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OXIDATIVE STRESS PARAMETERS IN PATIENTS WITH MIGRAINE WITHOUT AURA

Aurasız Migrenli Hastalarda Oksidatif Stres Parametreleri

Suat CAKİNA[1], Selma YÜCEL[2], Cemre Cagan POLAT[2], Şamil OZTÜRK[1]

[1] Canakkale Onsekiz Mart University, Health Service Vocational College, Çanakkale, TURKEY.
[2] Canakkale Onsekiz Mart University, Faculty of Medicine, Department of Neurology, Çanakkale, TURKEY.

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Abstract

Aim: Migraine is a multifaceted neurological disease whose molecular mechanisms are not yet clearly defined. Oxidative stress is also believed to play a role in the pathogenesis of migraine. The purpose of this study was to evaluate serum paraoxonase (PON) and arylesterase (ARE) activities, thiols levels, ischemia-modified albumin (IMA), the total oxidant status (TOS), total antioxidant status (TAS), and oxidative stress index (OSI) in patients with migraine without aura.

Materials and Methods: 30 patients (5 males and 25 females) and 30 matched healthy controls (8 males and 22 females) were enrolled. Serum PON and ARE activities, thiols levels, IMA, TAS, TOS and OSI were determined by using the spectrophotometric method in the study groups. Statistical analysis was conducted using Mann–Whitney U test and independent samples t-test, and $p < 0.05$ was considered as statistically significant.

Results: PON and ARE levels were significantly lower in the migraine without aura group compared with the control group ($p < 0.05$).

Conclusion: Our results suggested that the PON and ARE levels might be associated with migraine without aura. In migraine patients, it is recommended that oxidative stress markers be investigated with a larger population and these parameters are taken into consideration.

Keywords: Migraine, oxidative stress, without aura.

Öz

Amaç: Migren moleküler mekanizmaları henüz net bir şekilde tanımlanmamış çok yönlü bir nörolojik hastalıktır. Oksidatif stresin, migrenin patogenezinde de rol oynadığına inanılmaktadır. Bu çalışmanın amacı, aurasız migren hastalarında serum paraoksonaz (PON) ve arilesteraz (ARE) aktiviteleri , tiyol düzeyleri, iskemi-modifiye albumin (İMA), total oksidan kapasite (TOK), total antioksidan kapasite (TAK) ve oksidatif stres indeksini (OSİ) araştırmaktır.

Materyal ve Metot: Aurasız migrenli 30 hasta (5 erkek ve 25 kadın) ve 30 sağlıklı kontrol (8 erkek ve 22 kadın) çalışmaya dahil edildi. Çalışma gruplarında spektrofotometrik yöntemle serum PON,ARE, tiyol düzeyleri, İMA, TAK, TAK ve OSİ indeksi belirlendi. İstatistiksel analiz Mann-Whitney U testi ve bağımsız örneklem t-testi kullanılarak yapıldı ve $p < 0.05$ istatistiksel olarak anlamlı kabul edildi.

Bulgular: PON ve ARE düzeyleri kontrol grubuna göre aurasız migren grubunda anlamlı derecede düşük bulundu ($p < 0.05$).

Sonuç: Bulgularımız PON ve ARE düzeylerinin aurasız migren hastalığı ile ilişkili olabileceğini göstermektedir. Migren hastalarında oksidatif stress belirteçlerinin daha büyük bir popülasyona sahip ve bu parametreler dikkate alınarak araştırılması önerilir.

Anahtar Kelimeler: Migren, oksidatif stres, aurasız.

