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Evaluation of changes in myelination in the brain during infancy and childhood using ADC maps

Bebek ve çocukluk döneminde beyinde miyelinizasyon ile ilgili değişikliklerin ADC haritaları kullanılarak değerlendirilmesi

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Abstract

Aim: Myelinization has a critical role in achieving rapid synchronization between the neural system and high-grade cognitive functions. Because of this critical role, it is important to quantitatively determine the degree of myelination. Today, structural changes due to myelination can be evaluated quantitatively by diffusion magnetic resonance imaging (MRI) and apparent diffusion coefficient (ADC) measurements. The aim of this study was to evaluate myelination-related changes in different regions of the brain during infancy and childhood in the normal population by measuring ADC values in routine MRI examinations.

Methods: In this cross-sectional study, 109 patients aged 0-17 years who underwent brain MRI examination with 3.0T device and whose myelination and maturation were interpreted as normal in conventional sequences were evaluated. In all examinations, ADC maps from 30 different locations were evaluated and measured in the workstation based on T2-weighted images.

Results: There is a functional relationship between ADC values and the myelination process during infancy and childhood in the normal population. ADC values decrease in all localizations with increasing age, especially during the first 2 years. During the postnatal period, ADC values, which are higher in the white matter, decrease as maturation of white matter is completed and increase in the cortical gray matter. No significant difference was found between bilateral structures except the thalamus, caudate nucleus or centrum semiovale regions. There was no gender-dependent significant difference in the patients aged between zero and 2 years.

Conclusion: ADC values for each localization can be easily obtained by diffusion weighted imaging and ADC maps, which are frequently used in routine MRI examinations. The relationship between ADC values and myelination process can be revealed in the whole brain and normative values can be obtained for multiple regions in the brain.

Keywords: Myelination, Diffusion weighted imaging, Magnetic resonance imaging, Apparent diffusion coefficient

Öz

Amaç: Nöral sistem arasında hızlı senkronizasyonun gerçekleşmesinde ve yüksek dereceli bilişsel fonksiyonların sağlanmasında myelinizasyonun kritik bir yeri vardır. Bu kritik rolü nedeniyle myelinizasyonun derecesini kantitatif olarak belirlemek çok önemlidir. Günümüzde difüzyon manyetik rezonans görüntüleme (MRG) ve görünür difüzyon katsayısı (ADC) ölçümleri ile myelinizasyona bağlı oluşan yapısal değişiklikler kantitatif olarak değerlendirilebilir. Çalışmamızın amacı normal popülasyonda bebeklik ve çocukluk çağında beynin farklı bölgelerinde miyelinizasyonla ilişkili değişikliklerin rutin MRG incelemelerinde ADC değerleri ölçülerek değerlendirilmesidir.

Yöntemler: Bu kesitsel çalışmada, 3.0T cihaz ile beyin MRG incelemesi yapılan ve miyelinizasyonu ve maturasyonu konvansiyonel sekanslarda normal olarak yorumlanan yaşları 0-17 arasındaki 109 hasta değerlendirildi. Tüm incelemelerde T2 ağırlıklı görüntüler baz alınarak 30 farklı lokalizasyondan ADC haritaları iş istasyonunda değerlendirilerek ölçüm yapıldı.

Bulgular: Normal populasyonda bebeklik ve çocukluk çağında miyelinizasyon süreci ve ADC değerleri arasında fonksiyonel bir ilişki bulunmaktadır. Yaş arttıkça ADC değerleri ilk 2 yaşta daha belirgin olmak üzere tüm lokalizasyonlarda azalmaktadır. Postnatal süreçte beyaz cevherde daha yüksek olan ADC değerleri beyaz cevher maturasyonu tamamlandıkça azalmakta ve kortikal gri cevherde daha yüksek hale gelmektedir. Talamus, kaudat nükleus ve santral sentrum semiovale dışında her iki hemisferde karşılıklı yapılarda anlamlı farklılık bulunmamıştır. Yapılan karşılaştırmada 0 ile 2 yaş arasındaki hastalarda cinsiyete bağlı anlamlı bir fark yoktu.

Sonuç: Beyin MRG incelemelerinde rutin pratikte sıklıkla kullanılan difüzyon ağırlıklı görüntüleme ve ADC haritaları ile her bir lokalizasyon için ADC değerleri kolayca elde edilebilmektedir. Böylelikle ADC değerleri ile miyelinizasyon süreci ilişkisi tüm beyinde ortaya konabilmekte ve beyinde multipl bölge için normatif değerler elde edilebilmektedir.

Anahtar kelimeler: Miyelinizasyon, Difüzyon ağırlıklı görüntüleme, Manyetik rezonans görüntüleme, Görünür difüzyon katsayısı

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Introduction

Myelination is an extremely sensitive and multi-staged process that begins in fetal life and is largely completed during the 2nd postnatal year. While some structures complete their maturation process in the initial stages of fetal development, others may remain incompletely myelinated until the 3rd and 4th decades of life [1,2].

Brain myelination maturation extends from the inferior to the superior, from the central to the peripheral, and from the posterior to the anterior regions. For example, the brainstem is myelinated before the cerebellar hemispheres, the posterior limb of the internal capsule before the anterior limb and deep periventricular white matter before subcortical U fibers [3,4].

There is no improved technique for directly visualizing myelin structure. Myelin can only be evaluated qualitatively [5]. Commonly used magnetic resonance (MR) techniques include conventional anatomic imaging, i.e., T1-weighted and T2-weighted sequences, as well as MR spectroscopy and diffusion tensor imaging (DTI). Nowadays, standard magnetic resonance imaging (MRI) techniques are not particularly capable of determining the amount of myelin. Instead, these techniques evaluate changes in axonal size and density, membrane structure including lipid and protein content, and a combination of water and macromolecule content [5,6].

Diffusion-weighted imaging is sensitive to the movement of water molecules. It is frequently used with advantages such as image acquisition in brief time and no need for contrast material. Diffusion weighted images are evaluated together with apparent diffusion coefficient (ADC) maps and quantitative measurement of diffusion coefficient can be performed [7,8].

In our study, mean ADC values during the myelination process at each localization for each age group were determined by measurement of ADC values from 30 different localizations of the brains of children with normal cranial MRI findings, and ADC changes during myelination between the two hemispheres and the two genders were comparatively analyzed. The aim of our study is to contribute to the development of reference values for intracranial pathologies that lead to ADC changes but do not show signs in conventional sequences.

Materials and methods

The cranial MRI results of 109 patients who were referred to the Radiology Department of Dicle University, Faculty of Medicine with complaints of headache, nausea, convulsion and a prediagnosis of intracranial mass between December 2014-January 2018 were evaluated retrospectively by two neuroradiologists. Patients with pathological cranial MRIs or those not fit for evaluation due to artefacts were excluded. 50 males and 59 females between the ages of 0-17 years were included in our study.

MRI protocol

All cranial MRI examinations were performed with a 3.0 Tesla MRI device (Achieva, Philips Medical systems, Best, the Netherlands) using an 8-channel cranial coil and images were evaluated at the Philips Extended MR Workspace workstation. MRI protocol routinely used for brain imaging in our hospital includes T2-weighted TSE (turbo spin-echo) sequences in the axial and sagittal plane, FLAIR sequence (fluid-attenuated-inversion-recovery) and axial T1-weighted SE (Spin echo) sequences.

Evaluation method

Diffusion weighted images of the areas to be examined on routine MRI images were analyzed at the Philips Extended MR Workspace workstation. Basing on T2-weighted images, ROI was carefully placed in oval, round, or rectangular shape in the areas to be examined by cross-linking on 'b=0' images, which are better than the other maps in revealing anatomical detail. The minimum and maximum sizes of placed ROI according to the localization were 6 mm^2 and 300 mm^2, respectively. For each patient, the mean ADC values, standard deviation, minimum and maximum ADC values ($x10^{-3}$ mm^2/sec) in these areas were manually calculated on ADC maps (Figure 1).

Patients were divided into 10 groups according to age. Mean values in all localizations, distribution of mean values according to age, differences between males and females, differences between the right and left hemisphere of the brain at the same localization were calculated for each group.

Statistical analysis

ADC values were measured separately for each localization. To determine age-dependent changes, mean ADC values were calculated for each group at each location. Individuals were divided into subgroups depending on age range (0-3 months, 3-6 months, 6-12 months, 12-24 months, 24-36 months, 3-5 years, 5-8 years, 8-11 years, 11-14 years and 14 years) and age-dependent changes were calculated with 95% reliability.

Wilcoxon signed rank test was used to compare the same regions in both hemispheres and white matter, cortical gray matter and deep gray matter. In order to compare gender-dependent differences in gray and white matter, individuals were divided into two groups: 0-2 years and 2-17 years. Mann Whitney U test was used to evaluate gender-dependent differences between the same localizations.

Results

ADC values in infants and children decrease in all 30 regions as age increases, especially during the first year. For example, the mean ADC value for the right lentiform nucleus (Region 5) in the youngest age group (0-3 months) was 0.971 x 10^{-3} mm^2/sec, which decreased to 0.850 x 10^{-3} mm^2/sec between 6-12 months and 0.707 x 10^{-3} mm^2/sec in the oldest age group (14-17 years) (Figure 2). In the left frontal white matter (Region 14), the mean ADC value was 1.275 x 10^{-3} mm^2/sec in the youngest age group (0-3 months), 1.057 x 10^{-3} mm^2/sec in the 6-12 month range, and 0.752 x 10^{-3} mm^2/sec in the 14-17 year-old group (Figure 3). For the left occipital cortex (Region 10), the mean ADC value in the 0-3 month-old group was 1.080 x 10^{-3} mm^2/sec, 0.885x 10^{-3} mm^2/sec between 6-12 months and 0.793 x 10^{-3} mm^2/sec in the oldest age group (Figure 4). The mean ADC values and standard deviations by age groups for each localization are listed in Tables 1-4.

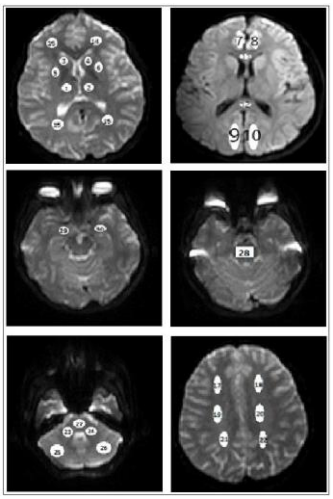

Figure 1: Localizations of ADC measurement

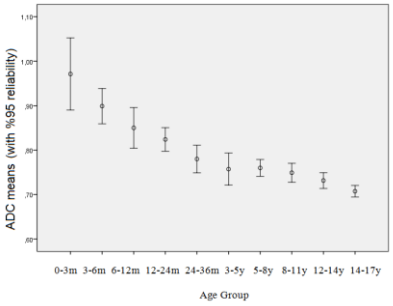

Figure 2: Mean age-dependent ADC values in right lentiform nucleus

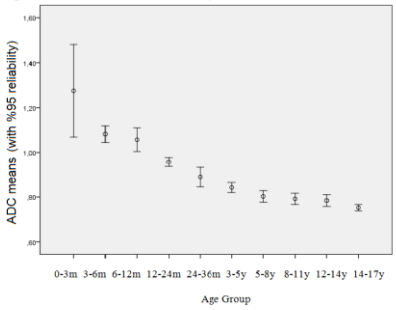

Figure 3: Age-dependent mean ADC values in left frontal white matter

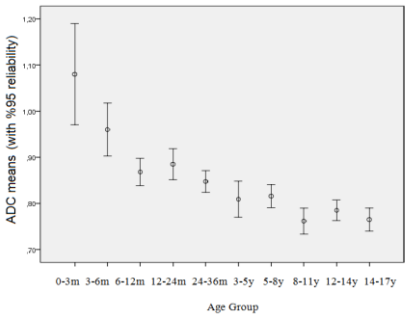

Figure 4: Age-dependent mean ADC values in left occipital cortex

Table 1: Cerebellum: ADC values with respect to age groups in middle cerebellar peduncle and hemispheres (Region 23-26)

23 (Right middle cerebellar peduncle)			24 (Left middle cerebellar peduncle)		
Age group	N	Mean (SD)	Age group	N	Mean (SD)
0-3 Months	8	0.93 (0.05)	0-3 Months	8	0.91 (0.07)
3-6 Months	9	0.80 (0.05)	3-6 Months	9	0.78 (0.06)
6-12 Months	11	0.78 (0.04)	6-12 Months	11	0.77 (0.05)
12-24 Months	10	0.77 (0.07)	12-24 Months	10	0.75 (0.04)
24-36 Months	12	0.75 (0.05)	24-36 Months	12	0.73 (0.06)
3-5 Years	11	0.70 (0.05)	3-5 Years	11	0.69 (0.03)
5-8 Years	12	0.71 (0.04)	5-8 Years	12	0.71 (0.04)
8-11 Years	12	0.68 (0.05)	8-11 Years	12	0.70 (0.04)
12-14 Years	12	0.70 (0.04)	12-14 Years	12	0.69 (0.05)
14-17 Years	12	0.68 (0.03)	14-17 Years	12	0.67 (0.03)
25 (Right cerebellar cortex)			26 (Left cerebellar cortex)		
Age group	N	Mean (SD)	Age group	N	Mean (SD)
0-3 Months	8	0.87 (0.12)	0-3 Months	8	0.88 (0.14)
3-6 Months	9	0.75 (0.07)	3-6 Months	9	0.76 (0.09)
6-12 Months	11	0.73 (0.02)	6-12 Months	11	0.75 (0.04)
12-24 Months	10	0.72 (0.05)	12-24 Months	10	0.73 (0.05)
24-36 Months	12	0.72 (0.04)	24-36 Months	12	0.70 (0.03)
3-5 Years	11	0.69 (0.02)	3-5 Years	11	0.67 (0.03)
5-8 Years	12	0.68 (0.02)	5-8 Years	12	0.68 (0.03)
8-11 Years	12	0.65 (0.02)	8-11 Years	12	0.65 (0.02)
12-14 Years	12	0.68 (0.03)	12-14 Years	12	0.65 (0.02)
14-17 Years	12	0.65 (0.02)	14-17 Years	12	0.64 (0.03)

N: number of patients, SD: standard deviation

Table 2: Deep Gray Matter and Brain Stem: ADC values with respect to age groups at levels of thalamus, caudate and lentiform nuclei and amygdala, mesencephalon and pons (region 1-6, 27-30)

1 (Right thalamus)			2 (Left thalamus)		
Age group	N	Mean (SD)	Age group	N	Mean (SD)
0-3 Months	8	0.92 (0.08)	0-3 Months	8	0.93 (0.09)
3-6 Months	9	0.87 (0.07)	3-6 Months	9	0.84 (0.05)
6-12 Months	11	0.82 (0.02)	6-12 Months	11	0.81 (0.03)
12-24 Months	10	0.83 (0.03)	12-24 Months	10	0.82 (0.02)
24-36 Months	12	0.82 (0.09)	24-36 Months	12	0.79 (0.10)
3-5 Years	11	0.77 (0.03)	3-5 Years	11	0.76 (0.03)
5-8 Years	12	0.78 (0.04)	5-8 Years	12	0.77 (0.04)
8-11 Years	12	0.72 (0.03)	8-11 Years	12	0.70 (0.04)
12-14 Years	12	0.75 (0.02)	12-14 Years	12	0.74 (0.01)
14-17 Years	12	0.71 (0.03)	14-17 Years	12	0.71 (0.03)
3 (Right caudate nucleus)			4 (Left caudate nucleus)		
Age group	N	Mean (SD)	Age group	N	Mean (SD)
0-3 Months	8	1.03 (0.12)	0-3 Months	8	1.01 (0.12)
3-6 Months	9	0.95 (0.06)	3-6 Months	9	0.93 (0.07)
6-12 Months	11	0.87 (0.06)	6-12 Months	11	0.86 (0.08)
12-24 Months	10	0.85 (0.04)	12-24 Months	10	0.85 (0.04)
24-36 Months	12	0.82 (0.08)	24-36 Months	12	0.81 (0.11)
3-5 Years	11	0.80 (0.04)	3-5 Years	11	0.79 (0.04)
5-8 Years	12	0.78 (0.03)	5-8 Years	12	0.78 (0.04)
8-11 Years	12	0.76 (0.02)	8-11 Years	12	0.75 (0.03)
12-14 Years	12	0.74 (0.02)	12-14 Years	12	0.73 (0.02)
14-17 Years	12	0.71 (0.03)	14-17 Years	12	0.70 (0.03)
5 (Right lentiform nucleus)			6 (Left lentiform nucleus)		
Age group	N	Mean (SD)	Age group	N	Mean (SD)
0-3 Months	8	0.97 (0.09)	0-3 Months	8	0.97 (0.11)
3-6 Months	9	0.89 (0.05)	3-6 Months	9	0.90 (0.05)
6-12 Months	11	0.85 (0.06)	6-12 Months	11	0.85 (0.09)
12-24 Months	10	0.82 (0.03)	12-24 Months	10	0.81 (0.04)
24-36 Months	12	0.78 (0.04)	24-36 Months	12	0.77 (0.07)
3-5 Years	11	0.75 (0.05)	3-5 Years	11	0.74 (0.04)
5-8 Years	12	0.76 (0.02)	5-8 Years	12	0.75 (0.04)
8-11 Years	12	0.74 (0.03)	8-11 Years	12	0.72 (0.04)
12-14 Years	12	0.73 (0.02)	12-14 Years	12	0.73 (0.02)
14-17 Years	12	0.70 (0.02)	14-17 Years	12	0.70 (0.03)
29 (Right amygdala)			30 (Left amygdala)		
Age group	N	Mean (SD)	Age group	N	Mean (SD)
0-3 Months	8	1.15 (0.12)	0-3 Months	8	1.08 (0.41)
3-6 Months	9	0.97 (0.02)	3-6 Months	9	0.97 (0.03)
6-12 Months	11	0.96 (0.09)	6-12 Months	11	0.95 (0.06)
12-24 Months	10	0.91 (0.03)	12-24 Months	10	0.89 (0.05)
24-36 Months	12	0.87 (0.06)	24-36 Months	12	0.83 (0.06)
3-5 Years	11	0.83 (0.04)	3-5 Years	11	0.83 (0.05)
5-8 Years	12	0.85 (0.05)	5-8 Years	12	0.85 (0.06)
8-11 Years	12	0.83 (0.04)	8-11 Years	12	0.83 (0.03)
12-14 Years	12	0.83 (0.03)	12-14 Years	12	0.80 (0.03)
14-17 Years	12	0.80 (0.03)	14-17 Years	12	0.81 (0.03)
27 (Mesencephalon)			28 (Pons)		
Age group	N	Mean (SD)	Age group	N	Mean (SD)
0-3 Months	8	0.91 (0.07)	0-3 Months	8	0.89 (0.10)
3-6 Months	9	0.90 (0.05)	3-6 Months	9	0.80 (0.03)
6-12 Months	11	0.87 (0.03)	6-12 Months	11	0.76 (0.02)
12-24 Months	10	0.82 (0.05)	12-24 Months	10	0.76 (0.06)
24-36 Months	12	0.78 (0.05)	24-36 Months	12	0.72 (0.04)
3-5 Years	11	0.79 (0.04)	3-5 Years	11	0.71 (0.07)
5-8 Years	12	0.76 (0.08)	5-8 Years	12	0.70 (0.07)
8-11 Years	12	0.74 (0.04)	8-11 Years	12	0.67 (0.05)
12-14 Years	12	0.73 (0.03)	12-14 Years	12	0.67 (0.03)
14-17 Years	12	0.69 (0.05)	14-17 Years	12	0.65 (0.03)

N: number of patients, SD: standard deviation

Table 3: Cortical Gray Matter: ADC values with respect to age groups at levels of frontal and occipital gray matter (regions 7, 8, 9, 10)

7 (Right frontal cortex)			8 (Left frontal cortex)		
Age group	N	Mean (SD)	Age group	N	Mean (SD)
0-3 Months	8	1.06 (0.08)	0-3 Months	8	1.09 (0.08)
3-6 Months	9	1.02 (0.05)	3-6 Months	9	1.0 (0.06)
6-12 Months	11	0.96 (0.03)	6-12 Months	11	0.97 (0.03)
12-24 Months	10	0.92 (0.05)	12-24 Months	10	0.92 (0.04)
24-36 Months	12	0.90 (0.09)	24-36 Months	12	0.91 (0.07)
3-5 Years	11	0.88 (0.03)	3-5 Years	11	0.88 (0.05)
5-8 Years	12	0.87 (0.03)	5-8 Years	12	0.87 (0.03)
8-11 Years	12	0.87 (0.03)	8-11 Years	12	0.87 (0.02)
12-14 Years	12	0.86 (0.02)	12-14 Years	12	0.86 (0.02)
14-17 Years	12	0.85 (0.02)	14-17 Years	12	0.86 (0.04)
9 (Right occipital cortex)			10 (Left occipital cortex)		
Age group	N	Mean (SD)	Age group	N	Mean (SD)
0-3 Months	8	1.06 (0.09)	0-3 Months	8	1.08 (0.13)
3-6 Months	9	0.92 (0.06)	3-6 Months	9	0.96 (0.07)
6-12 Months	11	0.88 (0.04)	6-12 Months	11	0.88 (0.04)
12-24 Months	10	0.87 (0.04)	12-24 Months	10	0.86 (0.04)
24-36 Months	12	0.84 (0.04)	24-36 Months	12	0.84 (0.03)
3-5 Years	11	0.83 (0.05)	3-5 Years	11	0.83 (0.05)
5-8 Years	12	0.83 (0.03)	5-8 Years	12	0.82 (0.03)
8-11 Years	12	0.82 (0.03)	8-11 Years	12	0.78 (0.4)
12-14 Years	12	0.82 (0.03)	12-14 Years	12	0.80 (0.3)
14-17 Years	12	0.80 (0.04)	14-17 Years	12	0.79 (0.03)

N: number of patients, SD: standard deviation

Table 4: Deep white matter, white matter: Frontal and peritrigonal white matter and centrum semiovale (regions 13-22).

