı istatistik olarak sürekli değişkenler ortalama ve standart sapma olarak, kategorik değişkenler ise yüzde olarak ifade edildi. Dağılımları Kolmogorow-Smirnow testi kullanılarak saptandı. İki grubun karşılaştırılmasında; normal dağılımdaki sayısal veriler Student T testi ile değerlendirildi; dağılımı normal olmayan sayısal verilerin karşılaştırılmasında ise Mann Withney U testi kullanıldı. İstatistiksel olarak p<0,05 veya %95 güven aralığı anlamlı olarak kabul edildi.

Bulgular

Bu çalışma 113'ü erkek, 79'u kadın olmak üzere toplamda 192 kişiyle gerçekleştirildi. Erkek hastaların yaş ortalaması 56,35±15,95, kadın hastaların yaş ortalaması ise 57,94± 17,40 olarak izlendi. Hastaların başlangıçtaki genel özellikleri ve biyokimyasal parametreleri Tablo 1'de gösterildi. Akut pankreatit geçirmiş hastaların akut pankreatit geçirmemiş hastalara göre AST, ALT, GGT, ALP, LDH, amilaz, lipaz, glukoz, CRP, WBC, HbA1c ve sedimantasyon değerlerinin istatiksel olarak anlamlı şekilde yüksek olduğu belirlendi (p <0,001; p 0,013; p 0,006).

Tablo 1: Hastaların başlangıçtaki genel özellikleri ve biyokimyasal parametreleri

	AKUT PANKREATİT GEÇİRMEMİŞ	AKUT PANKREATİT GEÇİRMİŞ	P
CİNSİYET Erkek/K	59/49	54/30	0,187
YAŞ	61,04± 14,38	51,81±17,73	**<0,001**
AST	28,24±3,10	94,95±16,74	**<0,001**
ALT	28,24±4,34	82,15±13,77	**<0,001**
GGT	44,58±11,20	152,96±25,08	**<0,001**
ALP	88,22±3,68	115,47±7,23	**<0,001**
LDH	185,59±3,58	285,08±18,77	**<0,001**
AMİLAZ	80,74±3,98	720,02±82,81	**<0,001**
LİPAZ	33,50±4,24	1686,85±197,45	**<0,001**
GLUKOZ	109,87±39,69	152,96±75,74	**<0,001**
HbA1c	6,09±1,01	6,67±1,87	**0,013**
CRP	13,18±2,35	43,52±6,77	**<0,001**
ÜRE	37,22±20,98	36,87±17,69	**0,012**
KREATİNİN	0,94±0,77	1,96±0,94	0,228
TOTAL PROTEİN	7,33±0,40	7,14±0,69	**0,015**
ALBUMİN	4,22±0,38	4,14±0,06	0,276
KOLESTROL	198,58±46,18	183,03±98,96	0,200
TRİGLİSERİD	151,68±75,39	245,40±433,88	0,063
HDL	46,60±12,39	40,61±23,79	**0,027**
WBC	6203,62±899,79	13559,29±666,37	**<0,001**
Plt	247333,33±73127,21	256285,71±80583,79	0,422
Hgb	13,52±1,83	13,74±2,22	0,456
SEDİMANTASYON	29,96±25,31	41,94±27,77	**0,006**
Ca	9,45±0,61	9,31±0,60	0,109
Na	140,41±2,46	136,08±3,77	**<0,001**
K	4,53±0,42	4,19±0,512	**<0,001**

AST:Aspartat aminotransferaz ALT:Alanin aminotransferaz GGT:Gama glutamil transferaz ALP:Alkalen fosfataz LDH:Laktat dehidrogenaz CRP:C-reaktif protein HDL:Yüksek yoğunluklu lipoprotein WBC:Beyaz kan hücresi Plt:Trombosit sayısı Hgb:Hemoglobin sayısı Ca:Kalsiyum Na:Sodyum K:Potasyum

Akut Pankreatit Geçirmiş Hastaların Biyokimyasal Parametreleri İle Abdominal Bilgisayarlı Tomografi Sonuçlarının Bir Yıllık Takip Sonrası Komplikasyon Gelişimi Açısından Değerlendirilmesi