INTRODUCTION

Migraine is a neurological disorder accompanied by a number of clinical features, such as headache and nausea, photophobia and phonophobia [1,2]. Oxidative stress may also increase as a result of increased oxidant products due to migraine attacks [3,4]. In recent years, many studies have investigated the relationship between oxidative stress and migraine [5]. In order to determine the role of oxidative stress in migraine, it would be beneficial to measure the oxidative stress markers and antioxidants simultaneously [4,6,7]. Paraoxanase (PON) and arylesterase (ARE) play a role in the plasma antioxidant system

Corresponding Author / Sorumlu Yazar:

Suat CAKINA
Adres: Canakkale Onsekiz Mart University, Health Service Vocational College, Canakkale / TURKEY.
E-posta: suatcakina@comu.edu.tr

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against oxidative stress [8,9]. Thiols have been reported to contain a sulfhydryl group (-SH) and to exhibit antioxidant protection. [10,11]. Ischemic-modified albumin (IMA) is a form of human serum albumin (HAS) and increased in cases of oxidative stress due to ischemia reperfusion injury [12,13].

In the present study, we aimed to evaluate PON and ARE activities, thiols, IMA, total antioxidant status (TAS), total oxidant status (TOS) and oxidative stress index (OSI) in Migraine without Aura (MWoA).

MATERIAL AND METHODS

This study was conducted in our Neurology clinic between February and October 2018. Thirty patients who presented at the Neurology Clinic of the Çanakkale Onsekiz Mart University Research and Education Hospital were prospectively included in the study. The MWoA population was obtained from patients in university hospitals in Çanakkale, Turkey, and the diagnosis was made by a neurologist according to the International Headache Society (IHS) [14]. Neurological disorders (e.g., epilepsy, neurodegenerative disorders, in migraine with aura) were excluded from both groups. The study was approved by Ethic Committee of Çanakkale Onsekiz Mart University Faculty of Medicine (2011-KAEK-27/2018-E.1800019374). Participants provided written informed consent to participate in the study. Blood samples were collected 30 MWoA (age: >18 years) between migraine attacks. A control group was formed, matching patients by gender and age, without a diagnosis of migraine in department of neurology.

Blood sample collection

After obtaining informed consent, venous blood samples were taken for PON, ARE, thiol, IMA, TAS and TOS measurements. The blood samples were centrifuged (3000g, 10 min, 4 ^{o}C) to prepare serum. Plasma samples were stored at −80 °C until the measurement of PON, ARE, thiols, IMA, TAS and TOS.

Measurement of paraoxonase and arylesterase activities

Serum PON and ARE levels were measured by spectrophotometric assay using commercially available kits (Assay Rel, Turkey).

Measurement of Thiol activities

Dynamic thiol-disulphide homeostasis in serum samples of maigraine patients and healthy individuals was identified using an automated method newly developed by Erel et al. [10].

Measurement of IMA activities

The IMA level was analyzed using the rapid colorimetric method developed by Bar-Or et al.[15].

Measurement of TAS and TOS activities

TAS and TOS levels were measured by spectrophotometric assay using commercially available kits (Assay Rel, Turkey). The OSI was defined as the ratio of the TOS level to TAS level.

Statistical analysis

Results are presented as mean ± SD. Statistical analysis was performed using SPSS, version 19.0. (SPSS, IBM Company). The normality of the data distribution was examined by the Kolmogorov-Smirnov normality test. In the comparison of the patients and controls, Kruskal-Wallis and Mann-Whitney U tests were used for continuous variables, and a chi-square test was used for categorical variables. P values less than 0.05 were accepted as the significance level.

RESULTS

The mean age of the MWoA patients (25 females, 83.3%) in this study was 36.5 ± 11.1 years while in control group (22 females, 73.3%) was 35.6 ± 10.4 years. The patient and control groups were similar given the age and sex (p >0.05) (Table 1.). Some of the patients were using prophylactic agents against migraine (6.66%). Newly diagnosed patients were included in the study (90%).

Table 1. Demographic and clinical details of MWoA patients and healthy controls.

	Patients (n=30, %)	Control (n=30,%)	*P* value
Age (mean years ±SD)	36.5 ± 11.1	35.6 ± 10.4	0.92
Sex (n,%)			0.53
Male	5 (16.7)	8 (26.7)	
Female	25 (83.3)	22 (73.3)	
Nausea	21 (70.0)		
Vomiting	5 (16.7)		
Photophobia	25 (83.3)		
Phonophobia	25 (83.3)		

SD: Standart Deviation, MWoA: Migraine without aura

Serum PON levels were lower in the patient group. (184.63±12.98 vs. 222.42±32.08 U/L, p value: 0.002). In addition, there were significant differences between groups regarding ARE levels (199.28±19.16 vs. 250.42±13.92, p= 0.001). We found no statistically significant difference between cases and controls in thiol, IMA, TAS, TOS and OSI levels. (Table 2).

