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Serum paraoxonase enzyme activity after balneotherapy in patients with fibromyalgia

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Abstract

Objective: The aim of this study was to compare the serum paraoxonase (PON 1) levels between patients with fibromyalgia syndrome (FMS) and healthy control subjects, and to investigate the possible effect of balneotherapy (BT) on PON 1 enzyme activity in FMS patients.

Methods: The study included 45 female patients with FMS, and 35 healthy female volunteers. To measure PON 1 enzyme activity, venous blood samples were taken twice from the FMS group, before and after BT, and once from the control group. The Visual Analogue Scale (VAS) and Fibromyalgia Impact Questionnaire (FIQ) scales were applied to the FMS patients before and after BT.

Results: There was no difference between the FMS group and healthy control group in terms of serum PON1 activity ($p>0.05$). The comparison of the serum PON 1 activity of the FMS group before and after BT revealed a statistically significant increase after BT ($p=0.001$). A statistically significant decrease was determined in the VAS and FIQ scores of the FMS group after BT compared to the pre-treatment values ($p=0.002$, $p=0.001$, respectively).

Conclusion: BT is an effective non-pharmacologic method in the treatment of FMS. There was an increase in serum PON 1 activity in patients with FMS after BT. BT may have a regulatory effect on the antioxidant system of patients with FMS.

Keywords: Fibromyalgia syndrome, balneotherapy, paraoxonase

Introduction

Fibromyalgia syndrome is a clinical condition that is characterized by chronic widespread pain, sleep disturbance fatigue, and cognitive dysfunction (1). Genetic, environmental and immunological factors, as well as central and peripheral mechanisms are known to play a role in the etiopathogenesis (2, 3). Despite the many clinical trials carried out to date related to the issue, the etiology of FMS is still not clearly understood, although recent clinical studies have indicated that oxidative stress may play a role in the pathogenesis of FMS (4,5).

Paraoxonase-1 (PON 1) is a protein that hydrolyzes lipid peroxides, and has the ability to protect low density lipoproteins (LDL) from oxidation. It also has an antioxidant function, being able to neutralize other radicals, including hydrogen peroxide (6,7). Previous studies have suggested that degradation of the antioxidant system in FMS may lead to oxidative damage in the muscles, and therefore, the antioxidant role of PON 1 may be important in FMS (8).

The management of FMS is based on symptomatic multidisciplinary treatment through pharmacological and non-pharmacological strategies. Balneotherapy (BT) is a non-pharmacologic treatment method that has seen success in the treatment of FMS, in which thermal and/or mineral waters, peloids and gases are applied repeatedly as a cure at various intervals (9). There is a regulatory effect of BT on the antioxidant system that removes free radicals from the body, and clinical trials have shown that after BT sessions, significant reductions have been noted in superoxide dismutase, catalase and glutathione peroxidase enzymes (9,10).

There have been reports in literature of clinical trials evaluating PON 1 enzyme activity levelsin patients with FMS. However, to the best of our knowledge there has been no clinical study examining the effects of BT on PON 1 enzyme activity levels in FMS treatment. Therefore, the aim of this study was to compare the serum PON1 levels between patients with FMS and healthy control subjects, and to investigate the possible effect of BT on PON 1 enzyme activity in FMS patients.

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Materials and methods

This study was conducted between June 2017 and June 2018, and included female patients aged 18–65 years who agreed to participate in the study. A total of 45 FMS female patients who were diagnosed with FMS according to the American College of Rheumatology (2010) criteria (11), were enrolled and a control group was formed of 35 female healthy subjects.

FMS patients with malignancy, rheumatic disease (osteoarthritis, Behçet's disease, rheumatoid arthritis, etc.) and those with a known history of systemic disease (hypertension, diabetes mellitus, neurological or psychiatric disease, etc.) were excluded. The control group was formed of subjects with no known disease and no medication use, recruited from hospital personnel and the relatives of patients. The age, height, weight and tobacco use of the patients in each group were recorded.

This study was approved by the Ethics Committee of our University (2015-12/07), and was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from each of the study participants.