Hastaların bir yıl sonraki biyokimyasal verileri ve vücut ölçümlerinin sonuçları Tablo 2'de gösterildi. Akut pankreatit geçirmiş hastalarda HgA1c (6,98±1,56/5,95±0,81) ve trigliserid (222,38±35,74/139,66±64,05) değerlerinin istatistiksel olarak anlamlı şekilde yüksek olduğu görüldü (p <0,001; p 0,003). CRP (15,04±5,31/7,23±2,24), sedimantasyon (26,10±17,76/19,00±16,19), WBC (9,33±5,14/7,45±2,04) değerlerinin ve bel çevresi kalınlığının da (108,33±9,07/102,52±16,56) akut pankreatit geçirmiş hastalarda akut pankreatit geçirmemiş hastalara göre yüksek olduğu belirlendi ancak istatistiksel olarak anlamlı fark bulunamadı (p 0,180; p 0,457; p 0,120; p 0,396). HDL değerinin ise akut pankreatit geçirmiş hastalarda akut pankreatit geçirmemiş hastalara göre düşük olduğu (43,29±13,19/48,83±13,09) belirlendi ancak istatistiksel olarak anlamlı fark bulunamadı (0,873).

Tablo 2: Hastaların bir yıl sonraki biyokimyasal verilerinin ve vücut ölçümlerinin sonuçları

	AKUT PANKREATİT GEÇİRMEMİŞ	AKUT PANKREATİT GEÇİRMİŞ	P
GLUKOZ	109,32±39,45	109,96±40,09	0,451
HbA1c	5,95±0,81	6,98±1,56	**<0,001**
TOTAL KOLESTROL	207,16±49,65	192,63±47,74	0,643
HDL	48,83±13,09	43,29±13,19	0,873
LDL	129,03±41,37	113,94±39,07	0,356
TRİGLİSERİD	139,66±64,05	222,38±35,74	**0,003**
CRP	7,23±2,24	15,04±5,31	0,180
SEDİMANTASYON	19,00±16,19	26,10±17,76	0,457
Hgb	13,74±1,71	13,00±1,91	0,525
WBC	7,45±2,04	9,33±5,14	0,120
Plt	243,98±70,56	244,42±55,86	0,810
VKİ	30,55±12,62	27,65±1,27	0,167
BEL ÇEVRESİ	102,52±16,56	108,33±9,07	0,396

HDL:Yüksek yoğunluklu lipoprotein LDL:Düşük yoğunluklu lipoprotein CRP:C-reaktif protein Hgb:Hemoglobin sayısı WBC:Beyaz kan hücresi Plt:Trombosit sayısı VKİ:Vücut kitle indeksi

Evaluation of Biochemical Parameters and Abdominal Computerized Tomography Results of Patients with Acute Pancreatitis in terms of Complication Development After One-Year Follow-up

Komplikasyon gelişiminin akut pankreatit geçirmiş ve geçirmemiş hastalarda karşılaştırılması Tablo 3'de gösterildi. Tekrardan akut pankreatit atağı geçirme oranının akut pankreatit geçirmiş hastalarda istatistiksel olarak anlamlı şekilde yüksek olduğu (%5/%0) belirlendi (p 0,015). Mortalite (%13/%6) ve kardiyovasküler hastalık gelişim (%16/%14) oranlarının da akut pankreatit geçirmiş hastalarda akut pankreatit geçirmemiş hastalara göre yüksek olduğu belirlendi ancak istatistiksel olarak anlamlı fark bulunamadı (p 0,139; p 0,842).

Tablo 3: Komplikasyon gelişiminin hasta grupları arasında karşılaştırılması

	AKUT PANKREATİT GEÇİRMİŞ	AKUT PANKREATİT GEÇİRMEMİŞ	P
MORTALİTE	11 (%13)	7 (%6)	0,139
KARDİYOVASKÜLER HASTALIK	14 (%16)	16 (%14)	0,842
MALİGNİTE	6 (%7)	13 (%12)	0,333
AKUT PANKREATİT	5 (%5)	0 (%0)	**0,015**

Abdominal BT sonuçlarına göre 22 bireyde hepatosteatoz saptanmış olup, geri kalan 170'inde hepatosteatoz mevcut değildi. Hepatosteatoz varlığına göre komplikasyon gelişiminin karşılaştırılması Tablo 4'de verildi. Akut pankreatit (%9/%1.7) ve kardiyovasküler hastalık (%18/%15) gelişim oranlarının hepatosteatoz saptanan hastalarda saptanmayan hastalara göre yüksek olduğu belirlendi ancak istatistiksel olarak anlamlı fark bulunamadı (p 0,101; p 0,755). Hepatosteatoz saptanan hastalar ile saptanmayan hastalar arasında tip 2 diyabet gelişimi, mortalite ve malignite gelişimi açısından istatistiksel olarak anlamlı farklar saptanmadı (p 0,600; p 0,699; p 0,703).