11 (Corpus callosum genu)			12 (Corpus callosum splenium)		
Age group	N	Mean (SD)	Age group	N	Mean (SD)
0-3 Months	8	1.17 (0.12)	0-3 Months	8	1.13 (0.12)
3-6 Months	9	1.10 (0.13)	3-6 Months	9	1.05 (0.12)
6-12 Months	11	1.00 (0.11)	6-12 Months	11	0.90 (0.13)
12-24 Months	10	0.84 (0.05)	12-24 Months	10	0.82 (0.06)
24-36 Months	12	0.83 (0.04)	24-36 Months	12	0.76 (0.09)
3-5 Years	11	0.78 (0.06)	3-5 Years	11	0.78 (0.06)
5-8 Years	12	0.79 (0.05)	5-8 Years	12	0.77 (0.07)
8-11 Years	12	0.76 (0.07)	8-11 Years	12	0.74 (0.11)
12-14 Years	12	0.75 (0.04)	12-14 Years	12	0.75 (0.06)
14-17 Years	12	0.75 (0.06)	14-17 Years	12	0.74 (0.03)
13 (Right frontal white matter)			14 (Left frontal white matter)		
Age group	N	Mean (SD)	Age group	N	Mean (SD)
0-3 Months	8	1.26 (0.23)	0-3 Months	8	1.27 (0.24)
3-6 Months	9	1.10 (0.04)	3-6 Months	9	1.08 (0.04)
6-12 Months	11	1.07 (0.07)	6-12 Months	11	1.05 (0.07)
12-24 Months	10	0.95 (0.03)	12-24 Months	10	0.95 (0.02)
24-36 Months	12	0.89 (0.04)	24-36 Months	12	0.88 (0.06)
3-5 Years	11	0.84 (0.03)	3-5 Years	11	0.84 (0.03)
5-8 Years	12	0.79 (0.04)	5-8 Years	12	0.80 (0.04)
8-11 Years	12	0.78 (0.04)	8-11 Years	12	0.79 (0.03)
12-14 Years	12	0.77 (0.05)	12-14 Years	12	0.78 (0.04)
14-17 Years	12	0.75 (0.03)	14-17 Years	12	0.75 (0.02)
15 (Right occipital white matter)			16 (Left occipital white matter)		
Age group	N	Mean (SD)	Age group	N	Mean (SD)
0-3 Months	8	1.25 (0.21)	0-3 Months	8	1.26 (0.23)
3-6 Months	9	1.13 (0.04)	3-6 Months	9	1.12 (0.08)
6-12 Months	11	1.13 (0.11)	6-12 Months	11	1.13 (0.09)
12-24 Months	10	0.98 (0.07)	12-24 Months	10	0.97 (0.27)
24-36 Months	12	0.92 (0.09)	24-36 Months	12	0.90 (0.08)
3-5 Years	11	0.86 (0.04)	3-5 Years	11	0.86 (0.03)
5-8 Years	12	0.85 (0.06)	5-8 Years	12	0.86 (0.07)
8-11 Years	12	0.81 (0.04)	8-11 Years	12	0.83 (0.05)
12-14 Years	12	0.81 (0.04)	12-14 Years	12	0.81 (0.04)
14-17 Years	12	0.79 (0.03)	14-17 Years	12	0.81 (0.03)
17 (Right frontal centrum semiovale)			18 (Left frontal centrum semiovale)		
Age group	N	Mean (SD)	Age group	N	Mean (SD)
0-3 Months	8	1.17 (0.06)	0-3 Months	8	1.15 (0.20)
3-6 Months	9	1.06 (0.07)	3-6 Months	9	1.03 (0.08)
6-12 Months	11	1.01 (0.04)	6-12 Months	11	1.00 (0.05)
12-24 Months	10	0.88 (0.05)	12-24 Months	10	0.89 (0.07)
24-36 Months	12	0.82 (0.02)	24-36 Months	12	0.82 (0.02)
3-5 Years	11	0.78 (0.04)	3-5 Years	11	0.79 (0.04)
5-8 Years	12	0.77 (0.04)	5-8 Years	12	0.77 (0.05)
8-11 Years	12	0.74 (0.03)	8-11 Years	12	0.73 (0.02)
12-14 Years	12	0.74 (0.03)	12-14 Years	12	0.74 (0.02)
14-17 Years	12	0.71 (0.03)	14-17 Years	12	0.70 (0.03)
19 (Right central centrum semiovale)			20 (Left central centrum semiovale)		
Age group	N	Mean (SD)	Age group	N	Mean (SD)
0-3 Months	8	1.15 (0.20)	0-3 Months	8	1.12 (0.16)
3-6 Months	9		3-6 Months	9	1.02 (0.09)
6-12 Months	11	0.98 (0.07)	6-12 Months	11	0.97 (0.09)
12-24 Months	10	0.85 (0.05)	12-24 Months	10	0.84 (0.04)
24-36 Months	12	0.82 (0.02)	24-36 Months	12	0.81 (0.03)
3-5 Years	11	0.76 (0.05)	3-5 Years	11	0.74 (0.05)
5-8 Years	12	0.77 (0.05)	5-8 Years	12	0.77 (0.08)
8-11 Years	12	0.73 (0.06)	8-11 Years	12	0.72 (0.04)
12-14 Years	12	0.74 (0.04)	12-14 Years	12	0.73 (0.04)
14-17 Years	12	0.69 (0.04)	14-17 Years	12	0.65 (0.05)
21 (Right posterior centrum semiovale)			22 (Left posterior centrum semiovale)		
Age group	N	Mean (SD)	Age group	N	Mean (SD)
0-3 Months	8	1.17 (0.22)	0-3 Months	8	1.16 (0.20)
3-6 Months	9	1.02 (0.05)	3-6 Months	9	1.00 (0.06)
6-12 Months	11	1.00 (0.07)	6-12 Months	11	1.03 (0.10)
12-24 Months	10	0.92 (0.06)	12-24 Months	10	0.89 (0.07)
24-36 Months	12	0.86 (0.05)	24-36 Months	12	0.84 (0.05)
3-5 Years	11	0.79 (0.05)	3-5 Years	11	0.79 (0.05)
5-8 Years	12	0.80 (0.05)	5-8 Years	12	0.82 (0.08)
8-11 Years	12	0.77 (0.06)	8-11 Years	12	0.75 (0.04)
12-14 Years	12	0.76 (0.03)	12-14 Years	12	0.77 (0.03)
14-17 Years	12	0.72 (0.02)	14-17 Years	12	0.72 (0.03)

N: number of patients, SD: standard deviation

Table 5: Comparison of ADC values at different localizations in both age groups ($x10^{-3}$ mm^2/sn

	0-2 Years			2-17 Years		
	DGM	WM	CGM	DGM	WM	CGM
N	38	38	38	71	71	71
Minimum	0.77	0.87	0.84	0.67	0.71	0.7
Maximum	1.18	1.51	1.22	1.04	0.94	1.03
Mean	0.8832	1.0459	0.9514	0.7563	0.7912	0.8022
SD	0.08083	0.13897	0.09442	0.05058	0.05331	0.04903

N: Number of patients, DGM: Deep Gray Matter, WM: White matter, CGM: Cortical Gray Matter, SD: Standard Deviation

The mean ADC values of white matter and gray matter were compared after all patients were divided into two subgroups according to age (0-2 years and 2-17 years).

Significant differences were found between all matched comparisons between white matter, cortical and deep gray matter in both age groups (P<0.001). Descriptive analytic results are presented in Table 5. There was a significant difference in all matched regions (P<0.001).

We analyzed the age-dependent distribution of ADC values in both subgroups (0-2 and 2-17 years). The mean ADC values of 0 to 2-year-old males and females were similar (P=0.645). There were no gender-related differences in any localization for this group. Mann-Whitney U test revealed distorted age distribution in the older age group, and no comparisons could be made.

When comparing the paired regions in both hemispheres, significant differences were detected between caudate nucleus (P=0.042) and central centrum semiovale (P=0.02). No significant differences were found in other matched regions.

Discussion

Until myelination is completed, ADC values decrease, especially during the first 2 years [9,10]. Changes in ADC values in response to structural adjustments due to increased anisotropy during cerebral development provide an objective, investigator-independent measurement of signal intensity. This decrease in ADC values is multifactorial due to the decrease in the total amount of water and the increase in lipid and macromolecules [11,12]. In addition, the increase in perfusion after birth as defined by Kehrer et al. [13] may also help explain changes in ADC values .

In their study performed on prenatal healthy children by obtaining measurements from 10 different localizations, Han et al.'s [14] results show similarities with our postnatal measurements. Accordingly, the supratentorial region had higher ADC values than the infratentorial region and the highest ADC values were observed in the frontal white matter, followed by occipital white matter.

The comparison of mean ADC values of white, cortical, and deep gray matter performed by Bültmann et al. [15] revealed comparable results to our study. They have found a significant difference between the structures compared. We found that ADC values were highest in supratentorial white matter after birth and higher than that in the gray matter, and cortical gray matter had the highest values after myelination and maturation of the brain. The significant difference they found in peritrigonal white matter between both hemispheres was not detected in our study, which can be explained by the fact that this region, called the terminal zone, is sensitive to differences in ROI positioning. In our study, the difference in the centrum semiovale and the caudate nucleus can be explained by the small differences in the standardization of ROI and the proximity of the caudate nucleus to the CSF.

Our findings are similar to the those of the study performed by Schneider et al. [16], in which they measured ADC values at 9 different sites in normal intrauterine fetuses (mean gestational age: 31 (3) weeks). Their values were higher than our postnatal results, but this can be explained by the decrease in ADC values as myelination increases. In addition, the researchers have been able to show that the brain stem, thalamus, and cerebellum have lower ADC values, which shows signs of earlier maturation with regards to the hypothesis of myelination occurring from the caudal towards the cranial areas. In our study, the postnatal ADC values in the brainstem and infratentorial structures were lower than the structures located cranially.

Schneider et al. [16] paid attention to the centrum semiovale, seen as loose white matter fibers after combining all deep white matter due to early myelin deposition and maturation in corticospinal tracts. Consistent with this observation, our ADC

values were slightly lower in the central, peri-rolandic part of the centrum semiovale than in the frontal and parietal parts, and, higher than the brain stem, which shows that the myelination of the centrum semiovale occurs slightly later when compared with sensory pathways in the brain stem and slightly earlier than the frontal and parietal regions. These findings support that myelination extends from the central regions toward the peripheral regions. In general, our measurements showed higher ADC values in all supratentorial deep white matter structures (except corpus callosum) compared to gray matter and infratentorial white matter, which showed later myelination.

The data on ADC values in neonatal brains with normal findings in the meta-analysis of Coats et al. [17] resembles those of ours. Higher ADC values were observed in the white matter than gray matter and the highest values were found in the frontal and occipital white matter, while the lowest ADC values were detected in the hind limb of the internal capsule and thalamus within the supratentorial part of the brain. In our study, the highest values were found in frontal and occipital white matter and the lowest values were observed in the thalamus and basal ganglia.

Our postnatal results are akin to those obtained by Engelbrecht et al. [18]. Increased ADC values in accordance with to monocyte expression function decreased with age in all investigated regions. Engelbrecht et al. [18] reportedly detected the highest values in the frontal and occipital white matter and the lowest values in the brain stem, which is consistent with our data.

Limitations

There are some factors limiting our study. Firstly, we selected patients without signal abnormalities or with focal anomalies which are not reflected in imaging, who had different clinical indications for conventional MRI examinations. Although we studied patients without any symptoms, our lack of a group without any complaints may be considered a deficiency. The disadvantage of our study is that there is a need for sedation or intubation during evaluation of healthy individuals during infancy or childhood. Another weakness of our study is that we use three directions instead of full diffusion tensor imaging. Therefore, examinations can yield different results depending on the position of the head or the orientation of the white matter fibers. Also, ADC measurements are extremely sensitive even to small motion artifacts and yield different results according to the size of the ROI used. Measurements in the regions close to CSF are easily affected by CSF volume. However, since we use diffusion sequences in routine MRI examinations in our clinic and obtain easily accessible results, these potential weaknesses are acceptable. The fact that our data is objective, reproducible, realistic, and comparable to the literature indicates that despite our weaknesses, our study is applicable in the evaluation of myelination.

Conclusion

The main result of our study is the ability to define ADC values for gray and white matter structures throughout the myelination process in the brain based on applicable diffusion weighted sequences. Using diffusion-weighted images and conventional sequences, we demonstrated reproducible ADC values in infancy and childhood. The obtained data show a close similarity when compared with the literature data. Our values showed a direct correlation with different myelination and maturation processes in different brain regions. For this reason, ADC values obtained from routine clinical MRI examinations can be used to assess whether postnatal maturation is appropriate for age. Our data will be useful in detecting faint or diffuse abnormalities that cannot be evaluated in conventional sequences. Our values can be used in clinical routine and diffusion-weighted imaging and ADC maps should be used as part of the standard evaluation of pediatric maturation and myelination.

References

1. Helen M. Branson. Normal Myelination A Practical Pictorial Review. Neuroimaging Clin N Am. 2013;183-95.
2. Bird CR, Hedberg M, Drayer BP, Keller PJ, Flom RA, Hodak JA. MR assessment of myelination in infants and children: usefulness of marker sites. AJNR Am J Neuroradiol. 1989;10:731–40.
3. Barkovich AJ, Kjos BO, Jackson DE Jr, Norman D. Normal maturation of the neonatal and infant brain: MR imaging at 1.5T. Radiology. 1988;166:173–80.
4. Baykan A, Ateşoğlu Karabaş S , Doğan Z , Solgun S , Özcan G , Şahin Ş, et al. Assessment of age- and sex-dependent changes of cerebellum volume in healthy individuals using magnetic resonance imaging. Journal of Surgery and Medicine. 2019;3(7):481-4.
5. Dietrich RB, Bradley WG, Zaragoza EJ IV, Otto RJ, Taira RK, Wilson GH, et al. MR evaluation of early myelination patterns in normal and developmentally delayed infants. AJR Am J Roentgenol. 1988;150:889–96
6. Deoni SC, Mercure E, Blasi A, Gasston D, Thomson A, Johnson M, et al. Mapping infant brain myelination with magnetic resonance imaging. J Neurosci. 2011;31(2):784–91.
7. Helenius J, Soinne L, Perkiö J, Salonen O, Kangasmaki A, Kaste M, et al. Diffusion-Weighted MR Imaging in Normal Human Brains in Various Age Groups. Am J Neuroradiol. 2002;23(2):194-9.
8. Mori S, Barker PB. Diffusion magnetic resonance imaging: its principle and applications. Anat Rec. 1999;257(3):102-9.
9. Yoshida S, Oishi K, Fairia AV, Mori S. Diffusion tensor imaging of normal brain development. Pediatr Radiol. 2013;43:15–27.
10. Jones RA, Palasis S, Grattan-Smith JD. The Evolution of the Apparent Diffusion Coefficient in the Pediatric Brain at Low and High Diffusion Weightings. Journal Of Magnetic Resonance Imaging. 2003;18:665–74.
11. Neil JJ, Shiran SI, McKinstry RC, Schefft GL, Snyder AZ, Almli CR, et al. Normal brain in human newborns: apparent diffusion coefficient and diffusion anisotropy measured by using diffusion tensor MR imaging. Radiology. 1998;209:57-66.
12. Huppi PS, Maier SE, Peled S, Zientara GP, Barnes PD, Jolesz FA, et al. Microstructural development of human newborn cerebral white matter assessed in vivo by diffusion tensor magnetic resonance imaging. Pediatr Res. 1998;44:584–90.
13. Kehrer M, Blumenstock G, Ehehalt S, Goelz R, Poets C, Schoning M. Development of cerebral blood flow volume in preterm neonates during the first two weeks of life. Pediatr Res. 2005;58:927–30.
14. Han R, Huang L, Sun Z, Zhang D, Chen X, Yang X, et al. Assessment of apparent diffusion coefficient of normal fetal brain development from gestational age week 24 up to term age: a preliminary study. Fetal Diagn Ther. 2015;37:102–7.
15. Bültmann E, Joachim H, Zapf A, Hartmann H, Nagele T, Lanferman H. Changes in brain microstructure during infancy and childhood using clinical feasible ADC-maps. Childs Nerv Syst. 2017;33:735–45.
16. Schneider JF, Confort-Gouny S, Le Fur Y, Viout P, Bennathan M, Chapon F, et al. Diffusion weighted imaging in normal fetal brain maturation. Eur Radiol. 2007;17:2422–9.
17. Coats JS, Freeberg A, Pajela EG, Obenaus A, Ashwal S. Meta-analysis of apparent diffusion coefficients in the newborn brain. Pediatr Neurol. 2009;41:263–74.
18. Engelbrecht V, Scherer A, Rassek M, Witsack HJ, Modder U. Diffusion weighted MR imaging in the brain in children: findings in the normal brain and in the brain with white matter diseases. Radiology. 2002;222:410–8.

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Polycystic ovary syndrome and Hashimoto's thyroiditis: An autoimmune relationship

Polikistik over sendromu ve Hashimoto tiroiditi: Otoimmün bir ilişki

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Abstract

Aim: Polycystic ovary syndrome (PCOS) and Hashimoto's thyroiditis (HT) are common and frequently comorbid diseases. A genetic predisposition and an inflammatory and autoimmune relationship have been posited between them. This study examines the role played by autoimmunity in the relation between PCOS and HT.

Methods: This case-control study was conducted at the Medical Park Hospital endocrinology and gynecology departments, Ordu, Turkey, from July 2015 to December 2018. Reproductive-age women diagnosed with PCOS based on the Rotterdam criteria, women diagnosed with HT, and healthy women with neither PCOS nor HT were included in the study. Thyroid function tests, thyroid autoantibodies, gonadotropins, androgen hormones, fasting glucose and insulin levels, and body mass index (BMI) were compared among the three groups. All patients also underwent pelvic and thyroid ultrasound examinations.

Results: Five hundred ninety-six women were included in the study, 254 in the PCOS group, 190 in the HT group, and 152 in the control group. BMI was significantly higher in the PCOS and HT groups than in the control group (P=0.012, and P=0.027, respectively). Menstrual and androgenic symptoms were also significantly higher in the patient groups than in the control group (P<0.001). The incidence of TPOAb and TgAb positivity was again significantly higher in the PCOS patients than in the controls (P<0.001).

Conclusion: This research demonstrated a higher prevalence of HT, together with elevated TSH, anti-TPO, and anti-Tg levels in PCOS patients. Our data suggest that thyroid functions and ovaries should be screened later in life in patients with PCOS and HT.

Keywords: Hashimoto's thyroiditis, Polycystic ovary syndrome, Thyroid autoantibodies, Autoimmunity

Öz

Amaç: Polikistik over sendromu (PKOS) ve Hashimoto tiroiditi (HT) sıklıkla birbirine eşlik eden yaygın hastalıklardır. Genetik, inflamasyon ve otoimmünite iki hastalığın arasındaki ilişkide mevcuttur. Bu çalışma otoimmünitenin PCOS ve HT arasındaki ilişkideki rolünü incelemektedir.

Yöntemler: Bu vaka-kontrol çalışması, Ordu Medical Park Hospital endokrinoloji ve jinekoloji bölümlerinde, Temmuz 2015 - Aralık 2018 arasında yapılmıştır. Rotterdam kriterlerine göre reprodüktif yaşlarda PKOS tanılı, HT tanılı kadınlar ve ne PCOS ne de HT tanısı olmayan sağlıklı gönüllüler çalışmaya dahil edildi. Üç grup arasında tiroid fonksiyon testleri, tiroid otoantikorları, gonadotropinler, androjen hormonları, açlık glukoz ve insülin düzeyleri ve vücut kitle indeksi (VKİ) karşılaştırıldı. Tüm hastalar ayrıca pelvik ve tiroid ultrason ile tarandı.

Bulgular: Çalışmaya toplamda beş yüz doksan altı kadın, PKOS grubunda 254, HT grubunda 190 ve kontrol grubunda 152 kişi dahil edildi. VKİ; PKOS ve HT grubunda kontrol grubundan anlamlı olarak daha yüksekti (sırasıyla P=0,012 ve P=0,027). Menstruel ve androjenik semptomlar hasta gruplarında kontrol grubundan anlamlı olarak daha yüksekti (P<0,001). TPOAb ve TgAb pozitifliği insidansı PKOS hastalarında kontrol grubuna göre anlamlı olarak yüksekti (P<0,001).

Sonuç: Bu araştırma PKOS hastalarında artmış TSH, anti-TPO ve anti-Tg düzeyleri ile birlikte HT sıklığının da yüksek olduğu gösterilmiştir. Çalışmamız, PKOS ya da HT hastalarının tiroid fonksiyonları ve overlerin ileri yaşamlarında taranması gerekliliğini göstermektedir.

Anahtar kelimeler: Hashimato Tiroiditi, Polikistik over sendromu, Tiroid antikorları, Otoimmunite

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Introduction

Polycystic ovary syndrome (PCOS) is a common endocrine disease. Various chronic diseases are associated with PCOS, such as diabetes mellitus and metabolic syndrome [1]. The etiology of PCOS remains unclear, although the evidence indicates a multifactorial origin on the basis of genetic predisposition [2]. Hashimoto's thyroiditis (HT) is characterized by elevated thyroid autoantibodies, leading to various degrees of thyroid dysfunction. Hypoechogenicity is seen at thyroid ultrasound due to lymphocytic infiltration, resulting in thyroid fibrosis. A relationship between HT and recurrent miscarriage, pregnancy loss and PCOS has been confirmed in many studies, but the adverse effects caused by thyroid autoantibodies in women of reproductive age are still an important problem [3, 4].

Thyroid hormone abnormalities can also be seen in PCOS. Thyroid hormone dysfunction in PCOS further complicates the clinical picture and may result in significant effects on comorbidity. The incidence of PCOS is increasing every year. Effective diagnostic and therapeutic methods need to be discovered for a better understanding of the causes of PCOS. The aim of our study was to determine the clinical and laboratory similarities between PCOS and HT, to identify the incidence of thyroid autoantibodies in PCOS cases, and to establish whether autoimmunity constitutes a risk factor for the transmissibility between the two diseases.

Materials and methods

This study was conducted at the Medical Park Hospital endocrinology and gynecology departments, Ordu, Turkey from July 2015 to December 2018. The study complied with the principles of the Declaration of Helsinki and was approved by the Ethics Committee of Ordu University (10.01.2019-91120269-000-E.00000031).

Participants, data collection and processing

The study population consisted of 596 women, those diagnosed with HT in our endocrinology and general surgery clinics, those diagnosed with PCOS in our endocrinology and gynecology clinics, and healthy volunteers. PCOS was diagnosed based on the ESHRE / ASRM (Rotterdam) 2004 criteria [5]. Subjects with ovulation disorder (oligo-ovulation or anovulation), clinical and / or biochemical hyperandrogenism, or those meeting the criteria for polycystic ovarian morphology were included in the study. Patients with a history of other autoimmune diseases, diabetes mellitus, coronary heart disease, hyperlipidemia, malignancy, or liver or kidney failure, women aged under 18 years or older than 52, or with menopausal status were excluded. Serum fasting glucose (70-100 mg/dl), TSH (0.35-4.94 mIU/L), free T4 (fT4) (9.01-19.05 pmol/L), TgAb (0-4.11 IU/mL), TPOAb (0-5.61 IU/mL), FSH (1.5-12.4 mlU/mL), LH (2.00-15.00 mlU/mL), serum testosterone (3,5-8.6 ng/ml), DHEA-S (82-338 ng/dL), and PRL (2-20 ng/mL) were studied using automated chemiluminescence immunoassay (ICMA) kits (Abbott, IL, USA). Pelvic ultrasonography was performed with a high-resolution apparatus equipped with a 5-1 MHz broadband convex array probe (Philips Affiniti 70 ultrasound; Philips North America Corporation, MA 01810, USA).

Statistical analysis

Data were analyzed on SPSS version 20.0 software [SPSS Inc., Chicago, IL, USA]. Mean standard deviation (SD) values for descriptive analysis were calculated with one-way ANOVA for intergroup comparisons. The Kruskal Wallis, chi-square, and independent samples t tests were used for further analysis. Categorical variables were evaluated using Pearson's chi-square test. Statistical data were considered significant if $P<0.05$.

Results

The PCOS group consisted of 254 patients, the HT group of 190 patients, and the control group, 152 healthy women. Mean (Standard Deviation) ages were 26.7 (8.2) years in the PCOS group, 25.4 (7.8) years in the HT group, and 24.1 (6.9) years in the control group.

BMI was significantly higher in the PCOS and HT than in the control group ($P=0.012$, and $P=0.027$, respectively). HOMA-IR was also significantly higher than in the control group ($P<0.001$, and $P=0.031$, respectively). Patients' menstrual and hyperandrogenic symptoms were also greater compared with the control group ($P<0.001$). The number of patients with polycystic ovary detected via ultrasound was significantly higher in the HT group than in the control group ($P<0.001$). The patient groups' clinical and biochemical data are summarized in Table 1.

Comparison of hormone levels between PCOS and HT groups and the control group revealed significantly higher testosterone levels ($P=0.002$, and $P=0.328$, respectively) and DHEA-S levels ($P<0.001$, and $P=0.016$, respectively) than in the control group. FSH, LH and PRL values were also significantly higher than in the control group ($P<0.001$). TSH values were significantly higher in the PCOS group than in the control group ($P=0.059$). Comparison of thyroid autoantibodies among the groups revealed significantly higher TgAb in the PCOS and HT groups than in the control group ($P<0.001$). TPOAb was significantly higher in both patient groups than in the control group ($P=0.043$, and $P<0.001$, respectively). A comparison of the patient groups' hormone levels with those of the control group is summarized in Table 2.

Table 1: Clinical and biochemical data for the study groups

Parameters	Control group (n=152)	PCOS group (n=254)	*P*-value (PCOS vs. Control)	HT group (n=190)	*P*-value (HT vs. Control)
Age (years) mean (SD)	24.1 (6.9)	26.7 (8.2)	0.647	25.4 (7.8)	0.853
BMI (kg/m^2)	23.8 (2.1)	28.6 (4.1)	0.012	25.9 (2.9)	0.027
Fasting glucose (mg/dl)	76.1 (24)	89.5 (22)	0.004	82.3 (18)	0.007
HOMA-IR	1.86 (0.4)	3.2 (1.2)	<0.001	2.73 (0.8)	0.031
Oligomenorrhea & amenorrhea n (%)	34 (22.3)	167 (65.7)	<0.001	94 (49.4)	<0.001
Hirsutism & acne n (%)	30 (19.7)	190 (74.8)	<0.001	85 (44.7)	<0.001
USG for polycystic ovaries n (%)	38 (25.2)	198 (77.9)	<0.001	89 (46.8)	<0.001

BMI: body mass index, HOMA-IR: homeostasis model assessment insulin resistance index, SD: Standard deviation

Table 2: Hormonal data for the patients and control group

Parameters	Control group (n=152)	PCOS group (n=254)	*P*-value (PCOS vs. Control)	HT group (n=194)	*P*-value (HT vs. Control)
Serum TE (ng/ml) mean (SD)	4.1 (1.2)	6.8 (1.9)	0.002	5.2 (2.2)	0.328
DHEA-S (ng/dL)	168.5 (65)	278.7 (107)	<0.001	253.9 (93)	0.016
FSH (mlU/mL)	4.6 (0.6)	9.2 (2.5)	<0.001	8.8 (2.1)	<0.001
LH (mlU/mL)	5.7 (2.1)	14.1 (4.1)	<0.001	10.3 (3.2)	<0.001
PRL (ng/mL)	12.9 (3.4)	35.7 (6.2)	<0.001	42.8 (7.3)	<0.001
TSH (μIU/L)	1.8 (0.6)	2.6 (1.1)	0.059	4.9 (2.1)	<0.001
fT4 (pmol/L)	15.8 (3.3)	13.6 (3.8)	0.383	11.2 (2.9)	0.032
TgAb (lU/mL)	1.2 (0.2)	3.5 (0.6)	<0.001	51.4 (12.1)	<0.001
TPOAb (lU/mL)	2.5 (0.5)	3.7 (1.2)	0.043	64.9 (28.4)	<0.001

TE: Testosterone, DHEA-S: Dehydroepiandrosterone-Sulfate, FSH: Follicle-stimulating hormone, LH: Luteinizing hormone, PRL: Prolactin, TSH: Thyroid-Stimulating Hormone, fT4: Free thyroxine, TgAb: Thyroglobulin antibody, TPOAb: Thyroid peroxidase anti-body, SD: Standard deviation

TgAb and TPOAb antibody positivity rates in the PCOS group were 15.7% for TgAb and 38.5% for TPO, both being significantly higher than the corresponding values in the control group (P<0.001). The results are shown in Table 3.

