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Concentration of selenium, zinc, copper, Cu/Zn ratio, total antioxidant status and c-reactive protein in the serum of patients with psoriasis treated by narrow-band ultraviolet B phototherapy: A case-control study

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ABSTRACT

Background: Psoriasis is a common, an inflammatory skin disease. Trace elements may play an active role in the pathogenesis of psoriasis.
Objective: The aim of this study was to estimate the concentration of selenium (Se), zinc (Zn), copper (Cu) and Cu/Zn ratio as well as total antioxidant status (TAS) and c-reactive protein (CRP) in the serum of patients with psoriasis.
Methods: In this case-control study sixty patients with psoriasis and fifty-eight healthy people were examined. Serum levels of Se, Zn and Cu were determined by atomic absorption spectrometry. Cu/Zn ratio was calculated. TAS was measured spectrophotometrically. CRP was analyzed by immunoturbidimetric method. Clinical activity of psoriasis was evaluated using Psoriasis Area and Severity Index (PASI).
Results: Serum concentration of Se in patients with psoriasis (71.89 ± 16.90 μg/L) was lower as compared to the control group (79.42 ± 18.97 μg/L) and after NB-UVB. Cu level of patients was higher (1.151 ± 0.320 mg/L) as compared to controls (1.038 ± 0.336 mg/L), but Zn level did not differ. We observed higher Cu/Zn ratio ($p < 0.05$) in examined patients than in the control group and after NB-UVB. We found decrease TAS before and after NB-UVB. CRP levels was found to be normal range. A significant correlation coefficient between CRP and Cu/Zn was observed.
Conclusions: The study showed some disturbances in the serum levels of trace elements and TAS in psoriatic patients.

1. Introduction

Psoriasis is a common, chronic and inflammatory disease of the skin, which affects approximately 2–3% of the world population [1,2]. It is characterized by erythematous plaques covered with a silvery-white scale. It ranges in severity from a few plaques to involvement of almost the entire body surface. [3,4]. Narrow band ultraviolet-B (NB-UVB) is one of the most common treatment methods of psoriasis [5].

The pathogenesis of psoriasis is still poorly understood. It results from the interactions between genetic predisposition and a large spectrum of environmental risk factors, such as diet, alcohol consumption, stress, obesity, smoking [6,7]. Psoriasis is an immune-mediated skin disease characterized by the production of reactive oxygen species due to the overexpression of pro inflammatory cytokines. Tumor necrosis factor alpha (TNF-α) is a cytokine which plays a crucial role in the pathogenesis of psoriasis, because it is thought to be an important factor in inducing and maintaining psoriatic lesions [8,9]. Lipid peroxidation and deficiency of natural antioxidants are involved in enhancing the toxic effects of free oxygen species [10].

Trace elements are essential to biochemical processes in the body and are involved in immunological and inflammatory reactions. The keratinization and melanin formation are enzyme-dependent processes and could be influenced by the deficiencies and excesses of trace elements [11]. Selenium, zinc and copper are involved in the destruction of free radicals through cascading enzyme systems [12]. The key role of Se in human metabolism is attributed to its presence in the glutathione

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Table 1
Patients and control group characteristic.

Variable	Control group (n = 58)	Psoriasis Patients (n = 60)
Gender (M/F)		
Male	17	30
Female	41	30
Age, years		
mean ± SD	40.12 ± 13.80	41.23 ± 12.46
Range	(19–65)	(19–68)
M – male, F – female		

peroxidase (GSH-Px), which protects cells against harmful effects of free radicals [13]. Zn and Cu are an integral part of as many as 40 metalloenzymes, including Cu/Zn superoxide dismutase with antioxidant and anti-inflammatory activity [14,15]. Total antioxidant status (TAS) of an individual is formed by enzymatic and non-enzymatic antioxidants in the body. Miller et al. [16] have defined total antioxidant status (TAS) as the sum of endogenous and food derived antioxidants of the extracellular fluid of an individual. Recent studies on the role of trace elements in the etiopathogenesis and treatment of psoriasis have shown controversial findings and are still limited [17–20]. C- reactive protein (CRP) has been suggested to be an inflammatory biomarker, in various conditions including psoriasis [21,22].

2. Materials and methods

2.1. Study participants

The study was performed as an case-control trial including 60 patients (Table 1) with psoriasis between the ages of 19–68 (with an average age of 41.23 ± 12.46 years) who were under the care of Outdoor-Patients Dermatological Department, Medical University of Bialystok Clinical Hospital. Eligible patients were those with definitive clinical diagnosis of plaque psoriasis confirmed by a dermatologist. Severity of psoriasis was assessed by PASI (Psoriasis Area and Severity Index) scores and the pre- and post-treatment scores. According to PASI moderate psoriasis were defined as mild ($3 < PASI \leq 12$), moderate ($12 < PASI \leq 18$), or severe ($PASI > 18$) [23]. The difference between the baseline PASI score and the final score was determined and PASI 75% was calculated based on Formula 1. (Formula 1: how to calculate the lesion recovery rates: $PASI\% = (PASI_1 - PASI_2)/PASI_1 *100$). Patients had skin phototype II. All the patients underwent 20 courses of narrow band ultraviolet (NB-UVB) treatment (Cosmedico Lamp GP 36 with UVB narrowband Philips TL-01). The mean of irradiation dose was 1515 J/cm^2. Exclusion criteria included pregnancy or lactation, diabetes, alcohol intake, taking mineral supplements containing Se, Zn, Cu, receiving any medication that could change serum level of trace elements, metabolic disorders, skin problems other than psoriasis, hypertension. The control group consisted of 58 healthy volunteers without any signs of skin disease. All control subjects were matched to study subjects by sex and age (19–65 years, an average age of 40.12 ± 13.80 years). There was no statistical difference between age of patients and controls ($p = 0.646$).