Table 2. Analysis of oxidative stress parameters in migraine without aura and control groups.

	Patients (mean±SD)	Control (mean±SD)	*P* value
PON (U/L)	184.63±12.98	222.42±32.08	0.002
ARE (kU/L)	199.28±19.16	250.42±13.92	0.001
TAS (mmol Trolox Equivalent/L)	1.96±0.27	2.07±0.36	0.260
TOS (µmol H_2O_2 Equiv/L)	5.32±2.30	5.47±2.90	0.732
OSI	2.98±1.78	2.72±1.89	0.671
Native thiol, µmol/L	522.75±94.99	520.10±87.80	0.932
Total thiol, µmol/L	616.98±105.92	608.27±98.85	0.802
Disulfide, µmol/L	47.11±2.21	44.08±2.19	0.682
IMA (ng/mL)	65.25±19.72	60.34±19.12	0.730

PON: Paraoxonase, ARE: Arylesterase, TAS: Total Antioxidant Status, TOS: Total Oxidant Status, IMA: Ischemic- Modified Albumin, OSI: Oxidative Stress Index, SD: Standart Deviation, MWoA: Migraine Without Aura, NA= <0.001.

DISCUSSION

Oxidative stress is a term used to describe situations during which a disturbance in the balance between the production of reactive oxygen species (free radicals) and antioxidant defences. The result can be damage to cell membranes, lipids, nucleic acids, proteins [16,17]. Oxidative stress is suggested to have been caused by free radicals may play role in migraine pathogenesis [18].

The role of oxidative stress in migraine has become a more important topic that has been investigated by many researchers [19-23]. Recent studies have shown that migraine patients have higher oxidative stress due to migraine attacks and migraine triggers (lipid peroxide) [24-28]. Eren et al. reported that no significant association was detected between patients and controls in thiols, TAS, TOS, OSI [29]. Triphati et al. showed that TAS levels were significantly reduced in migraine patients with aura. This finding further supports the role of oxidative stress in migraine headache [17]. In an experimental study of patients with MWoA, it was found that TAS levels decreased and TOS and OSI levels increased in the patient group [3]. They found lower levels of total thiol in MWoA patients. A study in Poland reported that IMA was significantly higher in migraine patients [13]. In our study, there was no difference between patient and control groups for TAS, TOS, OSI, IMA and thiols. The various techniques used in these conflicting results, patient subgroups and the biological samples analyzed, can be effective.

Eren et al. found no differences between PON and ARE activities levels of the patient and control group [29]. Yilmaz et al. reported that a higher activity in migraine patients without aura than in the control group, whereas PON and

ARE activity level was similar in these two groups [30]. Yıldırım et al. showed that patients migraine without aura had lower PON and ARE activities than the controls ($p<0.05$) [31]. In our study, it was found that PON and ARE levels were significantly lower in patient groups ($p <0.05$). Our results are consistent with the study of Yıldırım et al. Sedentary lifestyle, smoking, alcohol use, obesity, and diet rich in fat can decrease PON activity [32]. Furthermore, paraoxonase levels have been reported to decrease with aging [33]. In the light of the findings of this study PON and ARE activities decreases oxidative stress; consequently, headache duration also lessens.

One limitation of our study is the lack of migraine with aura subgroup in patients, this situation limits the reliability of comparison of these parameters between subgroups in migraine patients. For the validity of our results, larger sample studies are needed.

The results of our current study indicate that patients with MWoA have decreased serum PON and ARE activities, which may have clinical importance in the treatment of migraine. Our data suggest that oxidative stress may represent a key event in the pathophysiology of migraine and a suitable therapeutic target. Supplementation of regular treatment regimes with powered antioxidants may be considered in these patients.

Conflict of interest: None declared

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