Table 3: Thyroid autoantibody positivity in the PCOS and control groups

Parameters	Control group (n=152)	PCOS group (n=254)	*P*-value
TgAb, n (%)	10 (6.5)	40 (15.7)	<0.001
TPOAb, n (%)	19 (12.5)	98 (38.5)	<0.001

TgAb: Thyroglobulin antibody, TPOAb: Thyroid peroxidase anti-body

Discussion

As the prevalence of endocrinological diseases increases, the relationship between PCOS and autoimmune thyroid disease is becoming increasingly recognized. However, the reason for this relationship is still unclear, and the exact nature of the connection has not yet been elucidated. In polycystic morphology, the ovaries are also a clinical feature of hypothyroidism [6]. Thyroid function tests play an important role in the investigation of ovulatory dysfunction. Thyroid dysfunction should be ruled out before a diagnosis of PCOS, and correct diagnosis is particularly important in this patient group since PCOS can be treated medically.

A connection between PCOS and HT has been reported in several studies. However, the true pathogenesis has not yet been clarified [7]. Although there is no clear link between the underlying causes of hypothyroidism PCOS, studies have shown that the two conditions share many common features, such as chronic anovulation, decreased serum sex hormone binding globulin levels, and increased serum testosterone, LH and cholesterol [8]. We observed a significant increase in ovulatory dysfunction, and in serum testosterone and LH levels in the PCOS and HT groups compared to the control group. BMI, fasting glucose levels, and prevalences of ovulatory dysfunction, hirsutism and acne were also higher in both disease groups compared to the control group. Similarly, high fasting insulin and fasting glucose, and the presence of HOMA-IR in the PCOS and HT group mays indicate a pathogenic link between autoimmunity and insulin resistance [9]. Hormonal, clinical and ultrasonographic similarities have been reported in PCOS patients and in patients with thyroid dysfunction and thyroid antibody [10]. The results of these studies and our own research clearly show the connection between them.

TSH levels in this study were higher in the PCOS group compared to the control group, while fT4 levels were lower, although the differences were not statistically significant. While some studies have reported a significant increase in TSH levels, the increase is more generally reported to be slight [11,12]. The National Academy of Clinical Biochemistry (NACB) recommends the use of 2.5 μIU/mL instead of 4 μIU/mL for TSH levels [13]. In our study, the mean TSH level was 2.6 IU / mL. Occult hypothyroidism is seen in PCOS cases based on the NACB reference range definition.

In our study, the incidence of polycystic ovarian morphology in the HT group was 48.8% (n=89). Studies have shown that ovarian morphology becomes polycystic in the presence of hypothyroidism. Thyroid disorders should be excluded before PCOS is diagnosed [14]. The incidence of the characteristic ultrasonic characteristics of HT in a previous study was 42.3% in a PCOS group and 6.5% in the control group [15]. The presence of similar findings in the two diseases supports the idea of a connection between them.

Autoimmune thyroiditis is three times more common in patients with PCOS among women of reproductive age [16]. Statistically significant increases have been shown in TPOAb and TgAb positivity in PCOS cases [17-19]. In our study, TPOAb and TgAb levels were higher than in the control group. The incidence of TPOAb positivity was 3 times higher and that of TgAb positivity 2.4 times higher compared to the control group. The pathophysiological pathway that connects thyroid disorder with PCOS may thus involve autoimmunity.

There are several limitations to this study, including the small sample size and the population consisting of women from a single center.

Conclusion

Studies indicate a clear connection between PCOS and HT. There is sufficient evidence in the literature to suggest that one of the two diseases increases the prevalence of the other. The current unclear nature of the link between them may possibly be due to the complexity of the etiology of both diseases. We believe that autoimmune susceptibility contributes to the development of the two conditions. Our findings indicate a higher prevalence of TPOAb and TgAb in patients with PCOS. Our data also suggest that thyroid functions and the ovaries should be screened later in life in patients with PCOS and HT.

References

1. Söylemez S, Çaycı Sivri A, Şimşek E, Polat B, Çakır B. Melatonin, leptin, and ghrelin levels in nurses working night shifts. J Surg Med. 2019;3(1):22-6.
2. Karaköse M, Hepsen S, Çakal E, Saykı Arslan M, Tutal E, Akın Ş, et al. Frequency of nodular goiter and autoimmune thyroid disease and association of these disorders with insulin resistance in polycystic ovary syndrome. J Turk Ger Gynecol Assoc. 2017;18(2):85-9.
3. Boufas D, Vryonidou A, Mastorakos G, Ilias I. Thyroid function and autoimmunity versus number of pregnancies. J Reprod Infertil. 2016;17:240-2.
4. Chen CW, Huang YL, Huang RL, Tzeng CR, Chen CH. Idiopathic low ovarian reserve is associated with more frequent positive thyroid peroxidase antibodies. Thyroid. 2017;27:1194-200.
5. Geisthövel F, Rabe T. The ESHRE/ASRM consensus on polycystic ovary syndrome (PCOS)-an extended critical analysis. Reprod Biomed. 2007;14(4):522-35.
6. Singla R, Gupta Y, Khemani M, Aggarwal S. Thyroid disorders and polycystic ovary syndrome: An emerging relationship. Indian J Endocrinol Metab. 2015;19(1):25-9.
7. Ganie MA, Khurana ML, Eunice M, Gupta N, Gulati M, Dwivedi SN, et al. Comparison of efficacy of spironolactone with metformin in the management of polycystic ovary syndrome: an open-labeled study. J Clin Endocrinol Metab. 2004; 89(6):2756-62.
8. Arora S, Sinha K, Kolte S, Mandal A. Endocrinal and autoimmune linkage: Evidences from a controlled study of subjects with polycystic ovarian syndrome. J Hum Reprod Sci 2016;9(1):18-22.
9. Idris I, O'Malley BP. Thyrotoxicosis in Down's and Turner's syndromes: the likelihood of Hashimoto's thyroiditis as the underlying aetiology. Int J Clin Pract. 2000;54(4):272-3.
10. Mohammed S, Awooda HA, Rayis DA, Hamdan HZ, Adam I, Lutfi MF. Thyroid function/antibodies in sudanese women with polycystic ovarian disease. Obstet Gynecol Sci. 2017;60(2):187-92.
11. Al-Saab R, Haddad S. Detection of thyroid autoimmunity markers in euthyroid women with polycystic ovary syndrome: a case-control study from syria. Int J Endocrinol Metab 2014;12(3):e17954.
12. Janssen OE, Mehlmauer N, Hahn S, Offner AH, Gärtner R. High prevalence of autoimmune thyroiditis in patients with polycystic ovary syndrome. Eur J Endocrinol. 2004;150(3):363-9.
13. Baloch Z, Carayon P, Conte-Devolx B, Demers LM, Feldt-Rasmussen U, Henry JF, et al. Laboratory medicine practice guidelines. Laboratory support for the diagnosis and monitoring of thyroid disease. Guidelines Committee, National Academy of Clinical Biochemistry. Thyroid. 2003;13(1):3-126.
14. Sinha U, Sinharay K, Saha S. Thyroid disorders in polycystic ovarian syndrome subjects: a tertiary hospital based cross sectional study from Eastern India. Indian J Endocrinol Metab. 2013;17(2):304–9.
15. Kowalczyk K, Franik G, Kowalczyk D, Pluta D, Blukacz Ł, Madej P. Thyroid disorders in polycystic ovary syndrome. Eur Rev Med Pharmacol Sci. 2017;21(2):346-60.
16. Mobeen H, Afzal N, Kashif M. Polycystic Ovary Syndrome May Be an Autoimmune Disorder. Scientifica (Cairo). 2016;2016:4071735.
17. Arduc A, Aycicek Dogan B, Bilmez S, Imga Nasiroglu N, Tuna MM, Isik S, et al. High prevalence of Hashimoto's thyroiditis in patients with polycystic ovary syndrome: does the imbalance between estradiol and progesterone play a role? Endocr Res. 2015;40(4):204-10.
18. Petrikova J, Lazurova I, Dravecka I, Vrbikova J, Kozakova D, Figurova J, et al. The prevalence of non organ specific and thyroid autoimmunity in patients with polycystic ovary syndrome. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub. 2015;159(2):302-6.
19. Romitti M, Fabris VC, Ziegelmann PK, Maia AL, Spritzer PM. Association between PCOS and autoimmune thyroid disease: a systematic review and meta-analysis. Endocr Connect. 2018;26;7(11):1158-67.

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The effect of electroconvulsive therapy on subclinical inflammation in bipolar disorders

Elektrokonvülsif terapinin bipolar bozukluklarda subklinik inflamasyon üzerine etkisi

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Abstract

Aim: Growing evidence supports the role of inflammation in the etiology of bipolar disorder. Efficacy of electroconvulsive therapy (ECT) in the manic and depressive phases of bipolar disorder is well-known. We aimed to investigate the effect of ECT on the neutrophil/lymphocyte (NLR) and platelet/lymphocyte ratios (PLR), which are newly defined subclinical inflammatory markers in patients with bipolar disorder.

Methods: Patients who received ECT due to the diagnosis of bipolar disorder according to DSM-5 in the last two years and the same number of individuals as the control group were included in this case-control study. NLR and PLR were compared between the patient and control groups, and before and after ECT in the patient group.

Results: A total of 104 individuals were included in the study. Among included patients with bipolar disorder, 39 were in depressive episode and 13 were in manic episode. 52 healthy individuals were identified as control group. Patients' mean age was 36.0 (13.4) years. There were no significant differences between the groups in terms of age, gender, marital status, and smoking. NLR values were significantly higher in the patient group before and after ECT compared to the control group. No difference was found between PLR ratios. There was no significant difference between the NLR, PLR values before and after ECT in the patient group.

Conclusion: This study supports the hypothesis that subclinical inflammation exists in bipolar patients in both manic and depressive phases and it continues after ECT. Large-scale studies are needed to determine the effects of ECT on subclinical inflammation.

Keywords: Neutrophil, Lymphocyte, Monocyte, Electroconvulsive therapy, Bipolar disorder

Öz

Amaç: Biriken kanıtlar, bipolar bozukluğun etiyopatogenezinde enflamasyonun rolünü desteklemektedir. Elektrokonvülsif terapi (EKT) bipolar bozukluğun manik ve depresif dönemlerinde etkindir. Bu çalışmada bipolar bozukluk hastalarında EKT'nin remisyona ulaşan hastalarda yeni bulunan subklinik inflamatuar belirteçler olan nötrofil/lenfosit (N/L), platelet/lenfosit (P/L) oranlarına etkisini araştırmayı amaçladık.

Yöntemler: Bu olgu-kontrol çalışmasına son iki yılda DSM-5'e göre bipolar bozukluk tanısı ile kliniğe yatırılarak EKT uygulanan manik ve depresif dönem hastaları ile aynı sayıda kontrol grubu alındı. Hasta ve kontrol grubu N/L, P/L oranları açısından karşılaştırıldı. Elli iki hasta EKT öncesi ve sonrası N/L, P/L oranları açısından ayrıca karşılaştırıldı.

Bulgular: Çalışmamıza 39 bipolar bozukluk depresif dönem, 13 bipolar bozukluk manik dönem, 52 sağlıklı kontrol olmak üzere toplam 104 olgu alınmıştır. Yaş, cinsiyet, medeni durum, sigara içme açısından sağlıklı kontroller ve hastalar arasında anlamlı fark bulunmamıştır. EKT öncesi hasta grubunda N/L değerleri kontrol grubuna göre anlamlı oranda yüksek bulunmuştur. EKT sonrası N/L değerleri kontrol grubuna göre anlamlı oranda yüksek bulunmuş, P/L oranları arasında fark bulunmamıştır. Hasta grubunda EKT öncesi ve sonrası N/L, P/L değerleri arasında anlamlı fark bulunmamıştır.

Sonuç: Bu çalışma bipolar bozukluk manik/depresif dönem hastalarında subklinik enflamasyonun varlığını ve EKT sonrası bu durumun sürdüğünü desteklemektedir. EKT'nin enflamasyon üzerindeki etkilerini belirlemek için geniş ölçekli çalışmalara gerek vardır.

Anahtar kelimeler: Nötrofil, Lenfosit, Monosit, Elektrokonvülsif terapi, Bipolar bozukluk

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Introduction

The pathophysiology of bipolar disorder is not fully understood. Genetics, circadian rhythms, neurotransmitters, psychosocial factors including childhood traumas, and neuroanatomic changes were blamed in the etiology [1,2]. Accumulative evidence indicates that immune system dysfunction may play a role in the pathophysiology. Elevated levels of proinflammatory cytokines were detected in bipolar disorder [3]. The role of inflammation in mental disorders is not fully established, however, the connection between neurotransmitters and inflammation was shown. Proinflammatory cytokines interact with each other and neurotransmitters in the central nervous system via the cytokine network [4]. The neurotransmitter metabolism changes neuroendocrine function, synaptic plasticity, and related motor activity. These inflammatory cytokines could affect almost all aspects of brain function related to motivational behavior. These effects of the immune system in the brain could cause behavioral consequences and neuropsychiatric disorders [4].

One of the determinants of chronic inflammation is the number of white blood cells and subtypes. The neutrophil/lymphocyte ratio (NLR) is a new parameter indicating systemic inflammatory response [5-7]. Recently, platelet/lymphocyte and lymphocyte/monocyte ratios have been used to determine inflammation [8,9]. It has been reported that NLR and platelet/lymphocyte ratio (PLR), which are subclinical inflammatory markers, are increased in bipolar disorder [10].

Electroconvulsive therapy (ECT) is effective and safe in all manic, depressive, and mixed stages of bipolar disorder [11]. It is a frequently preferred method of treatment for inpatients [12]. Acute immune-inflammatory response increases as an acute stress reaction immediately after ECT sessions. However, after repeated ECT, the inflammatory response decreases at the end of the treatment process [13].

In this study, we report the results of our research on subclinical inflammatory markers, namely, NLR and PLR, and the improvement of symptoms after ECT in patients with bipolar disorder in manic and depressive stages.

Materials and methods

Patients who received ECT due to the diagnosis of bipolar disorder according to DSM-5 in the last two years in the Psychiatry Department of Gaziantep University, Faculty of Medicine and the same number of individuals as the control group were included in this case-control study. Ethics committee approval was obtained from Gaziantep University Clinical Studies Ethics Council (2018/360). 112 patients had undergone ECT for bipolar disorder in the last two years. Patients with severe neurological diseases, diabetes mellitus and other endocrinopathies, liver diseases, malignancies, intellectual disability, alcohol, substance use disorder or addiction history were excluded from the study. Among the remaining 63 bipolar patients in remission in the depression (HAMD<7) and manic (YMRS <12) phases, 11 patients were excluded due to lack of a complete blood count. Among the 52 included, 39 had depressive bipolar and 13 had manic bipolar disorder. Those who had no complaints in the 15 days following ECT (n=52) were identified as the study group. Prior to ECT, all patients had completed evaluations for anesthesia and did not have any active infections. The control group was selected from the last 52 healthy individuals without any disabilities, based on the report issued by the psychiatric outpatient clinic after general screening in the last six months. Sociodemographic variables such as age and gender of the patients were recorded.

ECT was administered bilaterally under general anesthesia after administration of 1 mg/kg propofol seven times a week, on Monday, Wednesday, and Friday at 800 mA with MECTA 5000Q ECT, allowing the patients to have seizures for a period of 30-60 seconds. Patients continued to use additional medication at the beginning of the study. Among 39 patients with bipolar depressive episode, 10 were using lamotrigine, 16 were using valproate, and 6 were using lithium. Five patients were using antidepressants in addition to mood stabilizers. Seven patients who did not use mood stabilizers had quetiapine in their combination. All of 13 the bipolar manic patients were on antipsychotics. 4 of them were using lithium and 4 of them were using valproate in combination with antipsychotics. Four patients with bipolar manic episode had discontinued their medication, and emergency hospitalization had been planned due to manic episode. Haloperidol, biperiden, chlorpromazine injections and additional antipsychotics were used for the treatment of these patients for 3 days and ECT was administered due to exacerbation. They continued to take antipsychotics orally during ECT. There were no patients who did not receive any medication.

52 patients and 52 healthy control individuals were compared in terms of NLR and PLR before and after ECT.

Statistical analysis

Descriptive statistics for demographic characteristics were used to evaluate the data of the patient group. $\chi 2$ test was used to compare categorical variables. T-test was used to compare normally distributed variables, and paired t-test was used for the pre-ECT and post-ECT comparisons of NLR and PLR. Data were analyzed with SPSS v24.0 (IBM Corporation York, United States) for Windows.

Results

The mean age of the patients was 36.05 (13.4) years. The average duration of education was 6.40 (3.5) years. The bipolar patient group consisted of 25 men and 27 women. No significant difference was found between healthy controls and patients in terms of age, sex, marital status, or smoking (Table 1).

Table 1: Sociodemographic data

		ECT	Control	*P*-value
Gender	Male n(%)	25(48.1)	24(46)	0.48
	Female n(%)	27(51.9)	36(54)	
Age mean (SD)		36.05 (13.4)	40.09 (14.8)	0.51
Education (years) mean (SD)		6.40 (3.5)	6.33 (3.99	0.92
Smoking	Yes	31	23	0.11
	No	21	29	

ECT: Electroconvulsive therapy, SD: Standard deviation

NLR values were significantly higher in patients with bipolar disorder than the control group before ECT (P<0.001). PLR did not differ between healthy and control groups (Table 2). After ECT, NLR remained significantly higher in the patient group than in the controls (P=0.003). There was no difference in PLR values (Table 2). No significant difference was found

between NLR and PLR in the pre-ECT and post-ECT evaluation (Table 3), and depressive and manic episodes.

Table 2: Comparisons of NLR and PLR between the patient and control groups before and after ECT

			NLR and PLR comparison before ECT		NLR and PLR comparison after ECT	
		n	Mean (SD)	*P*-value	Mean (SD)	*P*-value
NLR	patient	52	2.74 (1.24)	<0.001	3.22 (3.179	0.003
	control	52	1.91 (0.65)		1.91 (0.659	
PLR	patient	52	135.19 (49.68)	0.739	131.21 (59.77)	0.503
	control	52	138.43 (49.23)		138.43 (49.23)	

ECT: Electroconvulsive therapy, NLR: Neutrophil/lymphocyte ratio, PLR: Platelet/lymphocyte ratio, SD: Standard deviation

Table 3: Comparisons of NLR and PLR before and after ECT

		n	Mean (SD)	*P*-value
NLR	Before ECT	52	2,74 (1.24)	0.273
	After ECT	52	3.22 (3.17)	
PLR	Before PLR	52	135.19 (49.68)	0.611
	After PLR	52	131.21 (59.77)	

ECT: Electroconvulsive therapy, NLR: Neutrophil/lymphocyte ratio, PLR: Platelet/lymphocyte ratio, SD: Standard deviation

Discussion

The first finding of our study was that NLR was higher in patients with bipolar disorder who were on medication than healthy controls. Studies support the role of inflammation in bipolar disorder [3]. The prevalence of bipolar disorder has been shown to increase in patients with autoimmune disorders, cardiovascular diseases, and metabolic dysfunction [14]. Interleukin IL-4, IL-6, IL-10, soluble IL-2 receptor concentrations, tumor necrosis factor (TNF) -alpha, and soluble TNF receptor-1 were significantly higher in patients in the manic and euthymic periods compared to healthy controls [15]. TNF-alpha and IL-6 were found to increase in bipolar depressive period [16,17]. In another study, inflammation was reported as an important predictor of relapse in the course of bipolar disorder, especially during the depressive period [18]. Neutrophil-lymphocyte and platelet-lymphocyte ratios were significantly higher in bipolar disorder in both manic and euthymic patients than in the control group [10]. Our study, in which we found that the NLR values of patients using drugs due to bipolar disorder were higher, also supports these findings.

There were a few studies investigating the effect of ECT on the inflammatory system. More studies are focused on the alteration of inflammatory markers in the treatment of major depression in ECT [19,20]. In our literature review, we could not find a study directly investigating the effect of ECT on NLR and PLR in bipolar disorder. In a study which examined oxidant levels, total antioxidant levels increased with ECT in depressive bipolar patients, and total oxidant levels decreased in manic patients [21]. As an anti-inflammatory agent, celecoxib did not significantly affect BDNF level or treatment response after ECT in bipolar manic patients [22]. In our study, there was no significant alteration in NLR or PLR after ECT.

The retrospective design of the study, the scarce number of patients and the lack of the evaluation of body mass index were the limitations of our study. However, studies investigating the body mass index in relation to inflammation found a very low correlation [23]. Another limitation of the study was that patients were taking various medications. However, the inclusion of antidepressants in complex therapy is thought to alleviate chronic inflammation [24]. Studies reporting that mood regulators decrease inflammatory markers are dominant in the literature [25,26]. There was no significant relationship between antipsychotic use and inflammatory markers [27].

This study demonstrates the presence of subclinical inflammation in bipolar disorder, which continues after ECT. To determine the effects of ECT on inflammation, further studies are needed in large-scale patient groups who do not use drugs.

References

1. Freund N, Juckel G. Bipolar Disorder: Its Etiology and How to Model in Rodents. Psychiatric Disorders. Humana, New York, NY 2019;61-77.
2. Adigüzel V, Özdemir N, Şahin ŞK. Childhood traumas in euthymic patients with bipolar disorder in Eastern Turkey and its relations with suicide risk and aggression. Nordic Journal of Psychiatry. 2019;73(8):490-6.
3. Rosenblat JD, McIntyre RS. Bipolar Disorder and Inflammation. Psychiatr Clin North Am. 2016;39:125-37. doi: 10.1016/j.psc.2015.09.006.
4. Wang TY, Lee SY, Hu MC, Chen SL, Chang YH, Chu CH, et al. More inflammation but less brain-derived neurotrophic factor in antisocial personality disorder. Psychoneuroendocrinology. 2017;85:42-8.
5. Sunbul M, Gerin F, Durmus E, Kivrak T, Sari I, Tigen K, et al. Neutrophil to lymphocyte and platelet to lymphocyte ratio in patients with dipper versus non-dipper hypertension. Clin Exp Hypertens. 2014;36:217-21.
6. Yıldırım ÖT, Akşit E, Aydın F, Aydın AH, Dağtekin E. Can neutrophil to lymphocyte ratio and platelet to lymphocyte ratio be used as biomarkers for non-dipper blood pressure? J Surg Med. 2018;3(1):4-7.
7. Çelen S, Günseren KÖ, Özlülerden Y, Mete A, Tuncay ÖL, Yavaşcaoğlu İ. Does neutrophil-lymphocyte ratio show recurrence in patients who underwent curative resection for non-muscle-invasive bladder cancer? J Surg Med. 2019;3(4):324-7.
8. Krenn-Pilko S, Langsenlehner U, Thurner EM, Stojakovic T, Pichler M, Gerger A, et al. The elevated preoperative platelet-to-lymphocyte ratio predicts poor prognosis in breast cancer patients. Br J Cancer. 2014;13;110:2524-30.
9. Cummings M, Merone L, Keeble C, Burland L, Grzelinski M, Sutton K, et al. Preoperative neutrophil:lymphocyte and platelet:lymphocyte ratios predict endometrial cancer survival. Br J Cancer. 2015;14(113):311-20.
10. Kalelioglu T, Akkus M, Karamustafalioglu N, Genc A, Genc ES, Cansiz A, et al. Neutrophil-lymphocyte and platelet-lymphocyte ratios as inflammation markers for bipolar disorder. Psychiatry Res. 2015;30(228):925-7. doi: 10.1016/j.psychres.2015.05.110.
11. Perugi G, Medda P, Toni C, Mariani MG, Socci C, Mauri M. The Role of Electroconvulsive Therapy (ECT) in Bipolar Disorder: Effectiveness in 522 Patients with Bipolar Depression, Mixed-state, Mania and Catatonic Features. Curr Neuropharmacol. 2017;15:359-371. doi: 10.2174/1570159X14666161017233642.
12. Eroğlu MZ, İçbay E, Tamam L. Bir üniversite hastanesi psikiyatri kliniğinde elektrokonvülzif tedavi uygulanan hastaların demografik ve klinik özellikleri. Dicle Tıp Dergisi. 2012;39(3):371-6.
13. Yrondi A, Sporer M, Péran P, Schmitt L, Arbus C, Sauvaget A. Electroconvulsive therapy, depression, the immune system and inflammation: A systematic review. Brain Stimul. 2018;11:29-51. doi: 10.1016/j.brs.2017.10.013. Epub 2017 Oct 19.
14. Rosenblat JD, McIntyre RS. Are medical comorbid conditions of bipolar disorder due to immune dysfunction? Acta Psychiatr Scand. 2015;132:180-91. doi: 10.1111/acps.12414.
15. Modabbernia A, Taslimi S, Brietzke E, Ashrafi M. Cytokine alterations in bipolar disorder: a meta-analysis of 30 studies. Biol Psychiatry. 2013;1;74:15-25. doi: 10.1016/j.biopsych.2013.01.007.
16. Ortiz-Domínguez A, Hernández ME, Berlanga C, Gutiérrez-Mora D, Moreno J, Heinze G, et al. Immune variations in bipolar disorder: phasic differences. Bipolar Disord. 2007;9:596-602.
17. Brietzke E, Stertz L, Fernandes BS, Kauer-Sant'anna M, Mascarenhas M, Escosteguy Vargas A, et al. Comparison of cytokine levels in depressed, manic and euthymic patients with bipolar disorder. J Affect Disord. 2009;116:214-7.
18. Bond DJ, Andreazza AC, Hughes J, Dhanoa T, Torres IJ, Kozicky JM, et al. Association of peripheral inflammation with body mass index and depressive relapse in bipolar disorder. Psychoneuroendocrinology. 2016;65:76-83. doi: 10.1016/j.psyneuen.2015.12.012.
19. Freire TFV, Rocha NSD, Fleck MPA. The association of electroconvulsive therapy to pharmacological treatment and its influence on cytokines. J Psychiatr Res. 2017 Sep;92:205-11. doi:10.1016/j.jpsychires.2017.05.004.
20. Yrondi A, Sporer M, Péran P, Schmitt L, Arbus C, Sauvaget A. Electroconvulsive therapy, depression, the immune system and inflammation: A systematic review. Brain Stimul. 2018;11:29-51. doi: 10.1016/j.brs.2017.10.013.
21. Bulut M, Altındağ A, Deveci Z, Kaya MC, Bülbül F, Taşkın A, et al. Oxidative parameters in bipolar patients treated with electroconvulsive therapy and pharmacotherapy. Journal of Mood Disorders. 2013;3:93-9.
22. Kargar M, Yoosefi A, Akhondzadeh S, Artonian V, Ashouri A, Ghaeli P. Effect of Adjunctive Celecoxib on BDNF in Manic Patients Undergoing Electroconvulsive Therapy: a Randomized Double Blind Controlled Trial. Pharmacopsychiatry. 2015;48:268-73. doi: 10.1055/s-0035-1559667.
23. Howren MB, Lamkin DM, Suls J. Associations of depression with C-reactive protein, IL-1, and IL-6: a meta-analysis. Psychosom Med. 2009;71(2):171-86. doi: 10.1097/PSY.0b013e3181907c1b.
24. Huang G, Chen H, Wang Q, Hong X, Hu P, Xiao M, et al. High platelet-to-lymphocyte ratio is associated with post-stroke depression. J Affect Disord. 2018;246:105-11. doi: 10.1016/j.jad.2018.12.012.
25. Himmerich H, Bartsch S, Hamer H, Mergl R, Schönherr J, Petersein C, et al. Modulation of cytokine production by drugs with antiepileptic or mood stabilizer properties in anti-CD3-and anti-Cd40-stimulated blood in vitro. Oxid Med Cell Longev. 2014;2014:806162
26. Boufidou F, Nikolaou C, Alevizos B, Liappas IA, Christodoulou GN. Cytokine production in bipolar affective disorder patients under lithium treatment. Journal of Affective Disorders. 2004;82(2):309-13.
27. Mørch RH, Dieset I, Færden A, Hope S, Aas M, Nerhus M, Aukrust P. Inflammatory evidence for the psychosis continuum model. Psychoneuroendocrinology. 2016;67:189-97.