2.2. Study design

Blood samples were drawn from patients and control subjects using the vacutainer system test tubes containing clot activator (Becton Dickinson, France). The samples from psoriatic patients were drawn twice: before and after 20 courses of treatments with NB-UVB. The post-treatment blood drawn was collected 2 days after the last phototherapy treatment. Seven patients did not have their blood drawn after phototherapy – they resigned from participating in the study. The samples were allowed to clot within 30 min and then centrifuged within 10 min at approximately 2000 rpm until serum was separated from the blood. The serum samples were then removed, transferred to new capped experimental tubes and stored at −20 °C until the serum analysis.

The concentrations of trace elements in the serum were determined by the electrothermal (Se, Cu) and flame (Zn) atomic absorption spectrometry method with Zeeman background correction (Z-2000 instrument, Hitachi, Japan). Certified reference material of human serum (Seronorm Trace Elements, Serum Level 1, 0903106, Sero AS, Norway) was used to test the accuracy of this method. The results of the quality control analyses corresponded with the reference values. The accuracy of the method was 0.49, 0.93, and 0.55% and the coefficient of variation was 1.4, 2.4, and 1.2% for Se, Cu, and Zn, respectively. The detection limit of the methods was 1.4 μg/L, 0.4 μg/L and 0,014 mg/L for Se, Cu, Zn, respectively. The Department of Bromatology, Medical University of Bialystok participates in a quality control program for trace element analysis supervised by the National Institute of Public Health – National Institute of Hygiene and the Institute of Nuclear Chemistry and Physics. Content of Cu and Zn, after calculation on mmol/L, was used to determine the level of oxidative stress by the estimation of Cu/Zn ratio. TAS activity in the serum was measured using the ready-made sets of tests by Randox Laboratories Ltd. (USA) and UV − VIS spectrophotometer (Cintra 3030, GBC, Australia). ABTS (2.2′-azinodi-[3-ethylbenzthiazoline sulphonate]) was incubated with a peroxidase (metmyoglobin) and H_2O_2 to produce the radical cation ABTS+. This had a relatively stable blue-green color, which was measured at 600 nm. Antioxidants in the added sample caused suppression of this color production to a degree which was proportional to their concentration [24]. CRP levels were measured by immunoturbidimetric method using the ARCHITECT ci8200 system (Abbott Laboratories Inc. USA). Values < 5 mg/L were considered as normal.

Written informed consent was obtained from all study participants prior to the collection of blood samples. The study protocol was approved by the Ethics Committee of the Medical University of Bialystok (R-I-002/580/2013).

2.3. Statistical analysis

Statistical analyses were performed using Statistica v.10.0 software. Differences between independent and dependent groups were tested by the Mann-Whitney *U* test. Correlation was calculated and tested by Spearman rank test. A p value of < 0.05 was considered significant.

3. Results

Pre-treatment PASI scores in all patients was 13.98 ± 1.53 (range, 11.6–17.4), which suggest that all patients had moderate psoriasis. Among women PASI scores was 13.87 ± 1.54 (range, 11.6–17.0) and among men was 14.09 ± 1.55 (range, 11.6–17.4). After phototherapy PASI scores significantly decreased ($p < 0.05$), which was 3.7 ± 1.02 (range, 1.6–5.7). The number of patients, who achieved ≥75% reduction in PASI after phototherapy, was 25 (41,67%).

CRP concentration among psoriatic patients was 2.54 ± 3.82 mg/L (range, 0.2–22.3) and decreased after phototherapy (1.83 ± 1.65 mg/L), but the difference was not significant.

The serum levels of Se, Zn, Cu and total antioxidant status in the study patients and control subjects are presented in Table 2. The serum concentration of Se in patients with psoriasis (71.89 ± 16.90 μg/L) was significantly lower ($p < 0.05$) than in the control group (79.42 ± 18.97 μg/L). The concentration of Zn was lower in psoriatic patients (0.920 ± 0.309 mg/L) as compared to healthy controls (0.997 ± 0.292 mg/L). However, the Zn level did not differ significantly compared to healthy controls. We found significantly higher ($p < 0.05$) serum level of Cu in patients with psoriasis (1.151 ± 0.320 mg/L) than in healthy controls (1.038 ± 0.336 mg/