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ORIGINAL PAPER

A COMPREHENSIVE STUDY ON THE CONTENT OF SERUM TRACE ELEMENTS IN PSORIASIS

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Abstract

Psoriasis is one of the common autoimmune skin diseases that has become a main problem in healthcare. Autoimmune skin diseases can be accompanied by homeostatic imbalance of trace elements that may influence disease management. However, the recent data about the imbalance of trace elements in psoriasis patients are still insufficient. In the present study, the imbalance of trace elements in psoriasis patients and their influence on the extent of psoriasis were investigated. Serum levels of 21 trace elements, namely Li, B, Na, Mg, Al, K, Ca, Cr, Mn, Fe, Co, Cu, Zn, Se, Br, Rb Cd, Sn, I, Cs and Hg, were analyzed in serum samples of 60 patients and 20 healthy volunteers. The extent of psoriasis was investigated using the Psoriasis Area Severity Index (PASI) score of skin lesions. The samples were digested, then their content of trace elements was analyzed using inductively coupled plasma mass spectrometry (ICP-MS). The results revealed trace element imbalance that was accompanied by element – element interdependency. The serum level of lithium, boron and iron showed a highly significant decrease while the serum level of manganese, copper, zinc and selenium showed a highly significant increase in psoriasis patients in comparison to the control group. On the other hand, the remaining elements revealed insignificant differences in their serum level. Some trace elements may serve as biomarkers for diagnosing the disease and as a parameter of the efficacy of the treatment.

Keywords: lithium, iron, zinc, copper, selenium, trace elements imbalance, psoriasis.

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INTRODUCTION

Psoriasis is an autoimmune skin disease that has become a main problem faced in healthcare; it affects approximately 2-3% of the population (Bowcock, Krueger 2005). The major challenge is that the available therapies have been focused only on improving the symptom control whereas no cure has been approved for psoriasis. The initial cause of psoriasis remains medically unclear and only some explanations based on environmental and genetic roles have been proposed to describe the development of psoriasis (Rahman, Elder 2005). The environment and skin metabolism may contribute to the ment of psoriasis, as a skin disorder, by generating reactive oxygen species that cause harmful oxidative stress (Zhou et al. 2009). Many environmental factors can induce oxidative stress by elevating quantities of reactive oxygen species, e.g. drugs or radiation (Al-Jebory 2012). The state of imbalance between trace elements may disturb biochemical events, causing the development of psoriasis (Tahara et al. 2005). Because the content of trace elements influences the immune responses and enzymatic activities, the imbalance of trace elements may alter the activity of some enzymatic dependant bioprocesses such as keratinization and melanin formation (Bock et al. 2003). As antioxidants, some of the essential trace elements such as zinc, copper, selenium have an important role as cofactors for antioxidant enzymes (Al-Jebory 2012). Trace elements and their compounds have effective therapeutic and cosmetic effects on the skin (Afridi et al. 2006). The balance of trace element content in an organism provides basic evidence for good health (Kleczkowski et al. 2004). In last decades, many studies have attempted to determine and trace the unknown causes and development mechanisms of psoriasis (Portugal et al. 2007). In biochemistry, trace element imbalance may affect many of biochemical processes responsible for inducing or causing psoriasis (Tahara et al. 2005). Due to the unclear mechanisms behind the development psoriasis, it is suspected that variation in the content of trace elements and their imbalance can be associated with psoriasis and research in this field may help to understand the underlying mechanisms of the onset of psoriasis (Rashmi et al. 2012). Although both psoriasis and trace element homeostatic imbalance are associated with oxidative stress, studies concerned with the importance of trace elements in the etiopathogenesis and treatment of psoriasis are still limited. However, all the studies thus far have focused only on the effect of limited numbers of trace elements on psoriasis (Rashmi et al. 2012). Therefore, it is still necessary to analyze and evaluate most of trace elements so as to gain a comprehensive insight into the problem of trace element imbalance and psoriasis. The present study aimed to analyze and evaluate the levels of 21 trace elements in serum samples to provide a comprehensive insight into trace element imbalance in psoriasis patients and their role as a biomarker in diagnosis for psoriasis.

MATERIAL AND METHODS

Patients

The study comprised 60 psoriasis patients, 40 males and 20 females, of age between 10-80 years, including 17 females who were premenopausal women (10-45 years) and 3 post-menopausal women (50-80 years). The patients were randomly selected from the outpatient clinic of Dermatology and Venereology Department, Tanta University Hospital, Tanta, Egypt. The control sample contained 20 healthy volunteers and the age, sex, and body mass index matched those of the patients who were included in the study. All patients and controls were selected according to the following procedures: complete present and past history taking including personal and family history, general examination, complete dermatologic examination, informed consent signing, and laboratory investigations (a blood sample was taken to measure the serum level of some trace elements). Then, some patients were excluded if they had other skin disorders or received a topical or systemic treatment. Also, they are excluded if they were suffering from cardiac, diabetic, hypertension or psychiatric problems.

