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Is There Any Relationship Between Serum Endocan Levels and Carotid Intima-media Thickness in Patients with Fibromyalgia?

Fibromiyaljili Hastalarda Serum Endokan Düzeyleri ile Karotis İntima-medya Kalınlığı Arasında İlişki Var mı?

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Abstract

Objective: Although the pathophysiology of Fibromyalgia syndrome (FMS) has not yet been completely elucidated, it has been suggested that inflammation and endothelial dysfunction occur in patients with FMS. In recent years, endocan has been reported as an important biomarker for inflammation and endothelial dysfunction. It is important to assess carotid intima-media thickness (CIMT) in the evaluation of early atherosclerotic vascular diseases. In this study, we investigated this mechanism by measuring serum endocan levels and CIMT in patients with FMS and evaluated whether there is a correlation between them.

Materials and Methods: Serum samples collected from 40 female patients diagnosed with FMS (the patient group) for the first time and 40 healthy female participants' (the control group) endocan levels and CIMT ultrasonography were investigated, and the values of the two groups were compared.

Results: Serum endocan levels and CIMT results were significantly higher in the patient group than in the control group ($p<0.001$). In addition, a very weak correlation was found between CIMT and endocan levels in patients with FMS.

Conclusion: Increased subclinical inflammation, endothelial dysfunction, and early atherosclerosis play an important role in the pathophysiology of FMS. Increased endocan levels, CIMT, and the correlation between them will contribute to elucidating this mechanism.

Keywords: Carotid intima-media thickness, fibromyalgia, endocan, correlation

Öz

Amaç: Fibromiyaljinin patofizyolojisi henüz tam olarak aydınlatılmamış olmakla birlikte, fibromiyaljili hastalarda enflamasyon ve endotel disfonksiyonunun ortaya çıktığı ileri sürülmüştür. Son yıllarda, endokan enflamasyon ve endotel disfonksiyonu için önemli bir biyobelirteç olarak bildirilmiştir. Erken aterosklerotik vasküler hastalıkları değerlendirmede karotis intima media-kalınlığının (KİMK) değerlendirilmesi önemlidir. Bu çalışmada, fibromiyalji hastalarında serum endokan düzeylerini ve KİMK'yi ölçerek bu mekanizmayı araştırdık, aralarında bir korelasyon olup olmadığını değerlendirdik.

Gereç ve Yöntem: İlk kez fibromiyalji tanısı alan 40 kadın hastadan toplanan serum örnekleri ve 40 sağlıklı kadın endokan düzeyleri ve KİMK ultrasonografi ile incelendi ve iki grubun değerleri karşılaştırıldı.

Bulgular: Hasta grubunda serum endokan seviyeleri ve KİMK sonuçları kontrol grubuna göre anlamlı olarak yüksek olarak bulunmuştur ($p<0,001$). Ayrıca FMS'li hastalarda KİMK ile endokan seviyesi arasında çok zayıf bir korelasyon görüldü.

Sonuç: Fibromiyaljinin patofizyolojisinde artmış subklinik enflamasyon, endotelyal disfonksiyon ve erken ateroskleroz önemlidir. Artan endokan düzeyi, KİMK ve aralarında korelasyon görülmesi bu mekanizmayı aydınlatmaya katkı sağlar.

Anahtar kelimeler: Karotis intima-media kalınlığı, fibromiyalji, endokan, korelasyon

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Introduction

Fibromyalgia syndrome (FMS) is a chronic Pain syndrome characterized by widespread pain, sensitivity, sleep disturbance, fatigue, cognitive dysfunction, and emotional stress (1). Although the pathophysiology of FMS has not yet been completely elucidated, it has been suggested that inflammation and endothelial dysfunction occur in patients with FMS (2,3). Studies have shown that serum levels of proinflammatory cytokines (TNF-a, IL-6) and chemokines (Tarc, MIG) are higher in patients with FMS than in the healthy population (4-6). Furthermore, carotid intima-media thickness (CIMT) used to evaluate early atherosclerotic vascular diseases has been shown to be increased in FMS patients (2). Some studies have also shown that the level of endocan, which is a novel marker of inflammation and endothelial dysfunction, correlates with CIMT in various inflammatory diseases (7,8). The aim of this study was to evaluate serum endocan levels, which are important in the etiopathogenesis of FMS, and to evaluate the correlation between endocan levels and CIMT.