Tablo 4: Hepatosteatoz varlığına göre komplikasyon gelişiminin incelenmesi

		HEPATOSTEATOZ		P
		-	+	
TİP 2 DİYABET GELİŞİMİ	Yok	162	22	
	Var	8	0	0,600
AKUT PANKREATİT	Yok	167	20	
	Var	3	2	0,101
MORTALİTE	Yok	153	21	
	Var	17	1	0,699
KARDİYOVASKÜLER HASTALIK	Yok	144	18	
	Var	26	4	0,755
MALİGNİTE	Yok	152	21	
	Var	18	1	0,703

Abdominal BT sonuçları incelendiğinde toplamda 110 kişide pankreatik steatoz saptandı. Pankreatik steatoz varlığına göre komplikasyon gelişiminin karşılaştırılması Tablo 5'de verildi. Pankreatik steatoz saptanan hastalar ile saptanmayan hastalar arasında tip 2 diyabet gelişimi, akut pankreatit gelişimi, mortalite, kardiyovasküler hastalık ve malignite gelişimleri açısından istatistiksel olarak anlamlı farklar saptanmadı (p 0,726; p 0,636; p 0,533; p 0,549; p 0,578).

Tablo 5: Pankreatik steatoz varlığına göre komplikasyon gelişiminin incelenmesi

		PANKREATİK STEATOZ		P
		-	+	
TİP 2 DİYABET GELİŞİMİ	Yok	78	106	0,726
	Var	4	4	
AKUT PANKREATİT	Yok	80	107	0,636
	Var	2	3	
MORTALİTE	Yok	74	100	0,533
	Var	8	10	
KARDİYOVASKÜLER HASTALIK	Yok	71	91	0,549
	Var	11	19	
MALİGNİTE	Yok	74	99	0,578
	Var	8	11	

Tartışma

Akut pankreatit toplumda oldukça fazla görülmektedir. Etiyolojide safra taşları ve alkol sık izlenmekle birlikte; hiperkalsemi, infeksiyon ve hipertrigliseridemi de yer almaktadır. Pankreas bezinin inflamasyonu ile karakterize olan akut pankreatit tablosu klinik olarak hafif belirtiler verebileceği gibi şiddetli klinik tablolara da sebep olabilmektedir. Obezite toplumun her kesiminde oldukça sık izlenmektedir ve global epidemi olarak kabul edilmektedir. Her yıl obezite ve komplikasyonlarına bağlı olarak 3.5 milyon kişinin öldüğü düşünülmektedir. Obezite ve metabolik sendrom yağlanma için risk faktörüdür (6,7). Hepatosteatoz ve pankreatik steatoz yağ dokusu infiltrasyonunun karakteristik örnekleridir.

Diyabet, obezite ve metabolik sendrom inflamasyonu arttırıp, akut pankreatit için risk faktörü oluşturabilmektedir. Yapılan büyük retrospektif çalışmalarda tip 2 diyabet özellikle genç yaşlarda akut pankreatit riskini arttırmaktadır (8). Bizim çalışmamızda da benzer şekilde akut pankreatit geçiren grupta HgA1c (6,67±1,87/6,09±1,01) ve glukoz değerlerinin (152,96±75,74/109,87±39,69) akut pankreatit geçirmemiş gruba göre istatistiksel olarak anlamlı şekilde yüksek olduğu saptanmıştır. Toplumda diyabet prevalansı ve insidansının yüksek olması nedeniyle de akut pankreatit tablosunun daha sık izlenebileceği düşünülebilir. Akut pankreatit sonrası diyabet gelişebilmektedir fakat mekanizması tam olarak bilinmemektedir. Bazı çalışmalarda akut pankreatit geçirildikten sonraki bir yıl içinde %15 oranında diyabet gelişebildiği izlenmiştir (9).