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Survival outcomes of percutaneous endoscopic gastrostomy, comparison of cerebrovascular event and non-cerebrovascular event in malnourished patients

Perkütan endoskopik gastrostomi'nin sağkalım sonuçları, serebrovasküler olay geçiren ve geçirmeyen kötü beslenen hastaların karşılaştırılması

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Abstract

Aim: The number of comorbid diseases increased with the rise in the elderly population. In some cases, the state of deficient or absent nutrition emerges. Nevertheless, the contribution of percutaneous endoscopic gastrostomy (PEG) to the quality of life and the survival rate in the elderly with certain diseases remains controversial.

Methods: In this prospective cohort study, patients who underwent percutaneous endoscopic gastrostomy (PEG) procedure between 2009 and 2015 were divided into two groups: CVE group consisted of patients with cerebrovascular event (CVE) and non-CVE group comprised patients who suffered from esophageal tumors, head and neck tumors, brain tumors, amyotrophic lateral sclerosis and terminal dementia. In this study, the patients' pre-PEG and post-PEG body mass index (BMI) values, hemoglobin (Hb), albumin (alb), creatinine (Cr) and C-reactive protein (CRP) values, white blood cell counts, demographic characteristics, 30, 90, 180 and 365 day-survival rates, complications (mechanical, metabolic and infectious) and duration of patency of the PEGs were compared.

Results: The average age was lower while survival rate on the 90th day was higher in the CVE group. No significant difference was found in terms of other parameters. At the end of the one-year follow-up, 21% of the patients in the CVE group and 12% of those in the non-CVE group were able to be fed without PEG.

Conclusion: PEG patency was higher in the CVE group at 3 months but there was no statistically significant difference between the groups at one-year and overall follow-up periods.

Keywords: Cerebrovascular events, Enteral nutrition, Percutaneous endoscopic gastrostomy

Öz

Amaç: Yaşlı popülasyonda birden fazla hastalığın görülmesi gitgide artmaktadır. Bazı olgularda beslenme azlığı veya yokluğu acil durum yaratmaktadır. Bununla birlikte perkütan endoskopik gastrostominin (PEG), ciddi hastalıkları olan yaşlı hastalarda hayat kalitesi ve sağkalım oranına katkısı tartışmalıdır.

Yöntemler: Bu prospektif kohort çalışmada, 2009-2015 yılları arasında PEG açılan hastalar 2 gruba bölündü: Bu gruplar, SVO grubu denen serebrovasküler olay (SVO) geçiren hastalar ve özofagus tümörü, baş ve boyun tümörleri, beyin tümörleri, amiyotrofik lateral skleroz ve terminal demansı olan hastalardan oluşan non-SVO grubunu kapsamaktadır. Bu çalışmada, hastaların PEG öncesi ve sonrası olmak üzere vücut kitle indexi(VKİ) değerleri, hemoglobin (Hb), albümin (alb), kreatinin (Kr), C-reaktif protein (CRP), lökosit, demografik özellikleri, 30, 90, 180 ve 365 günlük sağkalım oranları, mekanik, metabolik ve infeksiyöz komplikasyonları PEG varlığı boyunca karşılaştırıldı.

Bulgular: SVO'lu olgularda ortalama yaş grubu düşük olanlarda 90. Gündeki sağkalım oranı daha yüksekti. Diğer parametrelerde belirgin bir fark yoktu. 1 yılın sonunda SVO'lu olguların % 21'i PEG'siz beslenebilirken, bu oran non-SVO'lu olgularda %12 olarak saptandı.

Sonuç: PEG'le beslenme 3 aylık izlemde SVO'lu olgularda daha yüksek oranda bulunurken; 1 yıllık ve total izlemde her iki grup arasında anlamlı farklılık bulunmadı.

Anahtar kelimeler: Serebrovasküler olay, Enteral beslenme, Perkütan endoskopik gastrostomi

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Introduction

If the enteral system is functional but the oral intake is not possible, feeding via percutaneous endoscopic gastrostomy (PEG) is preferred instead of the nasoenteral route [1]. Feeding via PEG is the most preferred long-term enteral feeding method due to easy and expeditious applicability and the lack of requirement for general anesthesia or operating room facilities. Due to the increased lifespan of the elderly population, accompanying diseases have also rocketed. Some of these patients encounter problems due to absent or improper nutrition. Stroke is the most prominent condition that negatively affects nutrition in the elderly patients. Pneumonia can increase mortality rates in stroke patients. Şimşek et al. [2] performed a cohort study about mortality factors, especially pneumonia, at stroke, and found mortality rate to be 30.4%. PEG feeding is a preferred feeding method which may reduce the risk of pulmonary infections in long-term coma patients due to stroke or traumatic brain injury [3]. Joundi and coworkers [4] reported that gastrostomy and jejunostomy placement after stroke was associated with lowering 30-day mortality. However, the contribution of PEG feeding to the quality of life and the survival rate is still controversial in the elderly population suffering from certain diseases.

In this study, we aimed to compare the demographic characteristics, 30, 90, 180 and 365-day survival rates, duration of PEG patency, clinical and laboratory nutritional parameters between patients in need of PEG for enteral feeding due to cerebrovascular event (CVE) or other causes.

Materials and methods

Ethics approval was obtained from Yeditepe University Clinical Trials Ethics Committee (Approval form number: 342) on 18 June 2013. Patients over 18 years of age who underwent PEG placement procedure between January 2009 and January 2015 at Yeditepe University Hospital were included in this study, and relevant patient information was obtained from patient files and hospital registry. This study was conducted in accordance with the principles of the Declaration of Helsinki, and in compliance with all international and national laws and regulations. Patients gave their written informed consent before any procedure was performed.

Investigators conducted the interviews by phone with the family members with their consent. A gastroenterologist performed the PEG placement procedures in the endoscopy unit under intravenous sedation, local anesthetics and using the pull method with a 20F silicone tube. Before the procedure, intravenous cefuroxime was administered for prophylaxis.

Patients were divided into CVE group and non-CVE group (those with esophageal tumors, head and neck tumors, brain tumors, amyotrophic lateral sclerosis (ALS), and terminal dementia) based on the indications for PEG placement.

A total of 130 patients underwent PEG placement procedure, among which 92 patients' data were obtained. All patients' pre-PEG and post-PEG body mass indexes (BMI), hemoglobin (Hb), albumin (alb), creatinine (Cr), and C-reactive protein (CRP) levels, white blood cell counts and complications (mechanical, metabolic, and infectious) were compared.

Statistical analysis

The data were expressed as mean (SD), median and with 95% confidence interval. Log-rank test and Kaplan Meier Curve were used for survival analysis. SPSS v22 software was used for statistical analysis.

Results

Among the 92 patients included, 27 were female and 65 were male. The mean age of all patients was 63 (39) years. Overall, the mortality rate during the six-year follow-up was 63%. The mean age, total survival and median survival rates according to follow-up visits after PEG, PEG patency, 30-day, 90-day, 180-day and one year total survival and median survival rates in CVE (65 patients) and non-CVE group (27 patients) are presented in Table 1.

The mean age was lower and 90-day survival rate was higher in the CVE group. There was no revelatory variation in terms of other parameters. Hemoglobin, CRP, albumin, creatinine, white blood cell count, and BMI parameters did not significantly differ between the groups before and after feeding via PEG (Table 2). Twenty six (40%) of the 65 patients with PEGs placed due to CVE had mechanical, five (8%) had metabolic and 29 (45%) had infectious complications, while 15 (55%) of the 27 patients with PEG placed due to non-CVE causes had mechanical, four (15%) had metabolic and 13 (55%) had infectious complications.

Table 1: Survival, lifespan of PEG and median survival at the CVE and non-CVE patients

	CVE (n=65) Mean(SD)	Non-CVE (n=27) Mean(SD)	*P*-value
Age (y)	58(18)	74(19)	0.001
After peg follow-up (month)	19(17)	14(13)	0.255
Lifespan with PEG (month)	12(10)	9(8)	0.374
Median survival (month)	20(13)	20(12)	0.274
Survival (%)			
30 d	94	92	0.694
90 d	78	55	0.041
180 d	61	50	0.391
1 y	56	50	0.637
Total (end of the study)	39	33	

CVE: Cerebrovascular event, PEG: Percutaneous Endoscopic Gastrostomy, SD: standard deviation, D: days, Y: year

Table 2: Comparing of the beginning and the last laboratory findings at the CVE and non-CVE patients

	CVE n: 65			Non-CVE n: 27		
	First Mean(SD)	Last Mean(SD)	*P*-value	First Mean(SD)	Last Mean(SD)	*P*-value
Hemoglobin (gr/dl)	11.9(1.8)	11.8(1.7)	0.145	10.8(1.4)	10.9(1.7)	0.156
CRP (mg/dl)	38(31)	52(45)	0.779	52(39)	39(29)	0.588
Albumin (gr/dl)	3.4(0.6)	3.3(0.4)	0.275	3.0(0.5)	3.4(0.4)	0.224
Creatinine (mg /dl)	0.67(0.31)	0.7(0.5)	0.135	0.69(0.29)	0.65(0.34)	0.423
Leucocyte	9.1(3.8)	8.9(3.3)	0.050	9.8(3.1)	9.2(2.7)	0.990
BMI (kg/m^2)	24.7(5.1)	22.8(3.5)	0.131	20.9(4.5)	19.5(3.2)	0.158

CVE: Cerebrovascular event, SD: standard deviation, CRP: C-reactive protein

In the CVE and non-CVE groups, the oral intakes of the patients were 4% and 13%, respectively (P=0.189), and the need of total parenteral nutrition (TPN) was 27% and 22%, respectively (P=0.594). Mixed feeding rates were 17% in the CVE group and 14% in the non-CVE group (P=0.077). At the termination of the study, PEG functionality in the CVE and non-CVE groups were 10% and 14%, respectively (P=0.334). The survival rates of the groups are presented in Figure 1. According to the Kaplan-Meier survival analysis, there was no significant difference between median survival rates (20 (13) months versus 20 (12) months (P=0.274)) (Figure 2).

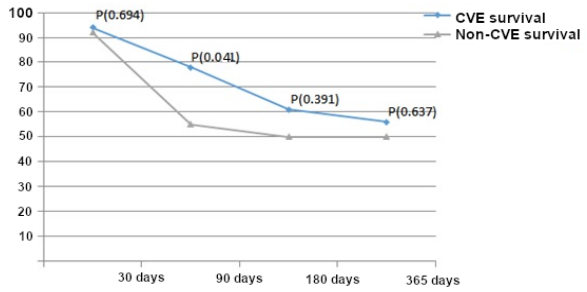

Figure 1: Survival rates of the groups

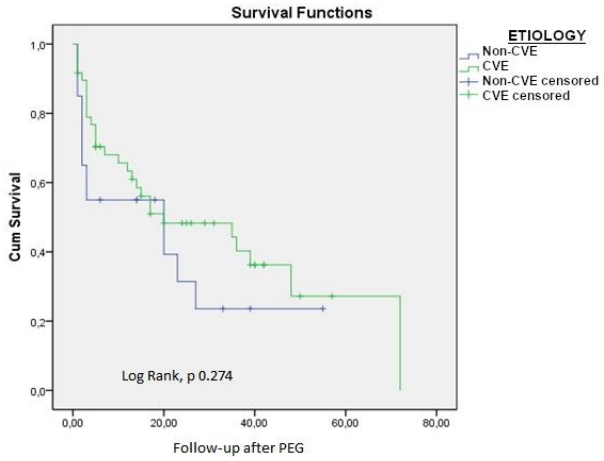

Figure 2: Median survival rates

The ratios of patients who were orally fed in the following months are shown in Table 3. At the end of one year, 21% of the patients in the CVE group and 12% in the non-CVE group were orally fed.

Table 3: Feeding without PEG ratios at the CVE and non-CVE patients at the proceeding months

Days (d)	CVE group Patient %	Patient feeding without PEG%	Patient feeding with PEG%	Non-CVE group Patient %	Patient feeding without PEG%	Patient feeding with PEG%
30 d	94	10	84	92	11	81
90 d	78	8	70	55	7	48
180 d	61	14	47	50	2	48
365 d	56	21	35	50	12	38

CVE: Cerebrovascular event, PEG: Percutaneous Endoscopic Gastrostomy, D: days

Discussion

In the last 20 years, seven international and 17 national studies on PEG case series have been conducted in this country. Among these, 15 neurological patients were studied by Bayraktar et al. [5] and 5 neurological patients were evaluated by Muftuoglu et al. [6]. In the remaining studies, neurological/paralytic subgroup analysis was not performed. Therefore, our study is a pioneer in this field in the country.

The 30-day mortality rate in the study was 6% in the CVE group, while in many studies the 30-day mortality after the PEG has been reported between 18% and 25% [7-11]. The lower 30-day mortality rate in this study may be associated with non-problematic values of baseline BMI, hemoglobin, albumin, creatinine, white blood cell count and a low average of subject ages. In the study conducted by Mitchell and Tetroe, factors such as age, malignancy, male sex, and hypoalbuminemia were found to be associated with increased mortality [12]. Albeit insignificant, higher CRP levels as well as lower BMI and albumin values before PEG placement in the non-CVE group may explain the significantly low 90-day survival rates compared to the CVE group (Table 1). Likewise, Blomberg et al. [13] also demonstrated a seven-fold increase in mortality rates in patients with low albumin, high CRP, BMI <18.5 and >65 years of age compared to patients with normal albumin and CRP values.

In this study, the prevalence of infectious complications after PEG placement was 55% in the non-CVE group and 45% in the CVE group. Higher CRP levels in the non-CVE group before PEG placement may be the reason for the rise in infectious complications.

In Malmgren et al.'s study [14] on 201 stroke patients with a mean age of 81 years, the 90-day and one-year mortality rates were 46% and 67%, respectively. The same rates in our study turned out lower with 22% 90-day mortality and 44% one-year mortality in the CVE group (mean age: 58 years). In a study performed by Callahan et al. [8] on 150 patients, the one-year mortality rate was similarly 47%. The lower average age in this trial could be the reason of lower mortality rate. Median survival span in James et al.'s study [15] was 305 days, while in the current study, it was twenty months (600 days) in the CVE group. James et al. [15] conducted this study in stroke patients with dysphagia between 1991-1995 and reported the demise of twenty-eight percent of the cases due to aspiration pneumonitis during hospital stay.

The low median survival rate may be related to the fact that in those years, experience with the PEG placement technique was constrained and patient monitoring was not as thorough as today.

Studies investigating the natural course of dysphagia following CVE showed that it spontaneously resolved in 7-14 days after the event in 73%-86% of patients [7,17,18]. Thus, it may be recommended to wait for 2-3 weeks before PEG placement in CVE cases.

In this study, 10% of the patients in the CVE group could be fed without PEG toward the finish of the first month, while 21% of the subjects could be orally fed at the end of the first year. In the non-CVE group, the ratios were determined as 11% and 12%, respectively. The proportion of feeding without PEG did not increment in the forthcoming time frames.

The ESPEN guideline [1] assesses the outcomes of the FOOD [17] and other studies on enteral nutrition in CVE patients with dysphagia and recommends that enteral nutrition should be initiated at the earliest opportunity except in contradictory cases in geriatric patients. Feeding via PEG should be favored over nasogastric tube due to better nutritional support and better long-term treatment outcomes [18].

Limitations

There are various limitations to our study, the first one being the unevenly distributed gender. There were 37 females and 65 males. Secondly, the time between the baseline laboratory tests obtained before PEG placement and the last laboratory tests was not equal in all patients. Both limitations may have confounded the results.

Conclusion

PEG is recently considered to reduce mortality in selective populations. In our study, although 3-month survival rates after PEG placement was higher in the CVE group, no significant difference was detected in terms of survival rates between the groups at one year and overall follow-up times. Mortality rate was lower than many other studies. However, there are also studies showing an increase in mortality in the first

months, especially in CVE patients. Mortality studies in elderly and PEG-placed patients have varying results. Further studies with higher number of patients and more homogeneously distributed age and gender groups are needed to illuminate the advantages and disadvantages of PEG placement.

References

1. Volkert D, Berner YN, Berry E, Cederholm T, Coti Bertrand P, Milne A, et al. ESPEN guidelines on enteral nutrition: geriatrics. Clin Nutr. 2006;25:330-60.
2. Şimşek KB, Özer G. Evaluation of stroke mortality and related risk factors: A single-center cohort study from Gaziantep, Turkey. J Surg Med. 2019;3(3):231-4.
3. Song RR, Tao YF, Zhu CH, Ju ZB, Guo YC, Ji Y. Effects of nasogastric and percutaneous endoscopic gastrostomy tube feeding on the susceptibility of pulmonary infection in long-term coma patients with stroke or traumatic brain injury. Zhonghua Yi Xue Za Zhi. 2018 Dec 25;98(48):3936-40.
4. Joundi RA, Saposnik G, Martino R, Fang J, Kapral MK. Timing of Direct Enteral Tube Placement and Outcomes after Acute Stroke. J Stroke Cerebrovasc Dis. 2019 Sep 28:104401.
5. Bayraktar Y, Koseoglu T, Sivri B, Kansu T, Kayhan B, Varli K, et al. PEG in patients with complete dysphagia due to neurological diseases. Turk J Gastroenterol. 1993;4(4):664-7.
6. Muftuoglu M, Erturk O, Karinoglu M, Gurer S, Yilmaz H, Akin O, et al. PEG in neurological diseases: Indications and complications. Turk J Gastroenterol. 1995;6(1):128-31.
7. Skelly RH, Kupfer RM, Metcalfe ME, Allison SP, Holt M, Hull MA, et al. Percutaneous endoscopic gastrostomy (PEG): change in practice since 1988. Clin Nutr. 2002;Oct;21(5):389-94.
8. Callahan CM, Haag KM, Weinberger M, Tierney WM, Buchanan NN, Stump TE, et al. Outcomes of percutaneous endoscopic gastrostomy among older adults in a community setting. J Am Geriatr Soc. 2000;48:1048-54.
9. Fisman DN, Levy AR, Gifford DR, Tamblyn R. Survival after percutaneous endoscopic gastrostomy among older residents of Quebec. J Am Geriatr Soc. 1999;47:349-53.
10. Fraser GM, Abuksis G, Mor M, Segal N, Shemesh I, Plout S, et al. Percutaneous endoscopic gastrostomy: high mortality rates in hospitalized patients. Am J Gastroenterol. 2000;95:128-32.
11. Ha L, Hauge T. Percutaneous endoscopic gastrostomy (PEG) for enteral nutrition in patients with stroke. Scand J Gastroenterol. 2003;9:962-6.
12. Mitchell SL, Tetroe JM. Survival after percutaneous endoscopic gastrostomy placement in older persons. J Gerontol A Biol Sci Med Sci. 2000;Dec;55(12):735-9.
13. Blomberg J, Lagergren P, Martin L, Mattsson F, Lagergren J. Albumin and C-reactive protein levels predict short-term mortality after percutaneous endoscopic gastrostomy in a prospective cohort study. Gastrointest Endosc. 2011;Jan;73(1):29-36.
14. Malmgren A, Hede GW, Karlström B, Cederholm T, Lundquist P, Wirén M, et al. Indications for percutaneous endoscopic gastrostomy and survival in old adults. Food Nutr Res 2011; 55:6037.
15. James A, Kapur K, Hawthorne AB. Long-term outcome of percutaneous endoscopic gastrostomy feeding in patients with dysphagic stroke. Age Ageing 1998;Nov;27(6):671-6.
16. Dennis MS, Lewis SC, Warlow C; FOOD Trial Collaboration. Effect of timing and method of enteral tube feeding for dysphagic stroke patients (FOOD): a multicenter randomized controlled trial. Lancet 2005;365:764-72.
17. Smithard DG, O'Neill PA, England RE, Park CL, Wyatt R, Martin DF et al. The natural history of dysphagia following a stroke. Dysphagia 1997;Fall;12(4):188-93.
18. Gordon C, Hewer RL, Wade DT. Dysphagia in acute stroke. Br Med J (Clin Res Ed). 1987 Aug 15;295(6595):411-4.

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Assessment of parotid gland masses with B-mode ultrasonography and strain elastography findings

Parotis bezi kitlelerinin B-mod ultrasonografi ve strain elastografi bulguları ile değerlendirilmesi

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Abstract

Aim: Ultrasound elastography (USE) has been found useful in differentiation between malignant and benign lesions of various tissues, such as the thyroid, breast, lymph node and prostate, however, there is limited data on the parotid gland. The aim of this study is to assess the diagnostic performance of B-mode ultrasonography (US) and USE findings in differentiating between benign and malignant parotid gland masses. A secondary goal is to evaluate results for the most frequent benign lesions.

Methods: In this cross-sectional study, 57 masses in 48 patients were evaluated. 2 radiologists examined each patient. B-mode US (size, contour, skin depth, internal structures, calcification, cystic component) and USE (a semiquantitative value strain index (SI)) findings were noted. We considered each feature individually. All patients underwent fine needle aspiration cytology (FNAC) and surgical resection.

Results: 50 masses were benign and 7 were malignant. Among B-mode US results, contour irregularity was found to have the highest accuracy (85.7%) in differentiating malignant lesions. When USE findings were considered, intra-observer agreement was moderate to fair and interobserver agreement was moderate. Malignant masses had mildly high SI scores. There was a wide range overlap between malignant and benign lesions. There was no statistically significant difference (P=0.422) and we could not attain a reliable SI cut-off value.

Conclusion: Despite the promising results of USE in breast and thyroid lesions, conventional US findings and FNAC are still the primary diagnostic tool to evaluate parotid lesions.

Keywords: Ultrasound elastography, Strain elastography, Strain index, Parotid gland

Öz

Amaç: Ultrason elastografi (USE) tiroid, meme lenf nodu ve prostat dokularının benign ve malign lezyonlarının ayrımında kullanışlı bulunmuştur. Bununla birlikte parotis bezindeki kullanımında sınırlı data mevcuttur. Biz bu çalışmada parotis bezi lezyonlarında benign malign ayrımında B-mod ultrasonografi (US) ve USE bulgularının tanısal performansını değerlendirmeyi amaçladık. İkincil hedef olarak da en sık rastlanan benign parotis bezi lezyonlarını kendi içerisinde değerlendirmeyi hedefledik.

Yöntemler: Bu kesitsel çalışmada 48 hastada 57 lezyon değerlendirilmeye alındı. Her hasta iki radyolog tarafından muayene edildi. B-mod US (boyut, kontur, ciltten derinlik, içyapı, kalsifikasyon, kistik komponent) ve USE (gerinim oranı olarak belirtilen yarı nicel değer) bulguları not edildi. Her bulgu ayrı ayrı değerlendirildi. Her hastaya ince iğne aspirasyon biyopsisi ve sonrasında cerrahi rezeksiyon uygulandı.