Clinical evaluation of patients

The extent and severity of psoriasis was investigated using the Psoriasis Area Severity Index (PASI) score of skin lesions according to Langley and Ellis (2004). Photographs of skin lesions were used to calculate the degree, area, scaling, indurations and erythema in the head, trunk, upper extremities and lower extremities. The severity of skin eruption in psoriatic patients is shown in Table 1. It was assumed that PASI <7.0, PASI 7.0-12.0, and PASI >12.0 corresponded to mild, moderate, and severe plaque psoriasis, respectively (Langley, Ellis 2004).

Table 1

Method for calculating the Psoriasis Area and Severity Index (PASI)

Surface involved per body region (%)		Degree of severity erythema, induration and scaling		Global overall assessment	
1=	< 10	0 =	no lesions	0 =	clear
2 =	10 - 29	1 =	slight	1 =	mild
3 =	30 - 49	2 =	moderate	2 =	moderate
4 =	50 - 69	3 =	marked	3 =	severe
5 =	70 - 89	4 =	very marked	4 =	extraordinarily severe
6 =	90 - 100				

Blood collection

For measurement of the serum level of 21 trace elements in the patients and controls, blood collection and serum separation were done under complete aseptic condition to avoid any possible metal contamination. 3cc venous blood samples were collected from patients and controls, then centrifuged at 3000 r.p.m. for 10 min to separate the serum. The serum was pipetted into a clean test tube and protected from exposure to light, after which it was frozen at −20°C until the digestion procedure.

Sample digestion and treatment

It is necessary to perform a sample treatment by acid digestion prior to analysis due to the high organic matrix content. 0.5 mL of centrifuged and standard serum was transferred to Teflon beakers, then 10 mL and 2.5 ml of concentrated nitric acid and perchloric acid, respectively, were added for digestion. For analysis of the volatile element Hg, the second preparation step consisted of the fixation of Hg. For the fixation of Hg at room temperature, 300 µl of a sample were treated with 300 µL of 10% tetramethyl ammonium hydroxide (TMAH) solution for one hour at room temperature. Trace element analysis was carried out by inductively coupled plasma mass spectrometry (ICP-MS: Finnigan element 2). For statistical analysis, SPSS software, version 12, was used to calculate the mean, standard error, Linear Correlation Coefficient and Student *t*-test (Unpaired).

RESULTS AND DISCUSSION

Clinical results

The present study was conducted on 60 psoriasis patients: 40 males (67%) and 20 females (33%), and their age ranged from 10-80 years with a mean of 42.059 ± 21.260 years. According to the PASI score, 6 patients were with mild psoriasis (PASI <7.0), 52 patients were with moderate psoriasis (PASI 7.0-12.0), and 2 patient with severe psoriasis (PASI >12.0). Evaluation of the progress and duration of psoriasis in relation to the PASI score is shown in Table 2. The results showed that the duration of psoriasis was less

Table 2

The duration of the disease in relation with the PASI score

Duration of the disease	Patients according to the PASI score (no = 60)		
	mild	moderate	severe
<1 month	4	2	-
1month - 1year	2	42	-
>1 year	-	8	2

than one month in 6 patients (4 mild, 2 moderate and zero severe), from one month to one year in 44 patients (2 mild, 42 moderate, and zero severe) and more than one year in 10 patients (8 moderate, zero moderate and 2 severe). The age of patients at the onset of the disease in relation to the PASI score is specified in Table 3. The results showed that the age at the onset of the

Table 3

Age of onset of the disease in relation to the PASI score

Age of onset of the disease	Patients according to PASI score (no = 60)		
	mild	moderate	severe
10-30 years	6	22	-
>30-60 years	-	20	2
>60 years	-	10	-

disease was 10-30 years in 28 psoriatic patients (6 mild, 22 moderate and zero severe), >30-60 years in 22 psoriatic patients (zero mild, 20 moderate and 2 severe) and >60 years in 10 psoriatic patients (moderate type).