Hipertrigliseridemi akut pankreatit geçirildikten sonra önlem alınmazsa devam edebilmekte ve tekrarlayan pankreatit ataklarına yol açabilmektedir. Hipertrigliseridemi akut pankreatit atağının şiddetini arttırabilmekte ve komplikasyonların daha sık izlenmesine neden olabilmektedir. Akut dönem geçtikten sonra yaşam tarzı değişikliği ve ilaç tedavisiyle gerekli önlemler alınmalıdır (10). Bizim çalışmamızda da literatüre benzer şekilde akut pankreatit geçiren hastaların bir yıl sonraki trigliserid değerlerinin akut pankreatit geçirmemiş hastalara göre istatistiksel olarak anlamlı şekilde yüksek olduğu (222,38±35,74/139,66±64,05) saptanmıştır. Bel çevresi oranı yüksekliği ile akut pankreatit gelişim riskinin arttığı bilinmektedir (11). Bizim çalışmamızda da akut pankreatit geçirmiş hastaların bir yıl sonraki bel çevresi kalınlığının akut pankreatit geçirmemiş hastalara göre yüksek olduğu (108,33±9,07/102,52±16,56) belirlenmiş ancak istatistiksel olarak anlamlı fark bulunamamıştır.

Bazı vakalarda akut pankreatit rekürren olarak izlenmektedir. Etiyolojisi idiopatik olan vakalarda tekrardan akut pankreatit geçirme sıklığı artmıştır. Genç yaşlarda izlenen akut pankreatit atağının sonradan tekrardan izlenme oranı yüksek saptanmıştır. Özellikle bu hastalarda altta yatan genetik sebeplerin iyi araştırılması gerekmektedir (12,13). Bizim çalışmamızda akut pankreatit geçirmiş hastaların bir yıl içinde tekrardan atak geçirme oranı %5 olarak saptanmış olup, bu oranın akut pankreatit geçirmemiş hastalara göre istatistiksel olarak anlamlı şekilde yüksek olduğu izlenmiştir. Bazı çalışmalarda bu oran %20-25 olarak görülmüştür (14). Çalışmamızda akut pankreatit geçirmiş hastaların bir yıl içindeki mortalite oranının akut pankreatit geçirmemiş hastalara göre yüksek olduğu (%13/%6) belirlenmiş ancak istatistiksel olarak anlamlı fark bulunamamıştır. Literatürde etiyolojide alkol olan akut pankreatit vakalarında mortalite yüksek izlenmiş olup, pankreas kanseri riskinin arttığı vurgulanmıştır (15).

Retrospektif olarak yapılan bir çalışmada tip 2 diyabet gelişiminde pankreatik steatoz varlığı risk faktörü olarak gösterilmiştir (16). Yapılan bir çalışmada obez farelerde pankreatik steatoz varlığının tip 2 diyabet gelişim riskini arttırdığı saptanmıştır (17). Bizim çalışmamızda ise pankreatik steatoz saptanan hastalar ile saptanmayan hastalar arasında tip 2 diyabet gelişimi açısından istatistiksel olarak anlamlı fark saptanmamıştır. Yapılan bir değerlendirme yazısında pankreatik steatoz ve tip 2 diyabet gelişimi arasındaki ilişkinin insanlar üstünde yapılan çalışma verileri incelendiğinde yetersiz olduğu belirtilmiştir. Uzun vadeli sonuçların yetersiz olduğu bildirilmiş ve yeni çalışmaların pankreatik steatozun dinamik bir şekilde incelenmesi gerektiğini bildirmiştir (18).

Obezite oranı dünya çapında gittikçe artmaktadır. Buna bağlı olarak tanı konması zor da olsa pankreatik steatoz saptanan hasta sayısı da artmaktadır. Pankreatik steatoz prevalansının %16-35 arasında olduğu düşünülmektedir (19,20). Literatürde pankreatik steatoz miktarında artış oldukça pankreas kanseri görülme oranının arttığı ve pankreatik steatozun pankreas kanseri mevcut olan kişilerde prognozu kötü etkilediği bildirilmiştir (21-23).