Bulgular: Lezyonların 50'si benign, 7'si malign olarak patolojik tanı aldı. B-mod ultrason bulguları dikkate alındığında düzensiz kontur özelliğinin malign lezyonların ayrımında en yüksek doğruluk oranına (%85,7) sahip olduğu görüldü. USE bulguları değerlendirildiğinde gözlemciler içi uyum orta-ortanın altında; gözlemciler arası uyum ise orta olarak saptandı. Malign kitleler benign olanlar ile kıyaslandığında hafif daha yüksek gerinim oranı değerlerine sahip olmakla birlikte istatistiksel olarak anlamlı fark tespit edilmedi (P=0,422) ve güvenilir bir eşik değer saptanamadı.

Sonuç: USE ile meme ve tiroid lezyonlarındaki umut verici sonuçlar elde edilmesine rağmen parotis kitlelerinin değerlendirilmesinde konvansiyonel US bulguları ve ince iğne aspirasyon biyopsisi hala temel tanı aracı olarak geçerliliğini sürdürmektedir.

Anahtar kelimeler: Ultrason elastografi, Strain elastografi, Gerinim oranı, Parotis bezi

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Introduction

Malignant or benign type of histology, superficial or deep localization of the tumor and differentiation between Warthin tumor and pleomorphic adenoma in benign tumors defines the type of the surgical approach [1]. Although FNAC is considered the gold standard in diagnosis, its sensitivity and specificity varies within a wide range, between 57-98% and 56-100% respectively, with an accuracy of 78-98% [2,3]. Ultrasonography (US) and magnetic resonance imaging (MRI) are the main non-invasive imaging techniques for the evaluation of parotid gland masses. Despite the fact that US and MRI characteristics of parotid lesions are already known, there is notable overlap in imaging findings [4,5]. Therefore, additional methods are needed. USE is an imaging technique based on the evaluation of the differences in tissue stiffness [6,7]. The method was found especially useful in differentiation of malignant and benign breast masses and thyroid nodules [8-12]. The current data regarding the use of this method in the parotid gland is limited. Our aim in this study is to compare strain elastography and B-mode US findings in differentiating between malignant and benign lesions of the parotid gland, and our secondary aim is to evaluate our results for differentiating between pleomorphic adenoma and Warthin tumor, which are the most frequently encountered benign tumors.

Materials and methods

Study design and patient selection

Patients who were diagnosed with intraparotid masses following clinical examination and radiological imaging for the first time, who were between the ages of 18-80 and had no previous surgical intervention were included in this study. Patients with recurring symptoms, extraparotid masses and those younger than 18 or older than 80 years were excluded. Our study was approved by the ethics review committee in accordance with the Declaration of Helsinki. All patients signed an informed consent.

Technique

Two experienced radiologists performed sonographic examinations in a dimly lit room. Patients were evaluated for both parotid glands while lying in supine position with their necks hyperextended. US and USE were performed with the same equipment, using a 17.5 MHz linear probe with elastography software (IU22 digital ultrasonography Philips, Bothell, Washington, USA). B-mode US and sonoelastography images of all cases were obtained. B-mode examination was performed first and size, contour, skin depth, internal structures, calcification, cystic component features of the masses were noted. USE examination followed, using the same transducer in elastographic mode for obtaining real time elastography images. Transducer was held perpendicular to the skin. Minimal compression was applied by the aid of pressure indicator located to the right side of the screen to improve intra and interobserver agreement. Elastograms were located to the right side of the screen and corresponding B-mode images were on the left. Examination frame including the whole mass and surrounding normal parotid tissue was adjusted. Depending on the degree of their stiffness, tissues were color-coded in red and blue with corresponding soft and hard areas with a colorimetric scale. A region of interest (ROI) circle was placed in the area thought to be the stiffest part of the mass while avoiding cystic parts and calcifications. Another ROI with the same diameter was placed at the same depth in the normal parotid tissue. The software assessed a semiquantitative value for SI within the ROI. Both radiologists reviewed two USE images of each mass. A total of four measurements were recorded for each lesion. The highest SI value was defined as SI_{max} after evaluation by each observer both individually and together (Figures 1-3).

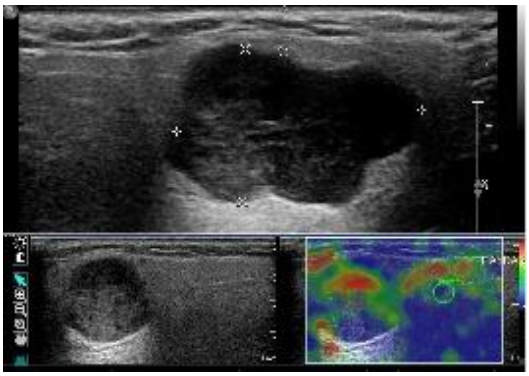

Figure 1: Hypoechogenic solid lesion with lobulated contours and posterior enhancement (SI value: 5.34. Mass is diagnosed as Pleomorphic Adenoma with FNAC.)

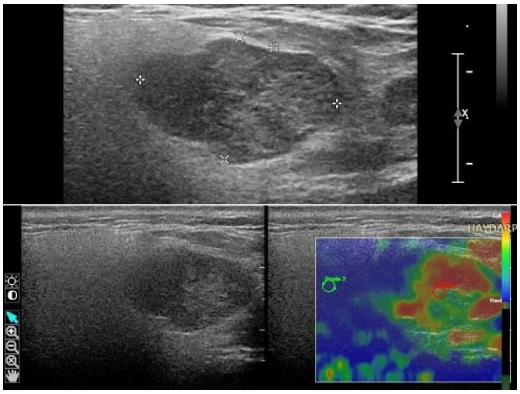

Figure 2: Well-defined hypoechoic lesion with internal microcystic spaces (SI value: 7.86, diagnosed as Warthin Tumor with FNAC.)

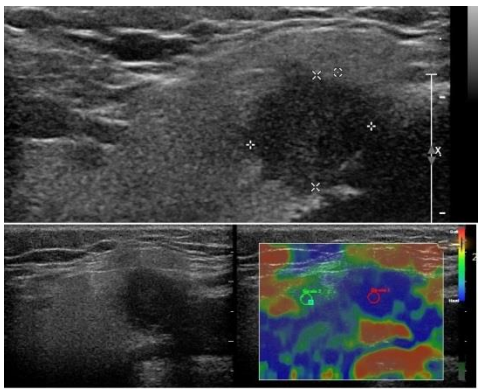

Figure 3: Ill-defined heterogeneous mass lesion with irregular contours (SI value: 2.58, diagnosed with mucoepidermoid carcinoma by FNAC.)

Histopathological diagnosis

The cytopathologist blinded to radiological findings evaluated FNAC. Each patient diagnosed on basis of pathologic examination underwent surgical resection.

Statistical analysis

Descriptive statistics were used to define the characteristics of the continuous variables (mean (standard deviation (SD)) and minimum-median-maximum). Independent and normally distributed two continuous variables were compared with the Student's t-test, while independent and non-normally distributed variables were compared using the Mann

Whitney U test. Chi-square or Fisher's Exact test were used to summarize the relations between categorical variables. To determine intraobserver and interobserver agreement degree, weighted kappa statistics were used. Interpretation was as follows: <0.00 poor agreement, 0.00–0.20: slight agreement, 0.21–0.40: fair agreement, 0.41–0.60: moderate agreement, 0.61–0.80: substantial agreement, and 0.81–1.00: excellent agreement [13]. P<0.05 was considered statistically significant. Analyses were performed with MedCalc Statistical Software version 12.7.7 (MedCalc Software bvba, Ostend, Belgium; http://www.medcalc.org 2013) program.

Power analysis was performed with G*Power 3.1.9.4 software. The power of this data was calculated as 1-β=0.82 with n1=50, n2=7, α=0.05 and an effect size of d=1.05.

Results

Forty-eight patients (24 females, 24 male) were included in the study. Age range was between 15-87 years (53 (15.5)). Two patients were excluded from the study due to the lack of a reliable elastographic measurement: The first case had a mass located 15mm deep from the skin surface with half of the lesion extending behind the mandible. The second case had a 4x4 cm mass protruding from skin surface, both of which prevented accurate elastographic examination.

Among 57 masses, 50 masses (87.7%) were benign and 7 masses (12.3%) were malignant. Histological subtypes included 2 lymphomas (3.5%), 5 basal cell adenomas (7.1%), 1 oncocytoma (1.7%), 1 large cell undifferentiated carcinoma (1.7%), 1 granuloma (1.7%), 1 hemangioma (1.7%), 1 metastasis (1.7%), 2 mucoepidermoid carcinomas (3.5%), 1 high grade acinic cell carcinoma (1.7%), 17 pleomorphic adenomas (29.8%), and 25 Warthin tumors (43.8%). FNAC results were confirmed after examination of the whole resection specimen.

Short axes of masses ranged from 4 mm to 37 mm (: 15 (6.8) mm) while long axes ranged from 8 to 45mm (: 15 (6.8) mm). Skin depth of the lesions ranged between 2 mm and 9 mm (: 3 (1.5) mm).

46 (95%) patients had unilateral, and 2 (5%) patients had bilateral (one basal cell adenoma, one Warthin tumor) masses. 39 patients (81.9%) had single, and 9 patients (18.1%) had multiple masses (8 Warthin tumors, 1 lymphoma).

During B-mode ultrasonography, contour, tumor size, internal structure, cystic component, calcification features were noted for each mass (Table 1).

Contour irregularity was the most useful parameter among all B-mode sonography findings (sensitivity 28.5%, specificity 93.8%, accuracy 85.7%) in differentiating between benign and malign masses (Table 2). Heterogeneity of internal structure wasn't found useful in differenting malignant masses (sensitivity 57.1%, specificity 44.1%, accuracy 46%) from benign ones. We observed calcification in both malignant (one high grade acinic cell carcinoma, one metastasis) and benign (two Warthin tumor) masses.

In differential diagnosis of the most frequent benign masses, contour lobulation of the pleomorphic adenoma and the presence of the cystic component in the Warthin tumor were evaluated (Table 3).

Following the B-mode examination, two radiologists recorded two sonoelastography measurements from each lesion. Upon consideration of SI_{max} values, intraoberserver agreement was moderate for the first (0.532) and fair for the second observer (0.375), and interobserver agreement was moderate (0.481).

The SI_{max} data from the elastography measurements were evaluated individually and together for each observer. Malignant masses showed mildly higher elastography scores than benign masses, which were statistically insignificant (Table 4).

Among malignant masses, large cell undifferentiated carcinomas showed the highest SI value (6.91), followed by lymphomas (4.6 (0.8)), mucoepidermoid carcinomas (3.97 (2,1)), metastases (3.9), and high grade acinic cell carcinoma (2.11).

Pleomorphic adenoma and Warthin tumor were the most common benign masses evaluated by USE. No reliable cut-off value could be demonstrated (*P*=0.990).

Table 1: B-mode US features of the masses

Feature	Benign n=50 Pleomorphic adenoma n=17	Warthin tumor n=25	Others n=8	Malignant n=7
Contour				
Regular	6	22	5	5
Lobulated	8	2	0	0
Irregular	1	1	1	2
Internal structure				
Homogenous	9	10	0	3
Heterogeneous	5	13	6	4
Cystic component				
Present	2	23	5	5
Absent	13	2	1	2
Calcification				
Present	0	2	0	2
Absent	17	23	8	5

Table 2: Diagnostic performances of irregular contour and heterogeneous internal structure (PPV: positive predictive value, NPV: negative predictive value, CI: confidence interval)

Feature	Sensitivity % (CI)	Specificity % (CI)	PPV % (CI)	NPV % (CI)	Accuracy %
Irregular contour	28.5 (3.67-70.96)	93.8 (83.16-98.72)	40 (11.82-76.83)	90.2 (85.14-93.66)	85.7
Heterogeneous internal structure	44.1 (29.08-60.12)	57.1 (18.41-90.10)	86.3 (71.64-94.07)	14.2 (7.68-25.03)	46

Table 3: Diagnostic performances of lobulated contour and cystic component in benign masses (PPV: positive predictive value, NPV: negative predictive value, CI: confidence interval)

Feature	Sensitivity % (CI)	Specifity % (CI)	PPV % (CI)	NPV % (CI)	Accuracy %
Lobulated contour	47 (22.98-72.19)	95 (83.08-99.39)	80 (48.61-94.42)	80 (72.84-86.92)	80.7
Cystic component	92 (73.97-99.02)	55.1 (35.69-73.55)	63.8 (53.76-72.92)	88.8 (67.04-96.92)	72.2

Table 4: USE SI_{max} score of benign – malignant lesions

	Biopsy	Mean (SD)	Range	*P*-value
Observer 1 SI_{max}	Malignant	5.5 (1.9)	2.4- 8.1	0.961
	Benign	5.5 (2.3)	1.1-11.1	
Observer 2 SI_{max}	Malignant	6.2 (2.6)	2.4-9.3	0.645
	Benign	5.8 (2.6)	2.1-13.2	
SI_{max} within two observers	Malignant	7.3 (1.6)	5.6-9.3	0.422
	Benign	6.6 (2.5)	2.1-13.2	

Discussion

A non-invasive, easily applicable, cost-effective, and repeatable method with high sensitivity, ultrasonography is the first step imaging method in the examination of the parotid gland pathologies [14,15]. However it has a low accuracy in differentiating between benign and malignant lesions [16]. Therefore, new diagnostic methods are under investigation. USE is a newly developed qualitative - quantitative reflective imaging method evaluating tissue stiffness. Theoretically malignant tissues are stiffer than the benign tissues. USE has been found useful for differentiating between malignant and benign nodules for breast, thyroid, prostate tissues. There are also a limited

number of studies evaluating lymph nodes and pancreas by USE [17-21].

There are studies using different methods of USE to measure tissue stiffness of parotid gland masses [8,22-25]. Bathia et al. used shear wave elastography as a quantitative method of USE to assess parotid masses. They found that SWE values of benign masses (18.3 (6) kPa) significantly overlap with malignant masses (13.5 (4.6) kPa), and that pleomorphic adenomas (22.5 (12.4) kPa) have higher SWE values than Warthin tumors (16.9 (4.8) kPa). In conclusion, they stated that according to the pathologic subtypes, parotid masses have wide range of overlap in the SWE values, which limits SWE use in routine practice to exclude malignancy [24].

Another study conducted on 65 salivary gland masses classified tissue stiffness with elastography score (ES) points between 1 – 4 relative to adjacent normal salivary gland parenchyma. They found that pleomorphic adenomas are stiffer than Warthin tumors and all primary malignant masses had 4 points, while noting the presence of many ES 4 lesions among benign ones. In conclusion, they emphasize that USE is an adjunctive technique in differential diagnosis between benign and malignant masses, but not a primary tool [8].

Yerli et al. examined 36 patients and assessed masses with a 4-point modified Itoh scoring system. They reported that benign masses (n:28) had a score between 1 and 4 and malignant masses (n:8), between 2 and 4. They considered masses scoring between 1 and 2 points as benign, and 3 and 4 as malignant, and found that 64.2% of benign masses were correctly identified. In their study, 10 patients had false positive malignant results [26].

Another study by Celebi et al. [27] included 81 masses in 75 patients, and correctly identified 30 of 49 benign masses and 19 of 32 malign masses using the 4-point scoring system. They determined that pleomorphic adenoma, Warthin tumor, adenoid cystic carcinoma and high-grade tumors had lower scores while low grade tumors (like mucoepidermoid carcinoma), acinic cell cancer, metastasis and basal cell adenocarcinoma had higher scores.

Cantisani et al. [22] evaluated 63 masses prospectively by B-mode US, colored Doppler US (CDUS) and USE. The noted findings for B-mode sonography were contour, echogenicity, and the presence of a capsule, for CDUS, central or peripheral vascularization and for USE, elasticity contrast index (a semiquantitative stiffness evaluation method). The evaluation of B-mode and CDUS results together yielded an accuracy of 61.8%, while the evaluation of ECI results alone with a 3.5 cut-off value yielded an accuracy of 90.3%. There was no statistically significant difference when conventional and USE finding criteria were compared.

Recently a meta-analysis published by Zhang et al. [28] evaluated the role of USE in the assessment of parotid masses, in which ten studies consisting of 711 patients with 725 parotid masses were included. They reported a pooled sensitivity and specificity of 67% and 64%, respectively. Heterogeneity was observed due to assessment method. Quantitative and semiquantitative methods showed higher pooled results compared to qualitative methods. Finally, they concluded that USE has limited and unsatisfactory value in the differential diagnosis between benign and malignant parotid masses.

In our study we evaluated 57 masses (benign: 50, malignant: 7). 17 of the benign masses were pleomorphic adenomas and 25 were Warthin tumors. 4 were primary and 3 were secondary salivary gland masses. The distribution of the malignant masses was consistent with the literature, but the rate of Warthin tumor was higher in our study compared to previous studies [14,29-31].

A well-defined contour on B-mode can be used with high accuracy as a benignity criterion, however, the homogenous inner structure can be observed in malignant lesions as well as benign lesions. Malignant masses also showed calcification that is normally expected in benign masses like hemangioma or vascular malformations. Strain elastography by means of SI was used as a semiquantitative USE method in assessment of parotid masses. We considered each observer's results both individually and together yet could not find a reliable threshold value for differentiating between benign and malignant masses.

The inner structure of malignant breast and thyroid lesions are relatively homogenous. The four-point semiquantitative scoring system was found useful in these tissues. On the contrary, parotid gland neoplasms show marked heterogeneity when histologic subtypes are analyzed. In adenoid cystic carcinoma and mucoepidermoid carcinoma (the most commonly encountered malignant tumors) soft and hard tissues coexist. So higher points (3 – 4) were rarely observed in malignant lesions of the parotid gland. For the above stated reasons, adapting this semiquantitative scoring system to parotid gland lesions was not considered suitable [18,20,32].

Technical aspects that can lead to difficulties and limitations are important in elastography imaging. Parotid gland is superficially located under the skin. Large, protruding lesions may be problematic to examine and get reliable elastography measurements because it's hard to adopt the transducer. Freehand compression, which was used to generate elastograms, presumably creates some subtle tissue displacement. We excluded one patient from our study with a mass located 15mm deep to the skin extending posterior to the mandible because no reliable measurement could be obtained. These controversies may explain why intra-observer agreement is fair-moderate and interobserver agreement is moderate in our study, unlike previous breast and thyroid studies.

Limitations

Our study has limitations. The prevalence of malignant lesions was consistent with the literature, but the number of primary parotid gland malignancy cases were limited. We considered each B-mode and USE features independently while assessing the lesions and did not include CDUS features. Combination of these features may improve diagnostic accuracy. Strain elastography is a semi-quantitative and operator-dependent method that influences intra/interobserver agreement.

Conclusion

Parotid gland lesions are suitable for elastography studies due to their superficial location. Differentiating between benign and malign cases is the key point to decide the choice of treatment. In our study we conclude that strain elastography is not a reliable tool to differentiate benign from malignant masses since there is a wide range overlap. While pleomorphic adenomas containing rigid fibrous tissue are expected to have

high SI values, upon evaluation of histological subtypes, no significant association between pleomorphic adenomas and malignant lesions or Warthin tumors were observed. We conclude that in daily practice and algorithm, conventional US findings along with FNAC remain the diagnostic tool to assess parotid gland lesions.

References

1. O'Brien CJ. Current management of benign parotid tumors--the role of limited superficial parotidectomy. Head Neck. 2003;25(11):946-52.
2. Khandekar MM, Kavatkar AN, Patankar SA, Bagwan IB, Puranik SC, Deshmukh SD. FNAC of salivary gland lesions with histopathological correlation. Indian journal of otolaryngology and head and neck surgery: official publication of the Association of Otolaryngologists of India. 2006;58(3):246-8.
3. Das DK, Petkar MA, Al-Mane NM, Sheikh ZA, Mallik MK, Anim JT. Role of fine needle aspiration cytology in the diagnosis of swellings in the salivary gland regions: a study of 712 cases. Med Princ Pract. 2004;13(2):95-106.
4. Okahara M, Kiyosue H, Hori Y, Matsumoto A, Mori H, Yokoyama S. Parotid tumors: MR imaging with pathological correlation. Eur Radiol. 2003;13 Suppl 4:L25-33.
5. Joe VQ, Westesson PL. Tumors of the parotid gland: MR imaging characteristics of various histologic types. AJR Am J Roentgenol. 1994;163(2):433-8.
6. Bhatia KS, Lee YY, Yuen EH, Ahuja AT. Ultrasound elastography in the head and neck. Part I. Basic principles and practical aspects. Cancer Imaging. 2013;13(2):253-9.
7. Yılmaz B, Şener ÖK, Çevik H. Shear Wave Velocity results of non-alcoholic fatty liver disease in diabetic patients. J Surg Med. 2019;3(1):27-30.
8. Bhatia KS, Rasalkar DD, Lee YP, Wong KT, King AD, Yuen HY, et al. Evaluation of real-time qualitative sonoelastography of focal lesions in the parotid and submandibular glands: applications and limitations. Eur Radiol. 2010;20(8):1958-64.
9. Alam F, Naito K, Horiguchi J, Fukuda H, Tachikake T, Ito K. Accuracy of sonographic elastography in the differential diagnosis of enlarged cervical lymph nodes: comparison with conventional B-mode sonography. AJR Am J Roentgenol. 2008;191(2):604-10.
10. Nazarian LN. Science to practice: can sonoelastography enable reliable differentiation between benign and metastatic cervical lymph nodes? Radiology. 2007;243(1):1-2.
11. Lyshchik A, Higashi T, Asato R, Tanaka S, Ito J, Hiraoka M, et al. Cervical lymph node metastases: diagnosis at sonoelastography--initial experience. Radiology. 2007;243(1):258-67.
12. Lyshchik A, Higashi T, Asato R, Tanaka S, Ito J, Mai JJ, et al. Thyroid gland tumor diagnosis at US elastography. Radiology. 2005;237(1):202-11.
13. Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics. 1977;33(1):159-74.
14. Guzzo M, Locati LD, Prott FJ, Gatta G, McGurk M, Licitra L. Major and minor salivary gland tumors. Crit Rev Oncol Hematol. 2010;74(2):134-48.
15. Lee YY, Wong KT, King AD, Ahuja AT. Imaging of salivary gland tumours. Eur J Radiol. 2008;66(3):419-36.
16. Gritzmann N, Rettenbacher T, Hollerweger A, Macheiner P, Hubner E. Sonography of the salivary glands. Eur Radiol. 2003;13(5):964-75.
17. Kim SJ, Ko KH, Jung HK, Kim H. Shear Wave Elastography: Is It a Valuable Additive Method to Conventional Ultrasound for the Diagnosis of Small (≤2cm) Breast Cancer? Medicine (Baltimore). 2015;94(42).
18. Hong Y, Liu X, Li Z, Zhang X, Chen M, Luo Z. Real-time ultrasound elastography in the differential diagnosis of benign and malignant thyroid nodules. J Ultrasound Med. 2009;28(7):861-7.
19. Asteria C, Giovanardi A, Pizzocaro A, Cozzaglio L, Morabito A, Somalvico F, et al. US-elastography in the differential diagnosis of benign and malignant thyroid nodules. Thyroid. 2008;18(5):523-31.
20. Itoh A, Ueno E, Tohno E, Kamma H, Takahashi H, Shiina T, et al. Breast disease: clinical application of US elastography for diagnosis. Radiology. 2006;239(2):341-50.
21. Kilic A, Colakoglu Er H. Virtual touch tissue imaging quantification shear wave elastography for determining benign versus malignant cervical lymph nodes: a comparison with conventional ultrasound. Diagn Interv Radiol. 2019;25(2):114-21.
22. Cantisani V, David E, De Virgilio A, Sidhu PS, Grazhdani H, Greco A, et al. Prospective evaluation of Quasistatic Ultrasound Elastography (USE) compared with Baseline US for parotid gland lesions: preliminary results of elasticity contrast index (ECI) evaluation. Med Ultrason. 2017;19(1):32-8.
23. Wierzbicka M, Kaluzny J, Ruchala M, Stajgis M, Kopec T, Szyfter W. Sonoelastography--a useful adjunct for parotid gland ultrasound assessment in patients suffering from chronic inflammation. Med Sci Monit. 2014;20:2311-7.
24. Bhatia KS, Cho CC, Tong CS, Lee YY, Yuen EH, Ahuja AT. Shear wave elastography of focal salivary gland lesions: preliminary experience in a routine head and neck US clinic. Eur Radiol. 2012;22(5):957-65.
25. Karaman CZ, Basak S, Polat YD. The Role of Real-Time Elastography in the Differential Diagnosis of Salivary Gland Tumors. 2018.
26. Yerli H, Eski E, Korucuk E, Kaskati T, Agildere AM. Sonoelastographic qualitative analysis for management of salivary gland masses. J Ultrasound Med. 2012;31(7):1083-9.
27. Celebi I, Mahmutoglu AS. Early results of real-time qualitative sonoelastography in the evaluation of parotid gland masses: a study with histopathological correlation. Acta Radiol. 2013;54(1):35-41.
28. Zhang YF, Li H, Wang XM, Cai YF. Sonoelastography for differential diagnosis between malignant and benign parotid lesions: a meta-analysis. Eur Radiol. 2019 Feb;29(2):725-35.
29. Jones AV, Craig GT, Speight PM, Franklin CD. The range and demographics of salivary gland tumours diagnosed in a UK population. Oral Oncol. 2008;44(4):407-17.
30. Liyanage SH, Spencer SP, Hogarth KM, Makdissi J. Imaging of salivary glands. Imaging. 2007;19(1):14-27.
31. Luukkaa H, Klemi P, Leivo I, Koivunen P, Laranne J, Mäkitie A, et al. Salivary gland cancer in Finland 1991–96: an evaluation of 237 cases. Acta Oto-Laryngologica. 2005;125(2):207-14.
32. Dumitriu D, Dudea S, Botar-Jid C, Baciut M, Baciut G. Real-time sonoelastography of major salivary gland tumors. AJR Am J Roentgenol. 2011;197(5):W924-30.