Concentrations of trace elements and statistical analysis

Studies and research data describing the correlation between trace elements and psoriasis are still limited. Therefore, there is a need for comprehensive investigaions correlating the levels of most of trace elements with psoriasis. Hence, twenty-one trace elements were analyzed in psoriasis patients and controls in our study. The analysis of the samples showed that 14 trace elements in the serum, i.e. Na, Mg, Al, K, Ca, Cr, Co, Br, Rb, Ca, Sn, I, Cs and Hg, differed insignificantly in all cases of psoriasis patients in comparison to the control group, while there were significant differences in 7 essential trace elements, Fe, Li, B, Zn, Cu, Se, and Mn, as shown in Table 4.

Table 4

Comparison between patients and controls as regards serum level of essential trace elements

Essential trace elements	Patients (no = 30)		Controls (no = 10)		T-test	
	range	mean ± SD	range	mean ± SD	*t*	*P*-value
Zn (mg L^{-1})	1.20-2.55	2.269±0.229	1.08-1.20	1.131±0.039	-15.527	0.001*
Cu (mg L^{-1})	1.28-1.66	1.494±0.078	0.24-1.29	1.104±0.307	-6.864	0.001*
Se (mg L^{-1})	9.99-13.11	11.436±0.644	7.31-9.27	8.510±0.588	12.864	0.001*
Fe (mg L^{-1})	0.41-0.65	0.550±0.067	0.66-0.84	0.764±0.072	8.798	0.001*
Mn (μg L^{-1})	2.31-3.02	2.632±0.187	0.62-0.69	0.654±0.030	-33.052	0.001*
Li (mg L^{-1})	0.10-0.14	0.120±0.011	0.17-0.21	0.187±0.013	16.115	0.001*
B (mg L^{-1})	1.38-1.67	1.540±0.074	2.22-2.40	2.314±0.054	30.704	0.001*

*significant *P*-value < 0.05

Of these trace elements, Fe, B, and Li, exhibited a highly significant decrease while Zn, Cu, Se, and Mn exhibited a highly significant increase in all psoriatic patients (mild, moderate and severe) as compared to healthy controls. These results are in partial agreement with Halevy et al. (2001), who demonstrated a significant decrease in the mean serum level of Li and B in psoriatic patients as compared to controls, and the mean serum level of Mn was significantly higher in patients compared to controls (Halvey et al. 2001). For the serum Fe level, it ranged from 0.44-0.58 and 0.41-0.65 mg L^{-1} in mild and moderate psoriasis patients, respectively, while in the severely ill patient it was 0.53 mg L^{-1}. In the control group, the Fe level ranged from 0.66-0.84 mg L^{-1}, but was significantly lower in patients. These results are in agreement with those of Basavaraj et al. (2009), who reported a significant decrease in the Fe concentration in both mild and severe psoriasis patients when compared to the control (Rashmi et al. 2012). Some studies mentioned that iron deficiency was found to be a metabolic consequence of skin diseases such as psoriasis and therefore anaemia may be caused by psoriasis (Sato 1991, Marks, Shuster 1970). The serum Li level ranged from 0.10-0.13 and 0.10-0.14 mg L^{-1} in mild and moderate psoriasis patients, respectively, while in the severely ill patients it was 0.14 mg L^{-1}. In the control group, lithium ranged from 0.17-0.21 mg L^{-1}; there was a significant decrease in patients compared to controls. These results are in accord with a study of Halevy et al. (2001), reporting a significant decrease in the serum level of Li in psoriatic patients compared to healthy controls. The low level of lithium in psoriasis may reflect a homeostatic compensatory mechanism. The serum B level ranged from 1.52- 1.62 and 1.38-1.67 mg L^{-1} in mild and moderate psoriasis patients, respectively, while in the severe case of psoriasis it was 1.67 mg L^{-1}. In the control group, the boron level ranged from 2.22-2.40 mg L^{-1}; there was a significant decrease in patients compared to controls. These results coincide the those reported by Halevy et al. (2001), who observed a significant decrease in the B concentration in psoriasis patients when compared to the control, but mentioned that the role of boron in psoriasis was obscure. Another study suggested that boron may play a role in the cell membrane function, mineral and hormone metabolisms, and enzyme reactions, and it is required or beneficial in humans and animals for immune functions (Penland 1994). The serum Zn level ranged from 2.20-2.54 and 1.20-2.55 mg L^{-1} in mild and moderate psoriasis patients, respectively, while in the severely ill patients it was 2.18 mg L^{-1}. In the control group, the zinc level ranged from 1.08-1.20; there was a significant increase in patients compared to controls. The results showed a negative correlation between the age of the onset of the disease and the serum level of Zn, meaning there was a higher in the Zn serum level in younger patients than in older ones. In the present study, the serum zinc level showed a statistically highly significant increase in all psoriatic patients (mild, moderate and severe) as compared to healthy controls. These results are consistent with the ones reported by Butnaru et al. (2008), who found that the serum Zn level was higher in the psoriatic patients than in

