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Trace elements in blood compartments in psoriatic patients and their impact on the course of the disease – literature review

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ABSTRACT

Psoriasis is an autoimmune disease resulting in para- and hyperkeratosis of the epidermis, which is manifested by specific skin lesions. It affects approx. 2% of the European and the US populations; however, it is less common in Asia and Africa. Psoriatic patients show certain changes in blood components due to chronic inflammation, and the concentrations of some micronutrients may differ from those observed in healthy individuals. In the literature, there are many studies analyzing the concentrations of various elements in the course of the disease. Our review summarizes the association of the following microelements with psoriasis: Cu, Se, Fe, Zn, Ni, Cr, Cd, and As. In the case of Cu, all researchers report an increase in its blood concentration, but the results concerning other microelements are inconclusive. The discrepancies may stem from differences between the studied populations, environmental conditions, and anthropogenic pollution. However, the role of trace elements is rather marginal in comparison to the well-documented factors that are the focal points for modern psoriasis therapy.

Keywords: trace elements; psoriasis; psoriatic patients; microelements in psoriasis; selenium and zinc in psoriasis.

INTRODUCTION

Psoriasis is a chronic inflammatory skin disorder characterized by keratinocyte hyperproliferation and cutaneous increased blood flow induced by the stimulation of tissue-resident immune cells and the marked alteration of cytokine profiles. The prevalence of this disease among adults is estimated to be around 3.2% and differs between populations; for instance, it is particularly high among Caucasians [1]. Many possible genes involved in the pathogenesis of psoriasis have been reported, indicating a polygenic model of inheritance [2].

The pathogenesis of psoriasis is still not fully elucidated. The disease is associated with genetic predisposition and a variety of environmental risk factors, such as: diet, smoking, alcohol consumption, stress, and obesity. Increased reactive oxygen species and lipid peroxidation are the main components of the inflammatory process in psoriasis, as well as many other dermatologic disorders [3, 4]. Cascading enzyme systems participating in this process are influenced by free radicals which can be neutralized by microelements such as Se, Zn, and Cu [5]. The glutathione peroxidase enzyme is responsible for protecting cells against the detrimental effects of free radicals and is predominantly dependent on Se. Zinc and Cu are also involved in anti-inflammatory activity by being part of metalloenzymes such as Cu/Zn superoxide dismutase. Available research on the role of microelements in the pathogenesis of psoriasis, as well as their influence on the disease course, still seems to be insufficient [6]. There are numerous inconsistent reports on whether the concentration of certain trace element remains elevated or decreased among psoriatic patients. Hence, the aim of this study is to analyze the literature data about the possible association between psoriasis and several trace elements in the blood.

COPPER

Serum Cu concentration in patients has been a subject of research for a long time. In all the available studies, authors found elevated serum Cu levels in cases with psoriasis (Tab. 1). This observation is important, especially considering the different populations studied, including Indian, American, Iranian, Iraqi, and Egyptian [7, 8, 9, 10, 11, 12, 13]. Furthermore, 2 analyses showed a positive correlation between the concentration of Cu and the psoriasis area severity index (PASI) [7, 10]. However, this was not confirmed in the study by Basavaraj et al., where serum Cu levels were higher in moderate psoriasis compared to severe psoriasis [8]. Several studies have observed that the Cu/Zn ratio, which decreases in patients with psoriasis, may

be a more precise indicator of the severity of the disease than the Cu level alone [7, 8, 12]. In their analyses, Zackheim and Wolf and Ala et al. observed different serum concentrations of Cu between men and women, as well as an increase in the level of this element with age, especially in the female population, which is likely related to estrogens. Therefore, it is important to consider age and gender stratification when conducting similar studies [11, 14]. Considering the increased concentration of Cu in the serum of psoriasis patients, studies have suggested exploring substances that can reduce its concentration or have antioxidant effects, such as Cu-chelating substances like penicillamine, or vitamins A and E [13, 14].