Çalışmamızın kısıtlılıkları incelendiğinde hastaların ilk başvuru anındaki antropometrik verilerine ulaşamamış olmamız, bir yıl sonraki antropometrik ölçümlere göre kıyaslama yapma imkanımızı kısıtlamıştır. Akut pankreatit geçiren hastaların etiyolojilerine yönelik verilerin, alkol ve sigara kullanım öykülerinin saptanamaması bazı değerlendirmelerde yetersizlikler oluşturmuştur. Hepatosteatozu olan hastaların alkol kullanımı bilinmediği için etiyolojiye yönelik bilgiler kısıtlıdır. Malignite gelişimi saptanan hastalarda primer odağın saptanamaması kısıtlılık yaratmıştır. Akut pankreatit geçiren hastalarda pankreatik steatozun saptanmasına yönelik belirsizlikler olduğu için bu konudaki verilerin yorumlanması problem oluşturmuştur.

Sonuç

Akut pankreatit toplumda oldukça sık izlenmekte ve gelecek yıllarda da bu tablonun devam edeceği düşünülmektedir. Bu düşüncemizin temelinde toplumda mevcut olan kötü beslenme alışkanlıkları, alkol kullanımı, genetik sebepler ve çevre koşulları gibi nedenlerle oluşan hipertrigliseridemi, obezite, kan şekeri yüksekliği yer almaktadır. Bu koşullar sonucunda oluşan hepatosteatoz ve pankreatik steatoz konusunda hem patofizyolojisi hem tedavi açısından daha çok araştırma yapılması gerekmektedir. Bu konuda literatür çalışmalarının yeni olması nedeni ile yetersiz sayıda çalışma olduğu düşünülmektedir. Bizim çalışmamız da hepatosteatoz ve pankreatik steatoz konusunda eksikliklere katkı sağlayacağı ve diğer çalışmalara yardımcı olacağı düşünülmüştür.

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OLGU SUNUMU /CASE REPORT
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Spontaneous Retroperitoneal Hemorrhage in A Patient Under Oral Anticoagulation Treatment: Case Report

Oral Antikoagulan Alan Bir Hastada Spontan Retroperitoneal Hemoraji: Olgu Sunumu

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Öz

Nadir ve ölümcül bir durum olan retroperitoneal hemoraji etiyolojik açıdan temel olarak travmatik ve non-travmatik olarak sınıflanmaktadır. Non-travmatik kanama iatrojenik bir yaralanmanın (Örn: femoral arter kanülasyonu) sonucu ya da spontan olarak gelişebilir. Bu yazıda, oral antikoagulan etki altında gelişen spontan retroperitoneal hemoraji vakası sunulmaktadır.

Anahtar Kelimeler: Spontan retroperitoneal hemoraji, oral antikoagülasyon, endovasküler embolizasyon

Abstract

Retroperitoneal hemorrhage, which is a life threatening and rare condition, is mainly classified as traumatic and non-traumatic by etiology. Non-traumatic bleeding may occur as a result of iatrogenic injury (e.g femoral artery cannulation) or spontaneously. In this paper, we report a case of spontaneous retroperitoneal hemorrhage (SRH) under oral anticoagulation therapy.

Keywords: Spontaneous retroperitoneal hemorrhage, oral anticoagulation, endovascular embolization

Introduction

In the absence of any trauma or medical manipulation, bleeding into the retroperitoneal space is defined as SRH.(1) Its pathogenesis is not fully understood. While retroperitoneal small vessel disease that renders these vessels more prone to rupture is suggested by some (2); others suggest that the hemorrhage may occur because of the unrecognized minor trauma in the microcirculation in patients under anticoagulation.(3) The risk of SRH is increased in older adults, women and oral anticoagulation users. (1,4)

Case Report

A 70-year-old woman was admitted to the cardiology ward with decompensated heart failure and was given intravenous diuretic therapy. Her rhythm was atrial fibrillation and she was taking warfarin for stroke prevention at the time of hospitalization. Her inital lab tests showed Hb to be 11.5 g/dL, WBC 10.6x 103/µL , PLT 242x 103/µL and INR 9.4; thus intravenous vitamin K was given for anticoagulation reversal. First control INR value was 1.5 and lower values detected thereafter. The reason that she showed no signs/symptoms of bleeding, full dose subcutaneous enoxaparin treatment was restarted after INR correction. During hospitalization she was followed with subcutaneous enoxaparin and after compansation of heart failure she was planned to be discharged with rivaroxaban 20 mg 1*1. The morning that rivaroxaban was initiated, in the routine daily visit, she complained right flank pain that had been started previous midnight.