the healthy controls. The serum Cu level ranged from 1.44-1.66 and 1.28-1.66 mg L^{-1} in mild and moderate psoriasis patients, respectively, while in the severe cases it was 1.49 mg L^{-1}. In the control group, the Cu level ranged from 0.24-1.29 mg L^{-1}; there was a significant increase in patients compared to controls. Regarding the serum copper level in the present study, a statistically significant increase was demonstrated in patients as compared to healthy control. These results are in accordance with the results given by Tasaki et al. (1993) and Basavaraj et al. (2009), who found a significant increase in the serum Cu level of both mild and severe psoriasis patients. Serum copper and ceruloplasmin levels were significantly increased in psoriasis. It is not known, however, whether psoriasis accelerates the release of synthesized protein (ceruloplasmin) into the blood serum or whether the synthesizing capacity is enhanced, or both. In spite of many efforts, no definite mechanism has been established which accounts for this increasing level of serum Cu in psoriasis patients (Yul et al. 1996). Furthermore, high concentrations of Cu may cause increased oxidative damage to lipids, proteins and DNA, which may contribute to inflammatory skin disorders (Gaetke, Chow 2003). The serum Se level ranged from 10.90-13.11 and 9.99-13.11 mg L^{-1} in mild and moderate psoriasis patients, respectively, while in the severe cases it was 11.23 mg L^{-1}. In the control group, the Se level ranged from 7.31-9.27 mg L^{-1}; there was a significant increase in patients compared to controls. In the present experiment, there was a highly significant increase in the serum level of Se in all psoriatic patients (mild, moderate and severe) compared to healthy controls. On the other hand, other studies found that there was no difference in the plasma concentration of Se between their psoriatic patients with different scores (mild, moderate and severe) and healthy subjects (Mohamad 2013, Sheikh et al. 2015). In contrast, Serwin et al. (2003) evaluated the serum Se level in psoriasis patients and their results found decreasing serum Se concentrations among psoriasis patients. Furthermore, Serwin et al. (2006) evaluated the Se level in the serum of psoriasis patients who had a recent onset of psoriasis, most having mild to moderate psoriasis, and they found that there was no difference in the serum level of this element between patients and healthy controls. But studies on the role of Se in the pathogenesis of psoriasis are scanty. The results of some previous investigations contradict the results of the current study, where the mean level of serum Se was statistically higher in patients than in controls, and most of the exaamined patients in the present study were newly diagnosed. The present study showed a statistically highly significant decrease in the serum level of lithium in patients compared to controls. The serum Mn level ranged from 2.43-2.68 and 2.31-3.02 μg L^{-1} in mild and moderate psoriasis patients, respectively, while in the severelz ill patients it was 2.40 μg L^{-1}. In the control group, Mn level ranged from 0.62-0.69 μg L^{-1}; there was a significant increase in patients compared to controls. Another study reported that there was a significant increase in the mean serum level of manganese in psoriatic patients as compared to healthy controls (Fidarov 1967).

Table 5

Comparison between patients and controls as regards the Cu/Zn ratio

Group	Cu/Zn ratio		T-test	
	range	mean ± SD	*t*	P-value
Patients (no. = 30)	0.560-1.267	0.669±0.115	5.272	0.000
Controls (no. = 10)	0.216-1.119	0.976±0.272		

Table 6

Comparison between patients and controls as regards the Fe/Mn ratio

Group	Fe/Mn ratio		T-test	
	range	mean ± SD	*t*	*P*-value
Patients (no. = 30)	0.164-0.259	0.209±0.025	45.489	0.000
Controls (no. = 10)	0.985-1.355	1.170±0.118		

Tables 5 and 6 compare the Cu/Zn and Fe/Mn ratio, respectively, between patients and controls. The Cu/Zn ratio in psoriasis patients ranged from 0.560 - 1.267, with mean ±SD (0.669 ± 0.115), and in control group it ranged from 0.216 - 1.119, with mean ±SD (0.976 ± 0.272). These results are consistent with the findings reported by Butnaru et al. (2008), who evaluated the Cu/Zn ratio at a mean 0.81 in psoriasis patients and 0.96 in healthy controls. There was a significant decrease in psoriasis patients compared to controls. In an earlier study of Nigam (2005), who evaluated the serum zinc and copper levels in psoriasis patients, no significant changes in either zinc or copper levels were demonstrated. The Fe/Mn ratio psoriasis patients ranged from 0.164-0.259, with mean ±SD 0.209 ± 0.025, and in control group it ranged from 0.985-1.355, with mean ±SD 1.170 ± 0.118. There was a significant decrease in psoriasis patients compared to controls. There are no previous studies that would investigate this ratio in psoriasis patients, but the Fe/Mn ratio was determined in plants by Kabata-Pendias, Mukherjee (2007). They reported that Fe and Mn were interrelated in their metabolic functions in plants. Interactions between several elements in humans may determine the availability of Fe, i.e. antagonistic relationships have been observed between Fe and Zn and between Fe and Mn. The antagonistic relationship between Fe and Cu is complex and associated with oxidation-reduction processes (Keen et al. 1986).