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The protective effect of caffeine and melatonin on antioxidant enzymes in rat fetal lung tissues

Kafein ve melatoninin sıçan fetus akciğer dokularındaki antioksidan enzimler üzerine koruyucu etkisi

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Abstract

Aim: Teratogenic substances such as nicotine, alcohol, caffeine, and derivatives, which pregnant women may get exposed to unconsciously or use consciously can harm the mother and directly or indirectly damage embryonal and fetal tissues. Melatonin has been shown to exert direct free radical trapping and indirect antioxidant effects in different organs and tissues. In this study, we aimed to biochemically evaluate the effects of melatonin, a powerful antioxidant battling the oxidative effects of high and low doses of caffeine administered to pregnant rats in fetal lung tissues.

Methods: In our study, 35 pregnant adult female Sprague-Dawley rats were used. Pregnant rats were divided into 7 groups with 5 rats in each. Caffeine and melatonin were administered for 20 days during the pregnancy. The gestational period lasted 21 days in average. The offspring were sacrificed, and lung tissues were removed. Superoxide dismutase (SOD), glutathione (GSH), glutathione disulfide (GSSG), total oxidant status (TOS), total antioxidant status (TAS), calcium (Ca) and vitamin D (Vit D) were measured by spectrophotometric assay. The oxidative stress index (OSI) and total glutathione (GSH/GSSG) were determinants of oxidative stress and were calculated as TOS/TAS and GSH/GSSG ratios, respectively.

Results: The highest TAS value was obtained in the Melatonin group (M) group. GSH and GSH/GSSG was highest in the control group, whereas GSSG was the highest in the high-dose caffeine group (HDC) group. HDC group had the highest SOD value compared to the other groups (P<0.05).

Conclusions: According to these data, it was determined that caffeine used during pregnancy delayed the development of lung, and melatonin, which is a strong antioxidant, minimized the delay.

Keywords: Rat, Caffeine, Melatonin, Lung, Fetus

Öz

Amaç: Hamilelik sırasında bilinçli olarak kullanılan veya bilinçsizce maruz kalınan nikotin, alkol, kafein ve türevler gibi teratojenik maddelerin embriyonal ve fetal dokulara doğrudan veya dolaylı olarak zarar vermesinin yanı sıra anneye de zarar verebilir. Melatoninin farklı organ ve dokularda doğrudan serbest radikal toplayıcısı ve dolaylı antioksidan etkileri olduğu gösterilmiştir. Bu çalışmada, fetus akciğer dokularında gebe sıçanlara uygulanan yüksek ve düşük dozdaki kafeinin etkisine karşı güçlü bir antioksidan olan melatoninin değerlendirilmesi amaçlanmıştır.

Yöntemler: Çalışmamızda 35 adet yetişkin dişi Sprague-Dawley sıçan kullanıldı. Gebe sıçanlar, her birinde 5 sıçan olacak şekilde 7 gruba ayrıldı. Gebelere 20 gün boyunca invaziv işlemler uygulandı. Deney grubuna kafein, kafein yanı sıra tedavi gruplarına melatonin uygulandı. Yavrular sakrifiye edildi ve akciğer dokuları çıkarıldı. Süperoksit dismutaz (SOD), Glutatyon (GSH), Glutatyon disülfür (GSSG) toplam oksidan durumu (TOS), toplam antioksidan durumu (TAS), Kalsiyum (Ca) ve D vitamini (Vit D)) spektrofotometrik analiz ile ölçüldü. Oksidatif stres indeksi (OSI) ve Total glutation (GSH/ GSSG), oksidatif stres dokularının yararlı göstergeleridir ve sırasıyla TOS/TAS ve GSH/ GSSG oranı olarak hesaplandı.

Bulgular: M grubunda elde edilen en yüksek TAS değeri, GSH ve GSH / GSSG kontrol grubunda en yüksek, GSSG ise HDC grubunda en yüksek değere sahipti. HDC grubunda SOD diğer gruplara göre en yüksek değere sahipti (P<0,05).

Sonuçlar: Bu verilere göre, gebelikte kullanılan kafeinin akciğer gelişimini geciktirdiği ve güçlü bir antioksidan olan melatonin gecikmeyi en aza indirdiği gözlendi.

Anahtar kelimeler: Sıçan, Kefein, Melatonin, Akciğer, Fetüs

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Introduction

Caffeine, an important stimulant, has been associated with many positive and negative effects on health. Teratogenic substances such as nicotine, alcohol, caffeine, and derivatives that pregnant women use consciously or get exposed to unconsciously can harm the mother and directly or indirectly damage embryonal and fetal tissues. The immature detoxification enzymes of the fetus and the failure of fetal renal excretion of these substances, which can easily pass through the placenta, are the two main reasons why the embryo is affected by these teratogenic substances [1].

Caffeine is naturally found in the seeds, leaves and fruits of many plants, including coffee and cocoa beans, tea leaves and cola seeds [2,3].

Caffeine [1,3,7-trimethylxanthine] is an alkaloid naturally found in coffee beans [4]. The caffeine content of coffee varies according to the preparation method and type. After caffeine is orally ingested, it is rapidly absorbed from the stomach and the small intestine, reaching its peak level in the blood. As a result of its metabolism in the liver, many metabolites such as paraxanthine, theobromine and theophylline are released [5-7]. Since there is no barrier for caffeine, it readily diffuses into the brain, testes, and other tissues throughout the body along with the placenta into the fetus [5]. It has also been reported to adversely affect bone health and increase the risk of post-menopausal osteoporosis, as high-dose caffeine increases the excretion of calcium and magnesium from the urine, leading to the development of osteoporosis [8].

Melatonin (5-methoxy-N-acetyl-tryptamine) is synthesized and secreted mainly from the pineal gland, ovary, lens and bone marrow cells and bile and gastrointestinal system in mammals [9]. Melatonin is synthesized from tryptophan in the pineal gland, secreted in the dark and binds to plasma proteins. It is metabolized in the liver and has been shown to have direct free radical trapping and indirect antioxidant effects in different organs and tissues [10-12].

To the best of our knowledge, there are no studies on the protective effect of melatonin against the oxidative stress caused by caffeine on fetal lung tissue in the literature. In this study, we aimed to biochemically evaluate the effects of melatonin, a powerful antioxidant battling the oxidative effects of high and low doses of caffeine administered to pregnant rats in fetal lung tissues.

Materials and methods

Animal selection and breeding

Sprague-Dawley female rats weighing between 200-250 g, obtained from Experimental Animals and Clinical Research Center of Erciyes University (DEKAM), were used in this study. Ethics approval was obtained from the Local Ethics Committee of Animal Experiments of Erciyes University on 13/09/2017 (no: 17/086), and rules set forth by this committee were adhered to. One male and two female rats were put into each cage at 17.00 pm on the day of mating. The following morning at 07.00, vaginal smear was obtained from the female rats. Those in which sperm was observed were considered 0.5 day pregnant. During the study, rats were kept in DEKAM at a constant temperature of 22ºC with 12 hours of light/dark cycles. All rats were fed pellets containing 21% crude protein and tap water ad-libitum.

Preparation of injections

Caffeine and Melatonin powder (CAS Number 73-31-4) were obtained from Sigma Aldrich. Drinking water was used as the solvent to adjust the amount of caffeine to be administered to the rats. Hanks Balanced Salt Solution (Hanks) was used for dissolving powdered melatonin. Both substances were prepared daily, and no stock solution was made.

Formation of experimental groups

Pregnant rats were randomly divided into 7 groups with 5 rats in each group, as listed below:

1.Control group (C): The rats were administered physiological saline solution (SF) (1 ml/kg/day) intraperitoneally (i.p.) at 17.00 for 20 consecutive gestational days.

2.Sham group (S): The rats were administered 0.1 ml Hanks i.p. at 17.00 for 20 consecutive gestational days.

3.Melatonin group (M): 10 mg/kg melatonin was administered i.p. for 20 consecutive gestational days.

4.Low-dose caffeine group (LDC): The rats were administered 30 mg/kg caffeine by gavage for 20 consecutive gestational days.

5.High-dose caffeine group (HDC): The rats were administered 60 mg/kg caffeine by gavage for 20 consecutive gestational days.

6.Low-dose caffeine+Melatonin group (LDC+M): The rats were administered 30 mg/kg caffeine by gavage and 10 mg/kg melatonin i.p for 20 consecutive gestational days.

7.High dose caffeine+Melatonin group (HDC+M): The rats were administered 60 mg/kg caffeine by gavage and 10 mg/kg melatonin i.p for 20 consecutive gestational days.

Obtaining fetuses from rats

Pregnant rats were anesthetized with ketamine (75 mg/kg) + xylazine (10 mg/kg) on the 20th day of pregnancy. The abdominal skins of the rats were cleaned with 70% alcohol and the anterior abdominal walls were removed by a 'V' shaped incision extending from the pubis to the rib cage. The uterus and fetuses were removed together with their placenta and dissected individually. The lung tissues of the fetuses were stored at -80ºC until biochemical parameters were evaluated.

Biochemical methods

Tissue preparation and protein quantification

Lung tissue used for analysis was placed into microcentrifuge tubes, washed 3 times with 1mL 100 mM PBS and aspirated. Stainless steel beads (1.6 mm blend) were used for homogenization with 100 mM PBS. After homogenization, homogenates were centrifuged at 10.000 RPM for 30 minutes at +4°C. Supernatants were used as protein samples. BioRAD DC Protein Assay Kit (BioRAD, 5000116) was used to assay the protein content.

Oxidative stress parameters

The parameters of oxidative stress (TAS, TOS and SOD levels) were determined with the spectrophotometric method. The TAS and TOS tissue levels were calculated based on Erel [13]. To compute antioxidant levels in samples, the antioxidant of a known amount (1.65 mmol/l) was used. TAS level is presented as mmolTrolox equivalent/l (mmolTrolox equiv./l). For determination of the TOS level, the assay was calibrated

with a standard hydrogen peroxide solution (39.16 µmol/l). The results are presented as µmol H_2O_2 equivalent/l (µmol H_2O_2 equiv./l). Other oxidative stress parameters such as GSH (Cat. No: E-BC-K030-M), GSSG (Cat. No: 703002, Cayman, USA) and SOD (Cat. E-BC-K020, Elabscience, USA) were calculated with a spectrophotometer (Multiskan, Thermo Fisher) according to the manufacturer's instructions. Commercial ELISA kits (EIA 5396 DRG, Germany) were utilized for Vitamin D analysis.

Ca^{+2} assay

Total Ca^{+2} was evaluated with the calcium colorimetric assay kit (ab102505; Abcam) according to the manufacturer's datasheet. 25 µL of standard solution and 25 µL of supernatant extracted from tissue (diluted 1:10) were mixed with 45 µL of chromogenic reagent and 30 µL assay buffer. The mixture was incubated at room temperature for 15 minutes in the dark. The signal was screened at 575 nm (ThermoVarioscan). The concentration of calcium in the samples was calculated according to the technique described by Sen et al. in 2018.

Statistical analysis

SPSS version 23.0 (IBM Co., NY, USA) was used for all analyses. Data were presented as mean (standard deviation). Differences among the groups were analyzed with one-way analysis of variance (ANOVA) and Post hoc Tukey's tests for continuous variables and parametric data, respectively. The Kruskal-Wallis and the Post hoc Dunn's tests were used for nonparametric data. *P*-value <0.05 was considered statistically significant.

Results

Assessment of oxidative stress parameters

The highest TAS and TOS values were obtained in the M and control groups, respectively. Melatonin administration increased antioxidant status significantly in a dose dependent manner when compared with the caffeine group. Dose-dependent melatonin exerted a more powerful antioxidant effect when used without caffeine. TOS values showed that the highest oxidant effect was observed in the HDC group. Control group had the lowest value. Oxidative stress index was calculated by the ratio of TOS/TAS. OSI was considerably higher in the HDC group and lower in the melatonin-administrated groups (Table 1).

GSH and GSH/GSSG were the highest in the control group, whereas GSSG was highest in the HDC group. Melatonin increased GSH and GSH/GSSG values while decreasing GSSG (Table 1).

SOD was highest in the SDC group. The intracellular calcium and vitamin D values of the M group were higher than all the other groups. According to these results, melatonin markedly decreased oxidative stress by stimulating the antioxidant system.

Discussion

In case of a disturbance in embryological and fetal lung development, congenital lung anomalies and malformations may be encountered [14-16]. It is emphasized by many researchers that cytotoxic agents adversely affect the development of organs during embryo-fetal development [17-22]. These studies evaluate the physiological, biochemical, and pathological changes related to anatomical structure and function of the lungs in the prenatal and postnatal periods [23-25]. In the literature, it is emphasized that information on the fetal development of lungs is of great significance in terms of early diagnosis and treatment of lung anomalies [14-16].

Lipids are the most sensitive to the toxic effects of reactive oxygen products in biological structures. Polyunsaturated fatty acids in the cell membrane readily react with free oxygen radicals and lipid peroxidation occurs. As a result of the damage of these unsaturated fatty acids, membrane fluidity decreases. MDA is the end-product of lipid peroxidation that develops as a result of oxidative stress and is an important indicator of lipid damage [26].

There are some studies about melatonin for its decreasing effect on lipid peroxidation. However, antioxidant enzyme activity shows various results with the use of melatonin [26,27]. Maarman et al. [26] found a decrease in the activity of plasma and lipoperoxidation of SOD and CAT enzymes in animals with Pulmonary Hypertension treated with Melatonin. Taşlıdere et al. [27] associated melatonin use with increased activity of CAT and Glutathione (GSH) enzymes in rat lung tissue after decreased lipoperoxidation and cirrhosis induced by carbon tetrachloride (CCl4). Borges et al. [23] showed that the use of melatonin reduced muscle lipoperoxidation induced by vigorous exercise and increased SOD activity, but there was no notable change in CAT and Glutathione Peroxidase (GPx) activity. Similarly, Rosa et al. [24] showed that melatonin reduced lipoperoxidation and increased SOD activity in the livers of animals with experimental Sleep Apnea models.

Oxidative stress is reportedly important in the pathogenesis of neonatal diseases. Giuffre et al. [29] reported that glutathione, lipid hydroperoxides and heat shock protein chaperone 60 may have functional and diagnostic importance for oxidative stress in newborns.

In the study of Taban et al. [30] the effects of lipid peroxidation product MDA, oxidative stress markers TAS, TOS and OSI, and the effect of bosentan were evaluated in rats by creating a hyperoxic lung injury model.

Table 1: The biochemical parameters of fetus lung

Value	Control	Sham group	M group	LDC group	HDC group	LDC+M group	HDC+M group	*P*-value
TAS	1.25(0.05)	1.12(0.06)[a]	1.36(0.07)[b]	0.80(0.06)[c]	0.59(0.03)[d]	0.88(0.08)[e]	0.74(0.03)[f]	<0.001
TOS	5.06(0.82)	6.09(0.49)[a]	5.46(0.22)[b]	7.03(0.44)[c]	8.81(0.42)[d]	5.45(0.66)[e]	5.57(0.36)[f]	<0.001
OSI	0.40(0.05)	0.54(0.07)[a]	0.40(0.02)[b]	0.88(0.10)[c]	1.47(0.13)[d]	0.62(0.10)[e]	0.74(0.04)[f]	<0.001
GSH	2.81(0.11)	2.56(0.14)[a]	3.13(0.16)[b]	1.86(0.13)[c]	1.38(0.06)[d]	2.01(0.18)[e]	1.70(0.07)[f]	<0.001
GSSG	0.39(0.06)	0.48(0.03)[a]	0.42(0.01)[b]	0.55(0.03)[c]	0.70(0.03)[d]	0.43(0.05)[e]	0.44(0.02)[f]	<0.001
GSH/GSSG	281.12(11.82)	61.38(2.91)[a]	313.96(16.20)[b]	186.50(13.40)[c]	138.53(6.58)[d]	201.15(18.99)[e]	170.42(7.13)[f]	<0.001
TBARS	0.68(0.11)	0.82(0.06)[a]	0.73(0.02)[b]	0.94(0.05)[c]	1.19(0.05)[d]	0.73(0.08)[e]	0.75(0.04)[f]	<0.001
SOD	8.56(1.38)	10.29(0.84)[a]	9.23(0.37)[b]	11.88(0.75)[c]	14.91(0.71)[d]	9.21(1.11)[e]	9.41(0.60)[f]	<0.001
Ca	8.23(0.35)	7.40(0.43)[a]	8.99(0.47)[b]	5.35(0.40)[c]	4.05(0.21)[d]	5.85(0.57)[e]	4.96(0.21)[f]	<0.001
VİT D	4.90(0.20)	4.39(0.26)[a]	5.35(0.28)[b]	3.13(0.24)[c]	2.32(0.13)[d]	3.46(0.34)[e]	2.91(0.12)[f]	<0.001

a, b, c, d, e, and f represent comparisons with the control group. a: Sham group vs Control group b: M group vs Control group c: LDC group vs Control group d: HDC group vs Control group e: LDC+M group vs Control group f: HDC+M group vs Control group

TAS levels were found to be significantly lower in the group with the highest room air + bosentan group and in groups with hyperoxic lung injury. TOS level was higher in the room air + bosentan group than the late bosentan group. There was no significant difference between the other groups. There were no significant differences between the groups in terms of OSI and MDA levels. With these results, they reported that bosentan reduced IL-6 and TNF-α in BPD-induced rats by a hyperoxic lung injury model and provided histopathological improvement with its anti-inflammatory effect.

Durceylan et al. [31] investigated the protective effects of melatonin with proven antioxidant activity on lung injury after TAV in rats. The biochemical analysis of lung tissue samples taken during and at the end of the experiment revealed that SOD levels were significantly higher in the melatonin-treated group after TAV and there was a significant decrease in MDA. It was concluded that preoperative melatonin use may reduce postoperative lung injury in patients with high tissue oxidation and inflammatory potentials.

Recent studies have emphasized the antioxidant properties of melatonin, and melatonin hormone has been shown to have a protective effect against lung damage due to oxidative stress [32-34]. Arslan et al. [32] reported that melatonin hormone prevents bleomycin-induced pulmonary fibrosis in the rat lung. Topal et al. [33] showed that melatonin administration has protective effects against oxidative stress in rat lung caused by hyperbaric oxygen exposure.

Harmless et al. [34] reported that melatonin prevented damage to lung tissue due to formaldehyde (FA) exposure. Showing that MDA, XO and SOD enzyme levels decreased and reached that of the control group in melatonin-treated rats with FA exposure, they explained that the increase in SOD enzyme activity due to FA exposure decreased with melatonin treatment. Crossley et al. [35] investigated the effects of acute caffeine administration on renal and pulmonary functions in preterm lambs. They found that caffeine did not affect blood flow to the pulmonary artery, patent ductus arteriosus or other renal, respiratory or cardiovascular parameters examined. However, they reported that caffeine increased neonatal heart rate and urine output.

In the current study, HDC group had the lowest GSH activity. After caffeine treatment following melatonin administration GSH increased in HDC+M group.

TAS, TOS, SOD and Vitamin D are crucial biomarkers to evaluate oxidative damage. In this study we detected that melatonin decreased TAS while increasing TOS levels in the HDC group. The highest value of SOD was observed in HDC group and the lowest value was recorded in the control group. Caffeine significantly increased SOD by stimulating the reactive oxygen system, and melatonin slightly decreased the effect of caffeine. We conclude that melatonin may exert its effect by reducing the production of superoxide radicals and suggest that melatonin is effective in reducing oxidative stress and impaired development of the lung induced by caffeine in rats.

Limitations

Melatonin dosage was not investigated in this study, and nor were its effect on different tissues, particularly liver and kidneys. Further studies on these aspects will illuminate the antioxidant properties of melatonin.

Conclusion

Melatonin therapy after caffeine administration markedly improved biochemical findings and prohibited oxidative stress and inflammation. According to these data we propose that melatonin at the dose of 10mg/kg may be used as a potential therapeutic agent to prevent the impaired development of the lung by caffeine. We believe that our results will be beneficial in model studies conducted on melatonin and caffeine.

References

1. Bosco AD, Schedler FB, Colares JR, Schemitt EG, Hartmann RM, Forgiarini Junior LA, et al. Melatonin effects on pulmonary tissue in the experimental model of Hepatopulmonary Syndrome. J Bras Pneumol. 2019;30;45(3):e20170164.
2. Barone JJ, Roberst H. Caffeine consumption. Food Chem Toxicol. 1996;34:119-29.
3. International Food Information Council Foundation Caffeine&Health: Clarifying The Controversies. Washington DC. March 2008.
4. Cano-Marquina A, Tarin JJ, Cano A. The impact of coffee on health. Maturitas. 2013;75(1):7-21.
5. Harland BF. Caffeine and nutrition. Nutrition. 2000;16(7-8):522-6.
6. Kendrick SF, Day CP. A coffee with your brandy, sir? J Hepatol. 2007;46:980-2.
7. Crews HM, Olivier L, Wilson LA. Urinary biomarkers for assessing dietary exposure to caffeine. Food Addit Contam. 2001;18(12):1075-87.
8. Weng X, Odouli R, Li D. Maternal caffeine consumption during pregnancy and the risk of miscarriage: A prospective cohort study. Am J Obstet Gynecol. 2008;198:279.
9. Reiter RJ. Exogenously administered and endogenously produced melatonin reduce hyperbaric oxygen induced oxidative stress in rat lung. Life Sci. 2004;75:461-7.
10. Altun A, Vardar A, Altun BU. Melatonin ve Kardiyovasküler Sistem. Kardiyoloji Derg. 2001;1:283-8.
11. Yildirim Z, Kotuk M, Erdogan H, Iraz M, Yagmurca M, Kuku I, et al. Preventive effect of melatonin on bleomycin-induced lung fibrosis in rats. J Pineal Res. 2006;40:27-33.
12. Aydoğdu N, Kanter M, Erbaş H, Kaymak K. Kadmiyuma bağlı karaciğer hasarında taurin, melatonin ve asetilsisteinin nitrik oksit, lipid peroksidasyonu ve bazı antioksidanlar üzerindeki etkileri. Erciyes Tıp Derg. 2007;29:89-96.
13. Erel O.A novel automated direct measurement method for total antioxidant capacity using a new generation, more stable ABTS radical cation. Clin Biochem. 2004;37(4):277-85.
14. Kreiger PA, Ruchelli ED, Mahboubi S, Hedrick H, Adzick NS, Russo PA. Fetal Pulmonary Malformations: Defining Histopatology. Am J Surg Pathol. 2006;30:643-9.
15. Kılıç C, Kocabıyık N, Yalçın B, Kırıcı Y, Yazar F, Ozan H. Akciğerin Aksesuar Fissürleri. SDU Tıp Fak Derg. 2006;13:12-6.
16. Kasparian G, Balassy C, Brugger PC, Prayer D. MRI of Normal and Pathological Fetal Lung Development. European J Radiol. 2006;57:261-70.
17. Jeffery PK. The Development of Large and Small Airways. Am J Respir Crit Care Med. 1998;157:174-80.
18. Chinoy MR. Lung Growth and Development. Front Biosci. 2003;1(8):392-415.
19. Sadler TW. Langman's Medical Embryology. 9th edition, Baltimore: Williams and Wilkins, 2004.
20. Groenman F, Unger S, Post M. The Molecular Basis for Abnormal Human Lung Development. Biol Neonate. 2005;87(3):164-77.
21. Avdalovic M, Putney L, Tyler N, Finkbeiner W, Pinkerton K, Hyde D. In Utero and Postnatal Exposure to Environmental Tabacco Smoke (ETS) Alters Alveolar and Respiratory ronchiole (RB) Growth and Development in Infant Monkeys. Toxicol Pathol. 2009;37(2):256-63.
22. Wallace J. The Respiratory Effects of tabacco Smoke Exposure on the Fetus and Child. SD Med. 2009;11:2.
23. Wigglesworth JS, Hislop AA, Desai R. Biochemical and Morphometric Analyses in Hypoplastic Lungs. Pediatr Pathol. 1991;11(4):537-49.
24. Cao L, Wang J, Tseu I, Luo D, Post M. Maternal Exposure to Endotoxin Delays Alveolarization During Postnatal Rat Lung Development. Am J Physiol Lung Cell Mol Physiol. 2009;296(5):726-37.
25. Hancox RJ, Poulton R, Greene JM, McLachlan CR, Pearce MS, Sears MR. Associations Between Birth Weight, Early Childhood Weight Gain and Adult Lung Function. Thorax 2009;64(3):228-32.
26. Gönül E. Yenidoğan sıçanlarda omega-3 yağ asitlerinin hiperoksik akciğer hasarı üzerine etkileri (Uzmanlık Tezi). İstanbul: GATA/Haydarpaşa Eğitim Hastanesi; 2013.
27. Maarman G, Blackhurst D, Thienemann F, Blauwet L, Butrous G, Davies N, et al. Melatonin as a preventive and curative therapy against pulmonary hypertension. J Pineal Res. 2015;59(3):343-53.
28. Taslidere E, Esrefoglu M, Elbe H, Cetin A, Ates B. Protective effects of melatonin and quercetin on experimental lung injury induced by carbon tetrachloride in rats. Exp Lung Res. 2014;40(2):59-65.
29. Giuffre M, Rizzo M, Scaturro G, Pitruzzella A, Marino GA, Cappello F, et al. Oxidative stress markers at birth: Analyses of a neonatal population. Acta Histochem. 2015;117(4-5):486-91.
30. Taban Ö. Hiperoksik akciğer hasarı oluşturulan yenidoğan ratlarda bosentanın akciğerdeki histopatolojik ve biyokimyasal etkileri Pamukkale Üniversitesi Tıp Fakültesi Çocuk Sağlığı Ve Hastalıkları Anabilim Dalı uzmanlık Tezi 2018.
31. DurceylanE. Melatoninin tek akciğer ventilasyonuna bağlı Akciğer hasarı üzerine koruyucu rolü Eskişehir Osmangazi üniversitesi tıp fakültesi göğüs cerrahisi anabilim dalı tıpta uzmanlık tezi Eskişehir 2014.
32. Arslan SO, Zerin M, Vural H, Coskun A. The effect of melatonin on bleomycin-induced pulmonary fibrosis in rats. Pineal Res. 2002;32:21-5.
33. Topal T, Oter S, Korkmaz A, Sadir S, Metinyurt G, Korkmazhan ET, et al. Exogenously administered and endogenouslyproduced melatonin reduce hyperbaric oxygeninducedoxidative stress in rat lung. Life Sci. 2004;75:461-7.
34. Zararsız İ, Kuş İ, Çolakoğlu N, Pekmez H, Yılmaz HR, Sarsılmaz M. Formaldehit Maruziyeti Sonucu Sıçan Akciğerinde Oluşan Oksidatif Hasara Karşı Melatonin Hormonunun Koruyucu Etkisi: Işık Mikroskobik ve Biyokimyasal Çalışma. Van Tıp Derg. 2004;11(4):105-12.
35. Crossley KJ, Allison BJ, Polglase GR, Morley CJ, Harding R, Davis PG, et al. Effects of caffeine on renal and pulmonary function in preterm newborn lambs. Pediatric Res. 2012;7:19-23.