SELENIUM

Selenium is an element that is tested in the course of many skin diseases. In each of the analyzes cited by us, covering the Polish, Western European, Egyptian and Pakistani populations, a decrease in the concentration of this element was found in plasma, serum or red blood cells, hair, or nails of patients with psoriasis (Tab. 2) [15, 16, 17, 18, 19, 20]. Kharaeva et al. showed a decrease in the oxidative stress markers and a reduction in psoriasis-induced changes after the oral administration of Q10 coenzyme, vitamin E, and Se in patients with erythrodermic and arthropathic psoriasis [21]. Fairris et al., on the other hand, used Se and vitamin E supplementation orally, which increased the concentration of this element in blood, but it did not affect the PASI, most likely due to the lack of an increase in the concentration of Se in the skin [19]. The study by Pinton et al. who observed a reduction in the PASI in the Western European population, to a greater extent in women than in men after taking a bath in Se-rich water in combination with oral intake, seems to confirm the thesis that it is necessary to supplement also reserves of this element in the skin [22]. However, the conclusion is not clear as Elhaddad et al. provide us with additional data concerning an increasing level of Se among psoriatic patients [12].

IRON

In the case of serum Fe concentration in patients with psoriasis, a decrease was found in most of the cited studies (Tab. 3). However, the data are inconclusive because in 2 reports there was an increase in this element, but only in its free form. The range of populations quoted in the research includes: Indian, Egyptian, and Polish [8, 10, 12, 23, 24, 25]. Apart from the concentration

TABLE 1. Overview of copper in blood compartments in psoriatic patients

First author and year of publication	Compartment	Measuring method	Association of copper with psoriasis	Number of psoriatic patients	Country
Gajjar et al., 2015 [7]	serum	ABA Minura 300	↑ ($p < 0.05$)	50	India
Zackheim and Wolf, 1972 [11]	serum	AAS	↑ ($p < 0.001$)	60♂	USA
Basavaraj et al., 2009 [8]	serum	ICP-AES	↑ ($p < 0.001$)	50	India
Ala et al., 2013 [14]	venous blood	AAS	↑ ($p = 0.003$)	25	Iran
Sheikh et al., 2015 [9]	serum	N/A	↑ ($p < 0.0001$)	100	India
Al-Wasiti et al., 2011 [13]	serum	AAS	↑ ($p < 0.01$)	50	Iraq
Elhaddad et al., 2017 [12]	serum	ICP-MS	↑ ($p < 0.05$)	60	Egypt
Sobhy Mohamad, 2013 [10]	serum	ICP-AES	↑ ($p < 0.05$)	60	Egypt

AAS – atomic absorption spectrometry; ICP-AES – inductively coupled plasma atomic emission spectroscopy; N/A – not available; ICP-MS – inductively coupled plasma mass spectrometry; ABA – abscisic acid

TABLE 2. Overview of selenium in blood compartments in psoriatic patients

First author and year of publication	Compartment	Measuring method	Association of selenium with psoriasis	Number of psoriatic patients	Country
Dilawar et al., 2019 [18]	serum	HGAAS	↓ ($p < 0.001$)	480	Pakistan
Serwin et al., 2003 [15]	plasma	FL	↓ ($p < 0.05$)	30	Poland
Seneczko, 2004 [16]	serum erythrocyte	ICP-AES	↓ ($p < 0.001$) ↓ ($p < 0.001$)	34	Poland
Fairris et al., 1989 [19]	whole blood serum	N/A N/A	↓ ($p < 0.001$) ↓ ($p < 0.001$)	69	UK
Elhaddad et al., 2017 [12]	serum	ICP-MS	↑ ($p < 0.05$)	60	Egypt

HGAAS – hydride generation atomic absorption spectroscopy; FL – fluoroscopy; ICP-AES – inductively coupled plasma atomic emission spectroscopy; N/A – not available; ICP-MS – inductively coupled plasma mass spectrometry