The correlations and interrelations between levels of serum trace elements in psoriatic patients are shown in Table 7. The results prove correlations between serum levels of trace elements of a significant value in psoriatic patients. The serum level of B revealed a negative correlation with Mn, Fe and Zn, while the serum levels of Mn and Se revealed a positive correlation. Table 8 shows correlations between serum trace elements in patients and patients' age at the onset of the disease. In patients less than 30 years old, the results showed a negative correlation between the age of onset of the

Table 7

Correlation between serum levels of trace elements with significant values in psoriatic patients

Elements		Lithium	Boron	Manga-nese	Zinc	Rubidium	Cadmium	Selenium
Lithium	*r*	1.000						
	P-value	0.000*						
Boron	*r*	0.276	1.000					
	P-value	0.115	0.000*					
Manganese	*r*	-0.019	-0.639	1.000				
	P-value	0.914	0.000*	0.000*				
Zinc	*r*	0.036	0.009	0.199	1.000			
	P-value	0.840	0.958	0.260	0.000*			
Rubidium	*r*	-0.143	-0.095	-0.039	-0.348	1.000		
	P-value	0.420	0.593	0.825	0.044*	0.000*		
Cadmium	*r*	0.040	-0.362	0.431	0.251	-0.310	1.000	
	P-value	0.821	0.035*	0.011*	0.152	0.074	0.000*	
Selenium	*r*	-0.100	-0.199	0.375	0.005	-0.074	0.569	1.000
	P-value	0.574	0.260	0.029*	0.979	0.679	0.000*	0.000*

*significant *P*-value < 0.05, *r* = correlation coefficient

Table 8

The correlation between serum levels of trace elements in patients and age at the onset of the disease

Trace elements	*r*	*P*-value
Lithium	0.046	0.797
Boron	0.203	0.250
Manganese	-0.299	0.086
Copper	-0.057	0.749
Zinc	-0.434	0.010*
Selenium	-0.214	0.224

*significant *P*-value < 0.05

disease and the serum level of Zn. With respect to correlations between serum trace elements with a significant value and trace elements with a non -significant value for all psoriatic patients, the results showed a positive correlation between selenium and copper in all psoriatic patients, as shown in Table 9.

Discrepancies in the serum levels of trace elements in psoriasis patients attributed to differences in the duration and severity of the disease between various studies may reflect the influence of dietary intake of food and the

Table 9

The correlation between serum trace elements with a significant value and trace elements with a non-significant value of all psoriatic patients

Elements		Lithium	Boron	Manganese	Zinc	Selenium	Iron
Copper	*r*	-0.186	-0.287	0.274	0.032	0.520	0.000
	P-value	0.292	0.100	0.117	0.856	0.002*	0.999

*significant *P*-value < 0.05, *r* = correlation coefficient

source of drinking water in each group of patients. Regarding the PASI score value in the present study, there were insignificant changes in the serum level of essential trace elements among the patients compared to controls. Therefore, there is no clear relationship between the severity of psoriasis and the serum concentrations of trace elements. This may be due to a relatively small number of the patients in the present study and the random selection of patients with respect to the severity of the disease.

CONCLUSION

The results showed significant changes in 7 essential trace elements, i.e. Fe, Li, B, Zn, Cu, Se, and Mn, which may serve as biomarkers for psoriasis and as parameters of the efficacy of the treatment. The serum level of B revealed a negative correlation with Mn, Fe and Zn while the serum levels of Mn and Se revealed a positive correlation. In patients less than 30 years old, the results showed a negative correlation between the age at which the disease began and the serum level of Zn. With respect to the correlations between serum trace elements with a significant value and trace elements with a non-significant value for all psoriatic patients, the results showed a positive correlation between selenium and copper in all psoriatic patients. There is no clear relationship between the severity of psoriasis and the serum concentrations of trace elements. In the future, use of salts rich in some trace elements in bathing water at home may help to improve the condition of patients suffering from psoriasis.

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