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Lower gastrointestinal endoscopic polypectomy: Cross-sectional study with 7503 consecutive endoscopic procedures

Alt gastrointestinal sistem endoskopik polipektomi: Ardışık 7503 endoskopik işlem ile kesitsel çalışma

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Abstract

Aim: Colonoscopic polypectomy is the most effective visceral cancer prevention tool in clinical medicine. Studies observed a 76-90% reduction in colorectal cancer incidence following colonoscopic polypectomy. We herein present a case series who underwent polypectomy by lower gastrointestinal system (GIS) endoscopy.

Methods: The study population consisted of 7503 lower GIS endoscopy (colonoscopy or rectosigmoidoscopy) procedures performed in the Department of General Surgery between 2009 - 2019 for screening, diagnostic and follow-up purposes. 612 (8.2%) of the patients who underwent polypectomy were evaluated. The patients' demographic data, clinical status, histopathology reports and follow-up findings were recorded.

Results: During the study period, 612 patients (38 patients, twice and 3 patients, thrice) underwent polypectomy with lower GIS endoscopy. 386 of the patients were male and 226 were female. The mean age of the patients was 57.3 (13.7) (range 24-89) years. A total of 813 polypectomies were performed, and 118 procedures included two or more polypectomies. The most common sites of polypectomies were rectum (n=233, 29.5%), sigmoid colon (n=208, 25.3%) and the descending colon (n=107, 13%). Histopathological examination revealed 25 adenocarcinomas (4.1%), 98 high grade dysplasias (16%) and 269 low grade dysplasias (44%). In terms of histopathological results, there were no significant differences between genders (P=0.098), however, younger patients (mean age: 51.7 years (14.7)) were more likely to have benign results and malignity was more often encountered in older patients (P<0.001). The mean ages of patients with adenocarcinoma and high-grade dysplasia were 61.2 (12.1) and 63.6 (11.1) years, respectively. Necessary treatments and follow-ups were performed for the related pathologies.

Conclusion: We observed that 8.2% of the patients undergoing lower GIS endoscopy had polyps and 20.1% of these polyps needed additional treatment, and 44% needed follow-up colonoscopy control. It should be noted that patients with various lower gastrointestinal tract symptoms may have malign polyps, potentially curable by polypectomy.

Keywords: Colonoscopic polypectomy, Adenoma, Adenocarcinoma

Öz

Amaç: Kolonoskopik polipektomi klinik tıpta en etkili visseral kanser önleme aracıdır. Çalışmalarda kolonoskopik polipektomiyi takiben kolorektal kanser insidansında %76–90 bir azalma sağlandığı rapor edilmektedir. Bu çalışmada alt gastrointestinal sistem (GİS) endoskopi ile polipektomi uygulanan olgu serisini sunmak amaçlanmıştır.

Yöntemler: Çalışma evrenini genel cerrahi servisinde 2009-2019 yılları arasında tarama, tanısal ve takip amaçlı uygulanan 7503 alt GİS endoskopi (kolonoskopi veya rektosigmoidoskopi) işlemi oluşturdu. İncelemede polip tespit edilen ve polipektomi işlemi gerçekleştirilen 611 (%8,2) endoskopi işlemi değerlendirildi. Hastalar demografik veriler, klinik durum, histopatoloji raporları ve takipler açısından kayıt edildi.

Bulgular: Çalışma döneminde alt GİS endoskopi ile polipektomi işlemi 557 hastaya (38 hastada iki kez, 6 hastada üç kez olmak üzere) 611 işlem yapıldı. Hastaların 386'sı erkek, 226'sı kadın idi. Hastaların ortalama yaşı 57,3 (13,7) (aralık 24-89) idi. Tek endoskopi işleminde gerçekleştirilen biyopsi sayıları değerlendirildiğinde; 118 işlemde iki veya daha fazla olmak üzere toplam 813 polipektomi yapıldı. Polipektomi lokalizayonları değerlendirildiğinde; en sık rektum 233 (%29,5), sigmoid kolon 208 (%25,3) ve inen kolon 107 (%13) olduğu görüldü. Histopatolojik inceleme sonuçları değerlendirildiğinde; 25 (%4,1) adenokarsinom, 98 (%16) high grade displazi, 269 (%44) low grade displazi tespit edildi. Patolojiler arasında cinsiyet açısından fark tespit edilmedi ancak yaş açısından fark tespit edildi (sırasıyla P=0,098 ve P<0,001). Malign hastaların ileri yaşta (adenokanser (61,2(12,1)) ve high grade displazi (63,6(11,1))) ve benign hastaların daha genç yaşta (51,7(14,7)) olduğu görüldü. İlgili malign patolojiler için gerekli tedavi ve takipler gerçekleştirildi.

Sonuç: Alt GİS endoskopi yapılan hastaların %8,2'sinde polip görüldüğü ve bu poliplerin %20,1'inde ek tedavilere ve %44'ünde kontrol endoskopik takiplere gerek duyabileceği görülmektedir.

Anahtar kelimeler: Kolonoskopik polipektomi, Adenom, Adenokanser

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Introduction

It has long been thought that colorectal cancers develop from a precursor lesion (adenomatous polyp). This concept was based on the pathology studies published by St Mark's Hospital, London, Lockhart-Mummery and Dukes in 1928 and resulted in the concept of the polyp-cancer sequence published in 1975 by Muto et al. [1]. The introduction of colonoscopy in the early 1970s, following the demonstration of colonoscopic polypectomy feasibility, provided the clinically applicable technology for this concept. It was assumed that colorectal cancers could be prevented by examining the entire colon and detecting and removing the polyps. The evidence for this belief was provided by Winawer et al. [2].

Gastrointestinal polyps are proliferative and neoplastic lesions originating from the mucosal and submucosal epithelium, forming a mass protruding into the stomach and intestine lumen. Gastrointestinal tract (GIS) polyps are more common in the colorectal area. Colonoscopic examination may reveal polyps with or without stalks, - varying in size [3,4]. Colorectal polyps are classified as non-neoplastic polyps (hyperplastic polyps, hamartomatous polyps, mostly seen in juvenile polyposis, Peutz-Jeghers syndrome, Cronkhite-Canada syndrome, Cowden's syndrome, and inflammatory polyps), neoplastic polyps and adenomas (tubular, tubulovillous, villous) [5,6].

Adenomas may show mild, moderate, and severe dysplasia. Tubular adenomas are generally small and mildly dysplastic. As the diameter of the polyp grows, dysplasia is expected to increase. Among tubular adenomas, 88% are mildly, 8% are moderately and 4% are severely dysplastic. The rates of mild, moderate and severe dysplasia are 58%, 26% and 16% for tubulovillous and 41%, 38% and 21%, respectively, in villous adenomas [4,5]. Inflammatory polyps, with a diameter of 2-3 cm, develop in response to chronic inflammation, such as inflammatory bowel diseases, and are mostly seen in the rectum. Hyperplastic polyps are the most common nonneoplastic polyps. They are characteristic lesions smaller than 5 mm in size. Large polyps may be stalked and are particularly observed in the distal colon and rectum [3,6].

The aim of this study is to document the types of polypectomy materials of the lower gastrointestinal system diagnosed in our center.

Materials and methods

Between January 2009 and December 2019, 7503 consecutive patients were admitted to the endoscopy unit for lower GIS endoscopy. 611 (8.2%) of them who had polyps and underwent polypectomy were included in this study.

Endoscopy procedure

Indications for lower GIS endoscopy included patients with a complaint of lower gastrointestinal system (rectal bleeding, bowel habit changes lasting more than two weeks, bloody mucus defecation, lower abdominal pain and tenesmus sensation), unexplained iron deficiency anemia detected during examinations in patients presenting with a different complaint (menopausal female patients and male patients of all ages), patients with first-degree relatives with colon cancer, patients with the presence of hematochezia or occult blood positivity in the stool. To prepare for the colonoscopy procedure, patients were advised to be fed with fluids for one day before the procedure. Also, all patients drank 1: 1 diluted 45mL sodium phosphate one day before the treatment at 23:00 and at 07:00 in the morning of colonoscopy. During the colonoscopy procedure, sedatives and antispasmodics were administered for better toleration of the procedure and pain control. The colonoscopy was performed with CF-30L Olimpus brand colonoscopy device and a rigid rectoscope (30 cm). Endoscopy and pathological results were then evaluated.

Statistical analysis

Categorical variables were expressed as frequency and percentage, parametric data with normal distribution were presented as mean (standard deviation), and non-normally distributed parametric as median (quarter range) and range. T-test for parametric data and Fisher's exact test for categorical data were used for comparison. *P*-value of less than 0.05 was statistically significant within 95% confidence interval.

Results

During the study period, 612 patients (38 patients, twice and 3 patients, thrice) underwent polypectomy with lower GIS endoscopy. 386 of the patients were male and 226 were female. The mean age of the patients was 57.3 (13.7) (range 24-89) years. A total of 813 polypectomies were performed, and 118 procedures included two or more polypectomies. The most common sites of polypectomies were rectum (n=233, 29.5%), sigmoid colon (n=208, 25.3%) and the descending colon (n=107, 13%) (Table 2). Histopathological examination revealed 25 adenocarcinomas (4.1%), 98 high grade dysplasias (16%) and 269 low grade dysplasias (44%) (Table 1). In terms of histopathological results, there were no significant differences between genders (P=0.098), however, younger patients (mean age: 51.7 years (14.7)) were more likely to have benign results and malignity was more often encountered in older patients (P<0.001). The mean ages of patients with adenocarcinoma and high-grade dysplasia were 61.2 (12.1) and 63.6 (11.1) years, respectively (Table 3). Necessary treatments and follow-ups were performed for the related pathologies.

Table 1: Histopathological examination results of polyps

	n	%
Benign	219	35.8
Adenocarcinoma	25	4.1
High grade dysplasia	98	16
Low grade dysplasia	269	44
	611	100

Table 2: Polypectomy locations

Polypectomy locations	n	%
Total	813	100
Rectum	233	28.7
Sigmoid colon	209	25.7
Descending colon	107	13.2
Anus	80	9.8
Transvers colon	48	5.9
Rectosigmoid	40	4.9
Ascending colon	37	4.6
Cecum	29	3.6
Hepatic flexure	18	2.2
Splenic flexure	12	1.5

Table 3: Age distribution of patients with various histopathological results

Histopathological results	Number of patients	Mean age (years)	Standard deviation
Benign	222	51.7	14.7
Adenocarcinoma	25	61.2	12.1
High-grade dysplasia	98	63.6	11.1
Low-grade dysplasia	268	59.3	12.2
Total	613	57.3	13.7

Discussion

In our country, lower GIS complaints are among the common gastroenterological problems. As a matter of fact, a significant proportion of our patients present to our outpatient clinic with complaints related to the GIS such as constipation and rectal bleeding. These symptoms may be indicative of a benign disease such as hemorrhoids, and treatment without further examination may delay the diagnosis of an important disease such as carcinoma. According to the American Cancer Society guidelines, everyone over the age of 50 should have a stool blood test and undergo rectosigmoidoscopic examination with 3-5 year intervals [1]. For this reason, rectosigmoidoscopy / colonoscopy or barium radiography should be performed to rule out malignant or inflammatory bowel diseases in patients presenting with rectal bleeding.

Most colorectal polyps are adenomatous polyps. Tubular adenomas constitute 80-86% of adenomatous polyps, villous adenomas constitute 3-16% and tubulovillous adenomas constitute 8-16% [3,7]. In a series of 675 cases, the rate of tubular adenoma was 80.7%, tubulovillous adenoma, 16.4% and villous adenoma, 2.9% [2]. Another study of 2506 cases revealed that 75% of adenomatous polyps were tubular adenomas, 15.3%, tubulovillous adenomas and 11.7%, villous adenomas [8]. Altınparmak et al. [9] reported that among 428 cases, 64.8% were tubular adenomas, 22.7% were hyperplastic polyps, and 3.7% were juvenile polyps. In Vatn et al.'s [10] study conducted on 914 cases, 68% turned out to be tubular adenomas, 7%, tubulovillous adenomas, 0.5% villous adenomas, 4.3% hyperplastic polyps, 6% serrated adenomas and 0.8%, adenocarcinomas. In our study, 35.8% were benign, 44% were low grade dysplasias, 16% were high grade dysplasias and 4.1%, adenocarcinomas.

The, incidence, size and dysplasia rate of adenomas increase with age [10-12]. Various studies in the literature report that 53-59% of adenomas are seen in males, 40-46% are seen in females and the age of patients with adenoma ranges between 43-61 years [3,9,11]. In our study, the mean age was 57.3 (13.7) years.

Adenomatous polyps are categorized into three groups based on diameter: <1 cm, 1-2 cm and >2 cm. Most adenomas are smaller than 1 cm. According to the literature, tubular adenomas are <1 cm in 77%, 1-2 cm in 20%, >2 cm in 4%. Tubulovillous adenomas are 1 cm in 25%, 1-2 cm in 47%, >2 cm in 29%. Villous adenomas are <1 cm in 14%, 1-2 cm in 26%, >2 cm in 60%. Large adenomas are more common in distal colon segments [10]. Polyps with diameters ≤5 mm are considered small, and they are almost always nonneoplastic. The rate of small polyps with villous or severe dysplasia foci is less than 1% [10-12]. In GIS, polyps occur most frequently in the rectosigmoid region and their incidence decreases towards the cecum. DiSario et al. [13] reported that 54% of the adenomas were localized in the proximal splenic flexure. Bech et al. [14] reported that adenomas were most commonly located in the sigmoid colon. Liebermann et al. [15] reported that 44% of the polyps were located in the distal 60 cm. In a series of 675 cases [3], 47% of the polyps were localized in the sigmoid colon, 18.7% in the descending colon, 13.6% in the transverse colon, and 12.5%, in the rectum. In another study conducted on 428 cases [9], 76.7% of the polyps were observed in the left colon and 23.3%, in the right colon. In our study, 28.7% of the polyps were observed in the rectum, 25.7% in the sigmoid colon, 13.2% in the descending colon. All our results were coherent with the literature.

Limitations

The retrospective nature of this study was the first limitation of our study. In addition, we did not compare the sizes of the polyps in terms of histopathological results, which would have illuminated this subject more.

Conclusion

We observed that 8.2% of the patients undergoing lower GIS endoscopy had polyps and 20.1% of these polyps needed additional treatment, and 44% needed follow-up colonoscopy control. It should be noted that patients with various lower gastrointestinal tract symptoms may have malign polyps, potentially curable by polypectomy.

References

1. Muto T, Bussey HJR, Morson BC. The evolution of cancer of the colon and rectum. Cancer. 1975:36;2251-70.
2. Winawer SJ, Zauber AG, Ho MN, O'Brien MJ, Gottlieb LS, Sternberg SS, et al. Prevention of colorectal cancer by colonoscopic polypectomy. The National Polyp Study Workgroup. N Engl J Med. 1993 Dec 30;329(27):1977-81.
3. Smith RA, Cokkinides V, Eyre HJ. American Cancer Society. American Cancer Society guidelines for the early detection of cancer, 2003. CA Cancer J Clin. 2003;53:27-43.
4. Konishi F, Morson BC. Pathology of colorectal adenomas: A colonoscopic survey. J Clin Pathol. 1982;35:830-41.
5. Boland CR, Hzkowitz SH, Kim YS. Colonic polyps and gastrointestinal polyposis syndromes. Gastrointestinal disease, Sleisenger MH, Fordran JSS, Philadelphia, WB Saunders Company 1989;2:1483-518.
6. Süleymanlar İ, Ertuğrul C, Işıtan F. Tanısal rektosigmoidoskopik incelemenin değerlendirilmesi. Turk J Gastroenterol. 1997;8(Suppl 1):28.
7. O'Brien MJ, Winaver SJ, Zauber AG, et al. The National Polyp Study: Patient and polyp characteristics associated with high-grade dysplasia in colorectal adenomas. Gastroenterolgy. 1990;98:371-9.
8. Williams AR, Balasoorriya BAW, Day DW. Polyp and cancer of the large bovel: A necropsy study in Liverpool. Gut. 1982;23:835-42.
9. Altınparmak E, Sezgin O, Parlak E, Altıntaş E. Colorectal polyps 'The Yüksek İhtisas experience'. Turk J Gastroenterol. 2001;12:49-52.
10. Vatn MH, Staisberg H. The prevalence of polyps of the large intestine in Osio: An autopsy study. Cancer. 1982;49:819-25.
11. Eminler AT, Sakallı M, Irak K, et al. Gastroenteroloji ünitemizdeki kolonoskopik polipektomi sonuçlarımız. Akademik Gastroenteroloji Dergisi. 2011;10:112-5.
12. Granqvist S, Cabrielsson N, Sundelin P. Diminutive colonic polyps clinical significance and managemant. Endoscopy. 1979;11:36-42.
13. DiSario JA, Fautch PG, Mai HD, et al. Prevalence and malignant potential of colorectal polyps in asymtomatic, avarage-risk men. Am J Gastroenterol. 1991;86:941-5.
14. Bech K, Kronborg O, Fenger C. Adenomas and hyperplastic polyps in screening studies. World J Surg. 1991;15:7-13.
15. Lieberman DA, Smith FW. Screening for colon malignancy with colonoscopy. Am J Gastroenterol. 1991;86:946-51.

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Coincidence of left isomerism, malposition of cecum, dorsal pancreatic agenesis, and retroaortic left renal vein: A case report

Sol izomerizmim çekum malpozisyonu, dorsal pankreas agenezi ve reroaortik sol renal ven varlığı ile birlikteliği: Olgu sunumu

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Abstract

Polysplenia / heterotaxy syndrome is a very rare condition that occurs as a result of the maldistribution of the thoracic and abdominal organs. It is examined in two groups with different clinical features and anatomical variations: right and left isomerism. This paper reports the case of a 47-year-old female patient who underwent a non-contrast computed tomography (CT) examination due to right flank pain and suspicion of a renal stone and presented with the findings of left isomerism; i.e., accompanied by intraabdominal variations. On abdominal CT examination, stomach and multiple spleen were localized in the right upper quadrant, and the liver had a midline localization. The interruption of the inferior vena cava with azygos continuation was also detected. The hepatic veins were draining directly into the right atrium. In the literature, a retroaortic left renal vein and dorsal pancreatic agenesis have been individually reported to coexist with left isomerism, but no other case of the coincidence of these three anomalies has been described, which makes the current case report significant. Having knowledge of anatomical variations and clinical status can prevent misdiagnosis, and imaging findings are crucial in the planning of a possible surgical procedure.

Keywords: Left isomerism, Computed tomography, Dorsal pancreatic agenesis, Retroaortic left renal vein, Malposition of cecum

Öz

Polispleni / heterotaksi sendromu, torasik ve abdominal organların yanlış dağılımı sonucu olarak ortaya çıkan çok nadir görülen bir durumdur. Farklı klinik özelliklere ve anatomik varyasyonlara sahip iki grupta incelenmiştir; sağ ve sol izomerizm. Sağ yan ağrısı ve böbrek taşı şüphesi nedeniyle kontrastsız bilgisayarlı tomografi (BT) çekimi yapılan 47 yaşındaki kadın hastada, sol izomerizm – polispleni sendromu ve eşlik eden abdominal organ varyasyonları saptandı. Abdominal BT incelemesinde sağ üst kadranda yerleşimli mide ve çok sayıda dalak, orta hat yerleşimli karaciğer tespit edildi. İnferior vena kava devamlılığında kesilme ve azigos devamlılığı tespit edildi. Hepatik venler doğrudan sağ atriyuma drene oluyordu. Tespit edilen bulgular, polispleni-sol izomerizm ile uyumlu olarak değerlendirildi. Retroaortik sol renal ven, çekum malpozisyonu ve dorsal pankreas agenezisine izomerizm eşlik ediyordu. Literatürde ayrı ayrı rapor edilen sol izomerizme eşlike eden retroaortik sol renal ven ve dorsal pankreas agenezisi olgu sunumları mevcuttu. Ancak bu üç anomalinin eşlik ettiği olgu sunumu yoktu ve bu özellikleriyle olgumuz tekdi. Anatomik varyasyonları ve klinik durumu bilmek yanlış tanıyı önleyebilir ve olası bir cerrahi işlemin planlanmasında görüntüleme bulgularını bilmek çok önemlidir.

Anahtar kelimeler: Sol izomerizm, Bilgisayarlı tomografi, Dorsal pankreatik agenezi, Retroaortik sol renal ven, Çekum malpozisyonu

Introduction

Heterotaxy syndrome is a very rare anomaly characterized with an incorrect position of the left and right abdominal and thoracic organs [1,2]. This syndrome has two types as right and left isomerism [2]. Right isomerism presents with a severe form of cyanotic cardiac disease associated with asplenia [3] and is accompanied by anomalies, such as bilateral epiarterial bronchi, bilateral three-lobed lungs, bilateral right atria, and intestinal malrotation. Left isomerism is often seen with the findings of multiple spleens, interruption of the inferior vena cava (IVC) with azygos continuation, non-orthotopic liver, bilateral hyperatrial bronchi, bilateral bi-lobed lungs, and bilateral left atria [4]. On computed tomography (CT), anatomical anomalies can be described in detail and other accompanying conditions can be detected. Although the coexistence of left isomerism with either dorsal pancreatic agenesis or left retroaortic renal venous variation has been reported in the literature, the coincidence of a left retroaortic renal vein, malposition of cecum, and dorsal pancreatic agenesis with left isomerism has not been previously described. In this study, we aimed to present the CT imaging findings of a rare left isomerism case presenting with these three anomalies.

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Informed Consent: The authors stated that the written consent was obtained from the patient presented with images in the study.
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Case presentation

A 47-year-old female patient underwent an abdominal CT scan using a 128-slice CT device (GE, Revolution EVO, USA) due to right flank pain and suspicion of a renal stone. A 6-mm renal stone was found at the lower pole of the right kidney and there were also heterotaxy findings of intraabdominal organs. The liver was located in the midline (Figure 1, Figure 2). While the normal appearance of the stomach and the spleen was not observed in the left upper quadrant, five spleen tissues of different sizes were detected instead of a normal spleen in the right upper quadrant (Figure 1). Duodenum and ileum were located on the left side of the abdomen, and stomach and jejunum were on the right. The vena cava inferior was located on the right but interrupted in the intrahepatic segment with azygos continuation. The azygos was dilated (Figure 2). The hepatic veins were draining directly into the right atrium. All these findings were consistent with left isomerism; i.e., polysplenia syndrome. In addition, the pancreatic head and uncinate process were normal, but the body and tail parts were not observed. The pancreas was short and had a vertical orientation. There was also dorsal pancreatic agenesis (Figure 3). CT showed retroaortic left renal vein variation (Figure 1). While the colon was not visible in the right half of the abdomen, the cecum and transverse column were located on the left half of the abdomen (Figure 4). To our knowledge, the coexistence of left isomerism with the malposition of cecum, dorsal pancreatic agenesis, and a retroaortic left renal vein has not been previously reported in the literature. Therefore, the current case is significant due to the rarity of observing these three anatomical anomalies in a patient with left isomerism. Written and informed consent was obtained from the patient for publishing this case report.