The FMS group engaged in 20-minute BT sessions every day for 21 days. During BT, the patients reclined and relaxed in a therapeutic pool containing thermo-mineralized water that was rich in bicarbonate (HCO3) and Calcium (Ca) at a temperature of 40°C. The mineral content of the thermal water included chloride, 257 mg/L; sodium, 337 mg/L; Ca, 655 mg/L; magnesium, 104 mg/L; sulfate, 65 mg/L; HCO3: 2003 mg/L; fluoride, 2.24 mg/L and silicate: 32 mg/L. Venous blood samples were taken from the patients both before and after the treatment, and the scales were applied.

Fibromyalgia Impact Questionnaire (FIQ): An FIQ comprising 20 questions was used to assess the patients' physical function, occupational status, pain, sleep, anxiety, depression, stiffness, fatigue and general health as a means of evaluating the functional status of the patients and the progression and results of the disease (12). The validity and reliability of the study was demonstrated in Turkey by Sarmer et al (13).

Visual Analogue Scale (VAS): The VAS was used to examine pain levels in the patients. On a 10 cm scale where 0 indicates no pain and 10 indicates the most severe pain, the patients were requested to mark the point corresponding to the level of pain they experienced.

Biochemical analyses: Blood samples were collected between 8:00 and 10:00 after 10–12 hours of fasting, before and after BT from the FMS group and once from the control group. The blood samples were centrifuged at 1500 rpm for 15 minutes and then separated into sera. The obtained serum samples were stored at -20 ° C until assay.

Paraoxonase activity analysis: The rate of paraoxone hydrolysis was assessed in accordance with the method described by Eckerson et al (14), with measurements made using an autoanalyzer (Beckman Coulter AU 5800, USA).

Statistical analysis

Data obtained in the study were analysed statistically using IBM SPSS Statistics vn. 22 software (IBM Corp., Armonk, NY, USA). Conformity of the data to normal distribution was analyzed using the Kolmogorov-Smirnov test. The Student's t-test and Pearson's correlation test were applied when the parametric test assumptions were met. When the parametric test assumptions could not be met, the Mann Whitney U-test was used, and the Chi-Square test was used to evaluate categorical data. The Wilcoxon sign test was applied in the comparison of pre-treatment and post-treatment variables. Continuous baseline variables were presented as mean ± standard deviation values, and categorical data as number and percentage (%). A value of $p<0.05$ was considered statistically significant. In this study, using $\alpha=0.05$ $\beta=0.10$ $(1-\beta)=0.90$, it was decided to include 45 FMS patients and 35 control subjects in the groups, and the power of the test was p=0.90120.

Results

The study was conducted on the data of 35 healthy female subjects and 45 female patients with FMS. Both groups were similar in terms of age, body mass index (BMI) and tobacco use (Table 1). Serum PON1 activity was found to be lower in the FMS group than in the healthy control group, but not at a statistically significant level ($p>0.05$). The mean serum PON1 activity of the patients with FMS was 95.66±70.84 before BT and 126.51±81.94 U/L after BT.

The serum PON1 activity after BT was significantly higher compared to the pre-treatment PON1 activity (p=0.01) (Table 1). There was no statistically significant correlation between PON1 activity and disease duration, VAS scores and FIQ scores of patients with FMS ($p>0.05$; r=0.207, r=0.202, and r=-0.051, respectively).

Table 1. Disease duration in patients with FMS and the sociodemographic data of the groups

	FMS (n=45) Mean ± SD	Control (n=35) Mean ± SD	p value
Age (years)	52.1 ± 10.1	48.6 ± 13.3	0.213
BMI (kg/m^2)	29.7 ± 5.6	28 ± 5.4	0.404
Disease duration (month)	57.4 ± 52.6	-	
Smoke, Negative n (%)	37 (82.2)	26 (74.3)	0.278
Smoke, Positive n (%)	8 (17.8)	9 (25.7)	

BMI: Body Mass Index; FMS: Fibromyalgia Syndrome; SD: Standard deviation; n: number of patients

Table 2. The VAS and FIQ score of FMS patients, and serum PON 1 levels of the controls and FMS patients