On examination, stiffness was detected on the right flank region and a blood test revealed a reduction in Hb value to 7.7 g/dL. Immediately, general surgery consultation was requested and through the suggestions of surgeon enhanced CT scan of the abdomen and pelvis was performed. Massive right retroperitoneal hematoma with active bleeding ***(Figure 1)*** was detected and then patient was consulted with urosurgeon who has better retroperitoneal surgery experience. Emergent operation wasn't planned by the surgeon because the rivaroxaban had been given to the patient and watchful waiting with agressive erythrocyte suspension (ES) and Fresh Frozen Plasma (FFP) replacement suggested. Patient was transferred to the Intensive care unit (ICU) , 3 units of ESs and 2 units of FFPs were given, concurrently contacted emergency center to refer the patient to a center with interventional radiology/endovascular embolization facilities. During ICU follow up, respiratory distress was developed with the increasing abdominal distension secondary to retroperitonal mass effect. Although the last Hb value was 8.9 g/dL, as a sign of nearly self-controlled bleeding, the patient suddenly collapsed because of the respiratory distress and possible compression of inferior vena cava by massive retroperitoneal hematoma. Despite the one hour advanced life support, the patient died. All procedures performed with patient's written and verbal consent.

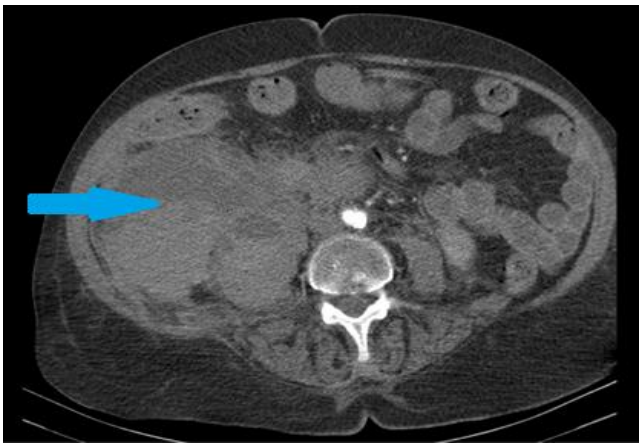

Figure1 .CT scan of the abdomen showing a huge retroperiteoneal hematoma (Blue arrow)

Discussion

Spontaneous retroperitoneal hemorrhage is a life threatening medical condition that may be managed medically or interventionally (angiographic or surgical). The main aspects of medical management are volume support with intravenous fluids and/or blood products and normalization of coagulation status.(5) When the patient's clinical condition doesn't respond to aggressive medical treatment, patient should promptly be evaluated and referred for angiography with possible embolization of the bleeding source or surgery. In the hospitals with interventional radiology capabilities, percutaneous arterial embolization is often the first-line intervention and surgery is generally reserved for patients with failed angiographic procedures, compressive symptoms from hematoma formation, or abdominal compartment syndrome .(1) With the regard to the identification and control of the bleeding site, surgery of SRH is difficult. Furthermore, anticoagulation effect makes the surgery of SRH much more complex. Unfortunately interventional radiology capabilities are not as prevalent as surgical facilities.

As long as the patient's medical condition allows, considering that the risk of surgery due to the anticoagulant effect is very high and percutaneous arterial embolization may be a method with a higher chance of success compared to surgery, it seems safer to refer the patient to a center with interventional radiology capabilities, as soon as the diagnosis is made and even if initial medical management is contemplated. LMWH therapy given in the period between the reversal of INR with intravenous vitamin K and pre-discharge rivaroxaban therapy is not aimed for bridging, since bridging therapy is no longer recommended in the latest guidelines.

Result

In cases of SRH, which is a life-threatening emergency, it should be planned to refer the patients to a center with interventional radiology facilities as soon as the diagnosis is made.

References

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