Materials and Methods

The study included patients admitted to the Physical Medicine and Rehabilitation Polyclinic of Kars Harakani State Hospital, who were diagnosed with FMS based on the 2016 ACR criteria. Exclusion criteria included patients aged <18 years or >70 years, the presence of any acute or chronic inflammatory disease, history of anti-inflammatory drug use, history of chronic illness (such as heart failure, coronary artery disease, liver failure, renal failure, chronic obstructive pulmonary disease, and diabetes mellitus), pregnancy or suspicion of pregnancy, and history of malignancy. The control group was formed of patients with Myofascial Pain syndrome with a trigger point in the upper trapezius muscle and pain durations were recorded.

Written informed consent was obtained from all the study participants. The study were approved by the Kafkas University Faculty of Medicine of Local Ethics Committee (protokol no: 80576354-050-99/131).

The demographic characteristics of patients, including age, weight, height, and body mass index, were recorded. Bilateral CIMT measurements of CIMT were taken using ultrasonography by an experienced radiologist using a linear probe (Figure 1) (7–12 MHz, B-mode, Toshiba Aplio 500, Japan). Serum endocan levels were measured using the commercial Human endothelial cell specific molecule 1 (ESM1) ELISA Kit (catalog no: E-EL-H1557).

Statistical Analysis

Conformity of the data to normal distribution was assessed using the Kolmogorov-Smirnov test. To determine any difference in CIMT and endocan values between the patient and control groups, the Student's t-test or the Mann Whitney U-test was applied. Correlations between endocan levels and CIMT values were assessed using the pearson or spearman correlation test.

Power Analysis: When data were evaluated by assuming that type I error was 0.05 and the power of the study was 80%**, the sample size was calculated as at least 28 patients necessary in each group.

Results

The demographic characteristics of the patient and control groups are shown in Table 1. Age, body mass index, and education level were not different between the groups. The sedimentation, C-reactive protein and lipid profile levels in the patients with FMS were found to be in the normal range and were significantly different from those of the control group.

The level of serum endocan was determined as 394.607±223.132 ng/mL and 235.998±190.812 ng/mL in the patient and control groups, respectively. The CIMT was measured as 0.64±0.13 mm and 0.47±0.15 mm in the patient and control groups, respectively. The serum endocan levels and CIMT were determined to be statistically significantly higher in the patient group than in the control group (p<0.001). In the FMS patients, a very weak correlation was determined between CIMT and endocan levels.

Discussion

The aim of this study was to evaluate serum endocan levels in patients with FMS and to evaluate any correlation between the serum endocan level and CIMT. The results demonstrated that serum endocan levels and CIMT were higher in patients with FMS than in the healthy population. Furthermore, a correlation between CIMT and endocan levels was determined in patients with FMS.

Table 1. Demographic and clinical characteristics of the patients

	Patient group Mean ± SD	Control group Mean ± SD	p
Age (years)	41.9±11.0	38.1±8.8	0.088
BMI (kg/m²)	24.4±3.3	23.5±1.5	0.126
Disease duration (months)	9.2±3.5	6.4±2.2	**<0.001**
CIMT (mm)	0.64±0.13	0.47±0.15	**<0.001**
Endocan (ng/mL)	394.6±223.1	235.9±190.8	**0.001**

BMI: Body mass index, CIMT: Carotid intima-media thickness, SD: Standard deviation

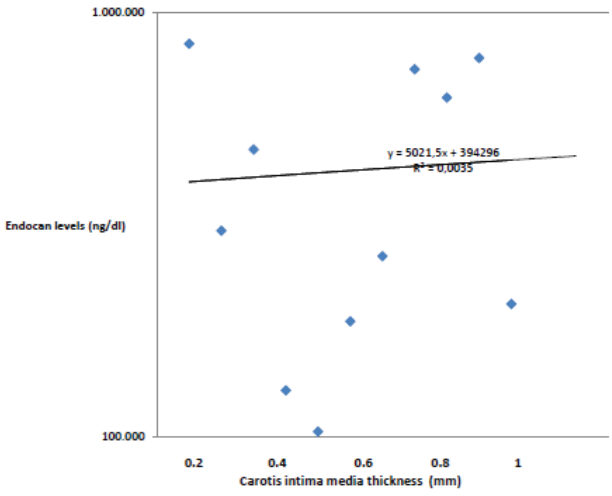

Figure 1. Correlations between serum endocan levels and carotid intima-media thickness values in patients with fibromyalgia