	FMS (n=45)		Controls (n=35)	
	(Before BT)	(After BT)		
VAS (Mean±SD)	7.6 ± 1.3	4.1 ± 1.7		0.002
FIQ (Mean±SD)	72.6 ± 12.1	49.6 ± 19.2		0.001
PON 1 (U/L) (Mean±SD)	95.6 ± 70.8	126.5 ± 81.9	120.1 ± 102.4	0.232[a] 0.001[b]

*p<0.05 VAS: Visual Analogue Scale; FIQ: Fibromyalgia Impact Questionnaire; FMS: Fibromyalgia Syndrome; PON 1: Paraoxanase 1; SD: standard deviation; n: number of patients [a] Comparison between controls and FMS (Before BT); [b] Comparison between FMS patients before BT and after BT

Discussion

The results of the present study showed that PON 1 enzyme activity in FMS patients was no different to that of the healthy individuals, which is a finding that differs from previous studies in literature (15,16). In addition, a decrease was found the VAS and FIQ scores after BT in the current study patients with FMS. However, no correlation was determined between the VAS and FIQ scores and the PON 1 activity of the FMS patients, and a similar finding has been previously reported in literature (17). The current study results showed an increase in PON1 enzyme activity after BT in the FMS patients. Furthermore, no statistically significant correlation was identified between the PON 1 activity of patients with FMS and disease duration. The present study is the first in literature to report such results.

PON 1 has been shown to act as an antioxidant in many clinical studies (18), and it has been suggested that decreases in PON 1 activity may play a role in the pathogenesis of cardiovascular disease, diabetes mellitus and metabolic syndrome (19). PON 1 activity levels have been found to be lower in rheumatoid arthritis (RA) and systemic lupus erythematosus, when compared to healthy individuals (20, 21). Only two clinical studies were identified in literature evaluating PON 1 enzyme activity levels in FMS. A clinical study by Altındağ et al (16) showed that PON 1 activity was lower in FMS patients than in healthy individuals, while Bozkurt et al. (15), reported no decrease in PON 1 activity in FMS patients, and no correlation between PON 1 activity and the VAS and FIQ scores. Similar to that study, no significant differences were noted in the present study between the PON 1 activity of FMS patients and healthy individuals, and no correlation was observed between PON 1 activity and the VAS and FIQ scores.

There is still no definitive treatment for FMS, and so the use of non-pharmacological and pharmacological methods together remains the optimum approach. BT, a non-pharmacological treatment, is known to have a positive effect on clinical parameters (17,22). In line with previous studies, the findings of the present study demonstrated a significant improvement in post-BT VAS and FIQ scores in patients with FMS. The regulatory role of the antioxidant system is believed to be one of the mechanisms of action of BT. Yamaoka et al. (23) determined the effect of BT on superoxide dismutase and catalase activities, while a further study found decreased superoxide dismutase activity as a result of BT in patients with rheumatoid arthritis (24), and Bender et al. (9) demonstrated the antioxidant effect of BT. The findings of the present study mirror those of previous studies as the serum level of PON1, an antioxidant enzyme, was seen to be elevated after BT in patients with FMS.

The limitations of this study include the narrow patient population studied, the absence of male patients with FMS, the lack of repeated measurements of PON 1 levels after 21 days in the healthy control group, and that no evaluation was made of other factors which can affect the FIQ score, and other antioxidant markers

Conclusion

BT is an effective non-pharmacological method in the treatment of FMS. The results of this study showed an increase in serum PON1 activity in patients with FMS after BT.Previous studies have also shown that the oxidant/antioxidant status could have a role in the pathogenesis of FMS. Therefore, these results suggest BT may have a regulatory effect on the antioxidant system in patients with FMS. The results of the present study may contribute to a better understanding of the pathogenesis of FMS and guide future clinical studies investigating the pathogenesis and treatment of FMS. Nevertheless, there is a need for further clinical studies examining antioxidant enzyme metabolism in FMS.

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Ethical issues: Author declare, originality and ethical approval of research. The study was conducted under defined rules by the Local Ethics Commission guidelines and audits.

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