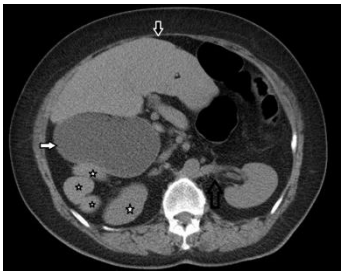

Figure 1: Axial section non-contrast CT showing the midline-located liver (black arrow), multiple spleens (stars), right-sided stomach (white arrow), and retroaortic left renal vein (empty arrow)

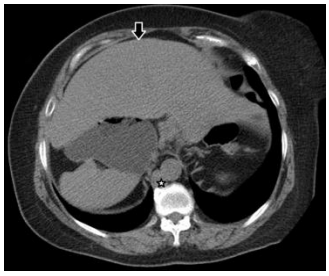

Figure 2: Axial section non-contrast CT showing the midline-located liver (black arrow) and dilated azygos vein (star)

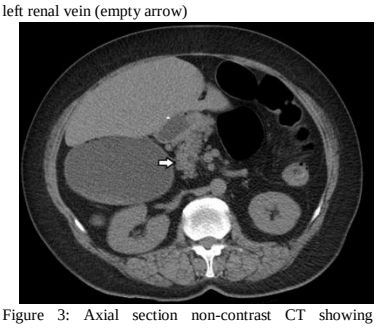

Figure 3: Axial section non-contrast CT showing vertically oriented short pancreas (white arrow)

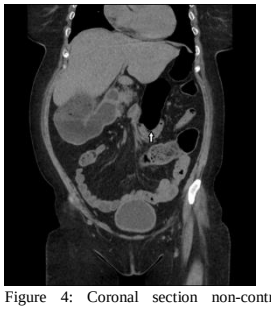

Figure 4: Coronal section non-contrast CT showing the cecum and transverse colon in the left upper quadrant (arrow)

Discussion

Situs solitus refers to the intraabdominal and thoracic organs being located in the normal anatomic position [5] while situs inversus is the opposite localization of these organs, which appears as a mirror image of the normal position [5,6]. Situs ambiguous is an incomplete mirror image anomaly, which describes the state between these two conditions [2,7] and it is divided into right and left isomerism. Right isomerism has severe cardiac anomalies with asplenia and is more common in the male gender. Infants with this condition often die in their first year due to both severe cardiac problems and severe infections caused by asplenia [3]. Left isomerism is more common in females, and it presents with milder, non-cyanotic cardiac anomalies. Immunodeficiency is not an expected finding because of functional spleen parenchyma. For this reason, it can be incidentally diagnosed in adulthood [4,8]. In our case, a 47-year-old female patient was diagnosed incidentally on CT.

Although the actual cause of polysplenia is unknown, many factors of embryological, congenital and teratogenic origin have been reported to play a role in its etiology [8]. Genetic defects in metalloproteinases (e.g., MMP21) that regulate normal right-left asymmetry and the failure of developmental regulatory transcription factors (e.g., FOX A2) may be responsible for the impairment of normal development at embryological stages [9]. Polysplenia is very rare with an incidence of 2.5/100,000.

The spectrum of polysplenia findings is very diverse and variable. Apart from typical IVC anomalies seen in polysplenia, there may be many accompanying vascular variations [1,4]. One of the most common accompanying vascular malformations is a preduodenal portal vein [4,7,8]. In addition, a retroaortic renal vein is common in both normal populations and patients with polysplenia, but it is not a specific finding or a diagnostic criterion for polysplenia. Thus, we consider that the presence of this finding was probably coincidental in our case, as well as in the limited number of previously reported polysplenia cases.

The pancreas may be completely normal in patients with polysplenia, but a short pancreas is a common pancreatic anomaly in this syndrome [1-3,9]. The head of the pancreas has a normal size, but the neck and tail of the pancreas are absent. In our case, while the pancreas had no tail or neck, a normal-size pancreatic head was seen with a vertical course.

In polysplenia syndrome, the stomach can be on the right or left side. Upper intestinal non-rotation/malrotation occurs frequently [2,9]. In our case, the stomach and jejunum were on the right side, and the ileum was located mostly on the left and partially on the right side. Position anomalies of the colon, as in many other organs, are expected findings in polysplenia syndrome. However, in this syndrome, there is no definitive finding of the colon position in the literature. In our case, there was evidence of the malposition of cecum. The cecal and ileocecal valves were located in the left upper quadrant of the abdomen.

Our case had typical features of polysplenia syndrome, but the interesting finding was the coincidence of dorsal pancreatic agenesis, a retroaortic left renal vein, and colonic malposition.

Conclusions

Polysplenia syndrome has a broad spectrum of findings, which are often combinations of various anomalies [1-4,7,8]. Besides the specific findings of polysplenia, common anomalies, such as a short pancreas, or completely incidental variations; e.g., a left retroaortic renal vein can be detected, as in our case.

Having knowledge of specific imaging findings is very important in diagnosis. Radiologists should be aware of this syndrome and should not consider these findings as separate entities. Asymptomatic patients with polysplenia syndrome can be diagnosed incidentally. Sometimes the initial examination can be ultrasound, but CT should be undertaken for definitive diagnosis since it is able to demonstrate all the components of associated congenital anomalies. When radiologists diagnose polysplenia syndrome, they should make an evaluation of the existence of other variations and anomalies. Having good knowledge of the whole anatomy is very important to prevent possible complications and decide on the necessity of a surgical procedure.

References

1. Jung JE, Hur JH, Jung MK, Kwon A, Chae HW, Kim DH, et al. Diabetes mellitus due to agenesis of the dorsal pancreas in a patient with heterotaxy syndrome. Ann Pediatr Endocrinol Metab. 2017 Jun;22(2):125-8.
2. Gupta AC, Herts B. Heterotaxia with polysplenia. J Urol. 2015 Sep;194(3):801-2.
3. Yildiz AE, Ariyurek MO, Karcaaltincaba M. Splenic anomalies of shape, size, and location: pictorial essay. Scientific World Journal. 2013 Apr 21;2013:321810.
4. De Wailly P, Metzler P, Sautot-Vial N, Olivier D, Meunier B, Faure JP. Pre-duodenal portal vein in polysplenia syndrome: clinical effects and surgical application. Surg Radiol Anat. 2011 Jul;33(5):451-4.
5. Gupta R, Soni V, Valse PD, Goyal RB, Gupta AK, Mathur P. Neonatal intestinal obstruction associated with situs inversus totalis: two case reports and a review of the literature. J Med Case Rep. 2017 Sep 18;11(1):264.
6. Douard R, Feldman A, Bargy F, Loric S, Delmas V. Anomalies of lateralization in man: a case of total situs inversus. Surg Radiol Anat. 2000;22(5-6):293-7.
7. Varga I, Babala J, Kachlik D. Anatomic variations of the spleen: current state of terminology, classification, and embryological background. Surg Radiol Anat. 2018 Jan;40(1):21-9.
8. Seo HI, Jeon TY, Sim MS, Kim S. Polysplenia syndrome with preduodenal portal vein detected in adults. World J Gastroenterol. 2008 Nov 7;14(41):6418-20.
9. Pagkratis S, Kryeziu S, Lin M, Hoque S, Bucobo JC, Buscaglia JM, et al. Case report of intestinal non-rotation, heterotaxy, and polysplenia in a patient with pancreatic cancer. Medicine (Baltimore). 2017 Dec;96(49):e8599.

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Case report
Olgu sunumu

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An unusual inguinal hernia presentation in an infant: Amyand's hernia with acute appendicitis

Süt çocuğu yaş grubunda nadir bir inguinal herni oluşumu: Amyand herni ve akut apandisit birlikteliği

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Abstract
Amyand's hernia is a rare condition defined as the presence of appendix vermiformis within the hernia sac, and it constitutes 1% (0.19-1.7%) of all inguinal hernias. Inflammation of the appendix within the inguinal sac is rarer, comprising 0.1% (0.07-0.13) of all Amyand's hernia cases. Although the clinical presentation of the disease varies depending on the inflammation of the appendix, the diagnosis is usually made during the operation. We herein present a 2-month-old male patient who underwent appendectomy during right inguinal herniotomy after visualization of the inflamed appendix adhering to the wall of the hernia sac.
Keywords: Amyand's hernia, Appendicitis, Infants, Appendectomy

Öz
Amyand herni, apendiks vermiformisin fıtık kesesi içinde bulunması olarak tanımlanan nadir bir durumdur. İnsidansı tüm inguinal herniler içinde %1 (%0,19-1,7)'dir. İnguinal kese içindeki apendiksin inflamasyonu daha nadirdir, tüm Amyand herni vakalarının % 0,1 (0,07-0,13)'ini oluşturur. Hastalığın kliniği apendiksin inflamasyonuna bağlı olarak değişmekle birlikte tanı genellikle operasyon esnasında konur. Bu çalışmada sağ inguinal herni nedeniyle operasyona alınan, operasyon esnasında kese duvarına yapışık, apendiks distalinde inflamasyon bulguları olması nedeniyle apendektomi yapılan 2 aylık bir erkek hasta sunuldu.
Anahtar kelimeler: Amyand herni, Apandisit, İnfant, Apendektomi

Introduction

Amyand's hernia is a rare condition defined as the presence of appendix vermiformis within the hernia sac. The disease was first described by Claudius Amyand in 1735 in an 11-year-old male patient during surgery for inguinal hernia, after he detected a perforated appendix in the sac [1]. It constitutes 1% (0.19-1.7%) of all inguinal hernias. Inflammation of the appendix within the inguinal sac is rarer and comprises 0.1% (0.07-0.13%) of all Amyand's hernia cases [2]. Although the clinical presentation of the disease varies depending on the inflammation of the appendix, the diagnosis is usually made during the operation.

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Informed Consent: The authors stated that the written consent was obtained from the parents of the patient presented with images in the study.
Hasta Onamı: Yazar çalışmada görüntüleri sunulan hastanın ailesinden yazılı onam alındığını ifade etmiştir.

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Case presentation

A 2-month-old male patient was admitted to the outpatient clinic with complaint of swelling in the right groin that began 10 days ago. Physical examination revealed a reducible right inguinal hernia. Preoperative examinations of the patient were performed, consent was obtained from the patient's family and elective surgery was planned. On the day of the operation, the hernia could not be reduced. The family stated that the swelling had persisted for the last 24 hours and the patient was restless. Under general anesthesia, a transverse incision was made in the right inguinal region, all fascial layers were incised, and the indirect inguinal hernia sac was identified. Dissection was performed with preservation of the cord and vessels and a distally hyperemic, erect appendix with impaired circulation was found adherent to the sac wall within the hernia sac (Figures 1, 2). Appendectomy was performed after ligation of the appendix vermiformis. The inguinal hernia sac was high-ligated, and the operation was completed. The patient was discharged uneventfully on the first postoperative day. Histopathological examination of the excised specimen was reported as consistent with appendicitis.

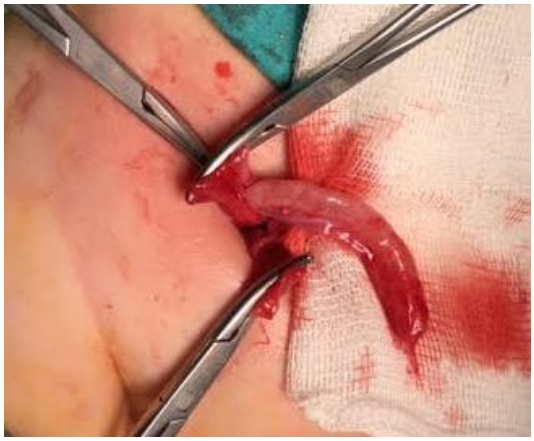

Figure 1: Appendix vermiformis within the hernia sac

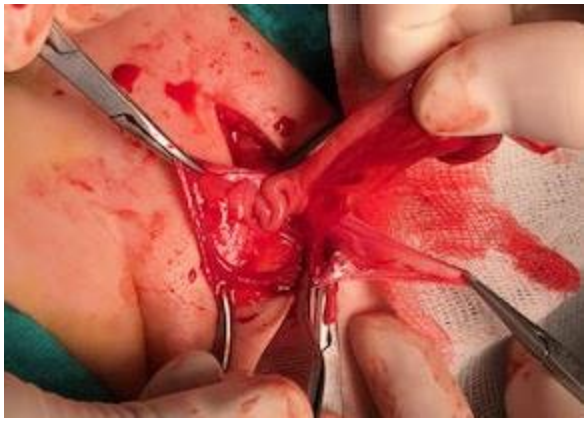

Figure 2: Appendix vermiformis mesentery adherent to the sac wall

Discussion

Indirect inguinal hernia is one of the most common surgical conditions in the pediatric age group. The incidence of this disease varies between 0.8% and 4.4% among pediatric patients [3]. The omentum, small intestine or the bladder are most commonly found within the hernia sac. Rarely, Meckel's diverticulum (Littre hernia), part of the intestinal wall (Richter's hernia) and an inflamed or non-inflamed vermiform appendix (Amyand's hernia) may also be observed. Amyand's hernia constitutes 1% of all inguinal hernias [2,4,5] and is more common in males than females. Inflammation of the appendix is observed in 0.13% of Amyand's hernia cases. It is usually located in the right and in rare cases, left inguinal regions [6].

The preoperative diagnosis of Amyand's hernia is difficult, and it is usually made during surgery. In a study by Cankorkmaz et al. [7], only one of the twelve newborns (median age 40 days) operated for Amyand's hernia in their clinic was diagnosed preoperatively. In our case, the diagnosis was made intraoperatively.

Amyand's hernia treatment may vary depending on the condition of the appendix in the sac and the presence of other pathologies. If there is evidence of inflammation or perforation in the appendix vermiformis, appendectomy is performed through the same incision, followed by hernioplasty [8]. There are many publications advocating appendectomy to eliminate the risk of appendicitis in Amyand's hernia with a non-inflamed appendix vermiformis [9,10]. However, many surgeons do not perform prophylactic appendectomy in the pediatric patient group due to insufficient data and the risk of infection during a non-contaminated surgery [7,11]. In this case, appendectomy was performed from the same incision due to inflammation and circulatory disturbance at the distal end of the appendix vermiformis.

Amyand's hernia is rare during the infantile period, and inflammation of the appendix vermiformis within the sac is even rarer. Since the diagnosis is usually made intraoperatively, the decision of the treatment should be given based on surgical findings. In cases of hernioplasty, the possibility of Amyand's hernia should be kept in mind and the contents of the hernia sac should be visualized.

References

1. Amyand C. Of an inguinal rupture, with a pin in the appendix coeci, incrusted with stone, and some observations on wounds in the guts. Philosophical Transactions. 1835;39:1735-6.
2. Patoulias D, Kalogirou M, Patoulias I. Amyand's hernia: An up-to-date rewiew of the literature. Acta Medica. 2017;60(3):131-4.
3. Bronsther B, Abrams MW, Elboim C. Inguinal hernias in children--a study of 1,000 cases and a review of the literature. J Am Med Womens Assoc. 1972;27:522-5.
4. Mewa Kinoo S, Aboobakar MR, Sigh B. Amyand's hernia: A serendipitous diagnosis. Case Report in Surg Volume. 2013;Article ID:125095.
5. Morales-Cardenas A, Ploneda-Valencia CF, Sainz-Escarrega VH, Hernandez-Campos AC, Navarro-Muniz E, Lopez-Lizarraga CR et al. Amyand hernia: Case report and review of the literature. Ann Med Surg. 2015;4:113–5.
6. Çığşar EB, Karadağ ÇA, Sever N, Dokucu Aİ. Amyand fıtığında apendektomi yapılmalı mıdır? İki olgu sunumu. Ulus Travma Acil Cerrahi Derg. 2013;19(5),488-90.
7. Cankorkmaz L, Ozer H, Guney C, Atalar MH, Arslan MS, Koyluoglu G. Amyand's hernia in the children: a single center experience. Surgery. 2010;147:140-3.
8. Thomas WE, Vowles KD, Williamson RC. Appendicitis in external herniae. Ann R Coll Surg Engl. 1982;64:121-2.
9. Ofili OP. Simultaneous appendectomy and inguinal herniorrhaphy could be beneficial. Ethiop Med J. 1991;29:37-8.
10. Livaditi E, Mavridis G, Christopoulos-Geroulanos G. Amyand's hernia in premature neonates: report of two cases. Hernia. 2007;11:547-9.
11. Sharma H, Gupta A, Shekhawat NS, Memon B, Memon MA. Amyand's hernia: a report of 18 consecutive patients over a 15-year period. Hernia. 2007;11:31-5.

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Successful management of hair follicles following urethroplasty with holmium:YAG laser epilation: A case report

Üretroplasti sonrası kıl foliküllerinin holmium:YAG laser epilasyon ile başarılı tedavisi: Olgu sunumu

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Abstract

A 27-year-old male presented with recurrent urinary tract infections, calculus formation and hair follicles in urine following urethroplasty. The patient was treated with urethroscopic holmium laser in 2012, which was performed by Beiko for the first time in the literature to remove stones and epilate hair follicles. At 3-month, 3-year and 6-year follow-ups, the patient was symptom and infection-free. Urethrocystoscopy was performed in the 6-year follow-up, and no stone formation was observed. There were only a few hair follicles that were too short to require re-surgery. Urethral hair follicles and stone formation are uncommon long term complications following urethroplasty. Endoscopic holmium laser hair epilation is a rarely performed treatment option for hair follicles and urethral stone. Holmium:YAG laser epilation may be an alternative, minimally invasive treatment option with successful long term outcomes.

Keywords: Laser, Urethroplasty, Hair follicles, Epilation, Stone

Öz

27 yaşında erkek hasta, tekrarlayan idrar yolu enfeksiyonu, idrarda taş oluşumu ve idrarla kıl gelmesi şikayetleri ile başvurdu. Hasta 2012 yılında, Beiko tarafından literatürde ilk kez uygulanan üretradan taş çıkarmak ve kıl köklerinin epilasyonu için yapılan üretroskopik olarak holmium lazer ile tedavi edildi. Kısa süreli 3.ay ve uzun süreli 3 ve 6 yıllık takiplerde hastada enfeksiyon gelişmedi. Üretrosistoskopi 6.yıl takibinde yapıldı. Üretrosistoskopide cerrahi gerektirecek taş ve kıl kökü oluşumu görülmedi. Semptom vermeyen ve cerrahi gerektirmeyecek kadar kısa olan birkaç kıl kökü görüldü. Üretral kıl folikülleri ve taş oluşumu, üretroplastiyi takiben nadir görülen uzun dönem komplikasyonlardır. Endoskopik holmium lazer epilasyonu kıl kökleri ve üretra taşı için nadiren uygulanan bir tedavi seçeneğidir. Holmium:YAG lazer epilasyonu minimal invaziv yaklaşım ve iyi uzun dönem sonuçlar ile alternatif bir tedavi seçeneği olabilir.

Anahtar kelimeler: Lazer, Üretroplasti, Kıl kökü, Epilasyon, Taş

Introduction

Urethral hair growth is an uncommon and historical complication of urethroplasty using hair-bearing skin as the graft. Although there is not enough data about the correct incidence of this complication, Rogers et al. [1] reported it as 5%. The hair-bearing urethra may cause obstruction, recurrent urinary infections or calculus formation [2]. This complication of urethroplasty has been solved by using nonhair skin flaps, preoperative epilation of the skin, clipping of urethral hair, Nd: YAG laser depilation or Holmium: YAG laser epilation [3]. Holmium: YAG laser treatment of the hair-bearing urethra was reported for the first time in 2011 [4]. We herein present a case of urethroscopic Holmium: YAG laser epilation of urethral hair follicles and long-term follow-up results.

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Hasta Onamı: Yazar çalışmada görüntüleri sunulan hastadan yazılı onam alındığını ifade etmiştir.

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Case presentation

A 27-year-old male presented with recurrent urinary tract infections and calculus formation in urine. His history included two urethroplasties and one urethral diverticulectomy. Seventeen years ago, urethroplasty was performed using an 8x2 cm skin graft from the scrotum due to a firearm injury causing urethral trauma. Physical examination revealed scarring of the ventral penile and perianal skin due to previous surgeries. Urinary system ultrasonography was normal, and his post-void residual urine volume was 53 mL. Retrograde urethrogram revealed a dilated posterior urethral segment (Figure 1). Under general anesthesia and in the dorsal lithotomy position, cystourethroscopy was performed using a 21 french urethroscope, during which hair-follicles and stone formation was observed in the dilated penile urethral segment (Figure 2). Using a 400-micron holmium: YAG laser fiber, hair follicles were epilated. The laser equipment was set to work at 1.0 J, 8 Hz and 8 W. Laser epilation of the hair follicles may damage the urethra, and like we did in our case, keeping the power as low as possible may help avoid that. Approximately 26 hair follicles were removed and around 600 laser pulses were required to remove all follicles and stones. We aimed to shoot the pulses towards the roots of the hair follicles (Figure 3). Urethral hair epilation was completed successfully, and all epilated hairs were removed with a grasper (Figure 4). There were no intraoperative or postoperative complications. The foley catheter placed during the surgery was removed 3 days later. The patient remained symptom and infection-free at 3-month, 3-year and 6-year follow ups. A repeat urethrocystoscopy was performed at the 6-year follow-up visit, no stones were observed, and only a few hair follicles were seen.

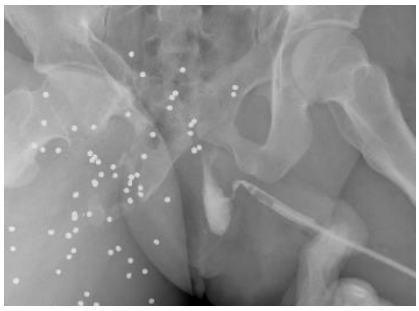

Figure 1: Retrograde urethrogram, dilated posterior urethral segment and small bullets

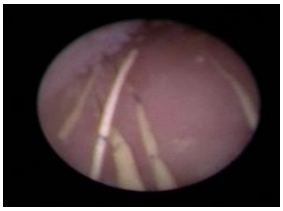

Figure 2: Urethroscope view: Stone formation and hair-follicles

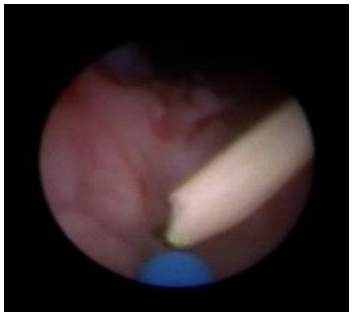

Figure 3: Ho-YAG laser shooting the most proximal parts of the hair follicles near the uroepitelium

Figure 4: A few hair follicles following epilation treatment

Discussion

Urethral hair and stone formation are historically uncommon long-term complications of urethroplasty [1]. However, urologists still encounter it today. Urethral hair may cause urinary obstruction, dysuria, and stone formation [2]. The diagnosis of urethral hair formation is usually based on the patient's suspicious history. The most common diagnostic tools include retrograde urethrogram and urethrocystoscopy. It is also important to assess residual urine volume. Currently, hair-free skin flaps such as the buccal mucosa are used for urethroplasty to avoid these complications. The most important method to prevent urethral hair growth and stone formation is to use hair-free skin flaps. However, some methods have been described to prevent hair follicle formation in patients with hair-bearing skin flaps, including using depilation agents, preoperative thermocoagulation, carbon dioxide (CO2) laser desiccation, neodymium: YAG laser photocoagulation, grasper extraction, surgical revision and Holmium: YAG laser treatment [3,4]. The use of laser in surgical practice has advanced significantly in the last 30 years. Laser technology is used in both non-urological procedures such as iridotomy and urological procedures, such as prostatic surgery, urinary-tract tumors, stricture of ureter and skin lesions [5]. Ho-YAG laser treatment of hair-follicles bares various disadvantages: Fever, urethritis, urethral stenosis, urethrocutaneous fistula and regrowth of hair-follicles can occur following laser treatment. However, we preferred this treatment modality because its advantages outweigh the disadvantages. First, it is easy to perform and can be safely used in luminal organs. Second, if one shoots the pulses as close to the epithelium and to the root of the hair follicle as possible, the success rate will increase [6]. To the best of our knowledge, there is no article reporting the long-term follow-up results of urethral laser epilation in the literature.

Limitations

In our institution, we can only use the 400-micron holmium: YAG laser, which prevents us from comparing this laser fiber with the others. The outcomes of the laser epilation can vary according to laser fiber type.

Conclusions

In the treatment of urethral hair follicles following urethroplasty, holmium: YAG laser epilation is an alternative, minimally invasive treatment option which can easily be performed by many endourologists. It constitutes an option in the treatment of symptomatic hair-follicles and calculi following urethroplasty in adults with favorable long-term results.

References

1. Rogers HS, Mc Nicholas TA, Blandy JP. Long-term results of one-stage scrotal patch urethroplasty. Br J Urol. 1992 Jun;69(6):621-8.
2. Crew JP, Nargund V, Fellows GJ. Symptomatic urethral hair ball and diverticulum complicating island flap urethroplasty. Scand J Urol Nephrol. 1996 Jun;30(3):231-3.

3. Singh I, Hemal AK. Recurrent urethral hairball and stone in a hypospadiac: management and prevention. J Endourol. 2001 Aug;15(6):645-7.
4. Beiko D, Pierre SA, Leonard MP. Urethroscopic holmium: YAG laser epilation of urethral diverticular hair follicles following hypospadias repair. J Pediatr Urol. 2011 Apr;7(2):231-2.
5. Bayraktar Ş, Çağman S, İzgi B, Örekici Temel G. Clinical characteristics and results of laser peripheral iridotomy of pigment dispersion syndrome. Journal of Surgery and Medicine. 2017 Dec;1(3):48-44.
6. Kaneko T, Nishimatsu H, Ogushi T, Sugimoto M, Asakage Y, Kitamura T. Laser hair removal for urethral hair after hypospadias repair. Nihon Hinyokika Gakkai Zasshi. 2008 Jan;99(1):35-8.

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