FMS is characterized by chronic musculoskeletal pain, fatigue, sleep disturbance, cognitive dysfunction, and depression (9,10). Stress and pain have been reported to increase the activity of the sympathetic nervous system (SNS) in patients with FMS (11-13). The arterial wall thickening process is significantly affected by SNS activity, leading to alterations in cardiovascular system responses and causing endothelial damage (14). It has also been suggested that a high catecholamine level may have a significant role in FMS pathophysiology (15). With consistent activation of calcium channels, membrane damage, and microvascular spasm may be responsible for catecholamine-induced endothelial dysfunction mechanisms (16).

Topal et al. (17) reported that asymmetric dimethylarginine levels associated with endothelial dysfunction are elevated in patients with FMS. They also determined a positive correlation between 8-iso-prostaglandin F2a (8-iso-PGF2α), which is an important indicator of oxidative stress and lipid peroxidation, and TNF-α, which is a proinflammatory cytokine (17). Another study demonstrated correlations between elevated IL-6 and IL-8 levels in patients with FMS and the severity of disease symptoms (18). Sánchez-Dominguez et al. (19) reported that TNF-α levels measured in skin biopsies were correlated with serum levels patients with FMS, suggesting that an increase in oxidative stress leads to inflammation. In conclusion, a greater risk of endothelial dysfunction and atherosclerosis may be inevitable in FMS patients (20).

Endocan is a novel human endothelial cell specific molecule. Elevated endocan levels may indicate endothelial dysfunction in different pathologies (21,22). CIMT is a strong indicator of early atherosclerosis and cardiovascular disease and is commonly used in rheumatological diseases to assess the risk of cardiovascular disease (23,24). In addition, CIMT values are associated with certain clinical parameters (such as lengthy disease duration, degenerations, high inflammatory parameters, and extra-articular symptoms) in diseases, such as rheumatoid arthritis (25). In the literature, studies have shown the presence of early atherosclerosis with increased CIMT values in ankylosing spondylitis, rheumatoid arthritis and Behçet's disease compared to a healthy population (26,27). In addition, high serum endocan levels and increased CIMT in patients with FMS have been shown in different studies (28,29) .

Previous studies have reported that endocan levels and CIMT are correlated in inflammatory diseases (7,8). Therefore, in the current study, serum endocan levels and CIMT were measured in patients with FMS. Although a correlation was determined between CIMT and endocan levels in the FMS patients, it is difficult to explain the increase in CIMT in this patient group by increased endocan levels alone, although this finding sheds light on a possible mechanism (Figure 1). Due to the complexity of the disease pathogenesis and presence of different risk factors that cannot be controlled, there is a need to investigate possible markers that may be associated with increased CIMT in a larger case series.

Conclusion

In conclusion, the results of this study demonstrated that serum endocan levels and CIMT were higher in patients with FMS than in the healthy population. Furthermore, a correlation was found between CIMT and endocan levels in the FMS patients. These results indicate the presence of increased subclinical inflammation, endothelial dysfunction, and early atherosclerosis in FMS and present a potentially significant mechanism in the pathophysiology of FMS. These patients should be followed up more carefully in terms of atherosclerotic and cardiovascular problems in the long term.

There were some limitations to this study, primarily that only females were included, so the effect of gender on CIMT in patients with FMS was not evaluated. Furthermore, the sample size was relatively small. There is a need for multicenter studies conducted with larger series of patients with FMS.

Ethics

Ethics Committee Approval: The study were approved by the Kafkas University Faculty of Medicine of Local Ethics Committee (protokol no: 80576354-050-99/131).

Informed Consent: Consent form was filled out by all participants.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: F.B., F.H.T., Concept: F.B., F.H.T., Design: F.B., Data Collection or Processing: F.B., F.H.T., Ö.K., Analysis or Interpretation: F.B., F.H.T., Ö.K., Literature Search: F.B., F.H.T., Ö.K., Writing: F.B.

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