TABLE 3. Overview of iron in blood compartments in psoriatic patients

First author and year of publication	Compartment	Measuring method	Association of iron with psoriasis	Number of psoriatic patients	Country
Basavaraj et al., 2009 [8]	serum	ICP-AES	↓ ($p < 0.001$)	50	India
Ghosh et al., 2008 [25]	stroma-free hemolysate	N/A	↑ ($p < 0.001$)	16	India
Rashmi et al., 2012 [23]	serum	ICP-AES	↓ ($p < 0.05$)	81	India
Ponikowska et al., 2015 [24]	serum	ELISA	= ($p = 0.29$)	39	Poland
Elhaddad et al., 2017 [12]	serum	ICP-MS	↑ ($p < 0.05$)	60	Egypt
Sobhy Mohamad, 2013 [10]	serum	ICP-AES	↑ ($p < 0.05$)	60	Egypt

ELISA – enzyme-linked immunosorbent assay; ICP-AES – inductively coupled plasma atomic emission spectroscopy; N/A – not available; ICP-MS – inductively coupled plasma mass spectrometry

TABLE 4. Overview of zinc in blood compartments in psoriatic patients

First author and year of publication	Compartment	Measuring method	Association of zinc with psoriasis	Number of psoriatic patients	Country
Afridi et al., 2011 [26]	blood	ETAAS	↓ ($p < 0.001$)	418	Pakistan
Gajjar et al., 2015 [7]	serum	ABA Miura 300	↓ ($p < 0.05$)	50	India
Basavaraj et al., 2009 [8]	serum	ICP-AES	↓ ($p < 0.0001$)	50	India
Ala et al., 2013 [14]	venous blood	AAS	= ($p = 0.57$)	25	Iran
Sheihk et al., 2015 [9]	serum	N/A	↓ ($p < 0.0001$)	100	India
Al-Wasiti et al., 2011 [13]	serum	AAS	↓ ($p < 0.0001$)	50	Iraq
Elhaddad et al., 2017 [12]	serum	ICP-MS	↑ ($p < 0.05$)	60	Egypt
Butnaru et al., 2008 [29]	serum	AAS	↑ ($p = 0.04$)	21	Romania
Sobhy Mohamad, 2013 [10]	serum	ICP-AES	↓ ($p < 0.05$)	60	Egypt

AAS – atomic absorption spectrometry; ICP-AES – inductively coupled plasma atomic emission spectroscopy; N/A – not available; ICP-MS – inductively coupled plasma mass spectrometry; ABA – abscisic acid; ETAAS – electro thermal atomic absorption

of Fe itself, some authors have also investigated other elements important for Fe balance. Interestingly, Ponikowska et al. observed a decreased level of transferrin saturated with Fe and an increase in soluble transferrin receptor. In the case of transferrin, it would seem normal as it is a negative acute phase protein. However, the study also showed a decreased level of hepcidin, which contradicts the theory of the increase in this protein in response to the inflammatory process [24], Rashmi et al. found a higher ferritin-to-Fe ratio, although the ferritin level itself did not show significant differences [23]. In both studies, relationships between Fe concentration and PASI were also excluded, and Ponikowska et al. only noticed a correlation between its low concentration and low body mass index [23, 24]. Ghosh et al., due to an increase in the concentration of free Fe in steep free hemolysate in ill patients, proposed further research on Fe chelators as a therapeutic option [25]. Elhaddad et al., in their study, found that Fe levels in patient's serum were decreased and suggested supplementing it in the form of mineral salts [12].

ZINC

The concentration of Ze has been tested in patients with psoriasis in serum, whole blood, urine, and hair (Tab. 4) [7, 8, 9, 10, 12, 13, 26, 27]. Afridi et al. found an increase in the concentration of this element only in patients' urine [26]. Al-Wasiti et al. and Sobhy Mohamad suggest a possible association of low Zn levels in serum with the loss of this element through excessive peeling of the epidermis [10, 13]. In the Nigam review, a decrease in serum Zn concentration was observed to be inversely proportional to disease severity [27]. It has also been proven that its concentration is lower in the serum of patients with a positive family history, and Elhaddad et al. showed a gradual decrease in serum Zn with the duration of the disease and the age of patients [12, 27]. A therapeutic option in the treatment of psoriasis may be a correction of Zn deficiency and an antioxidant activity (Zn deficiency may increase oxidative stress). Al-Wasiti et al. suggest the use of vitamins A and E as well as additional Zn supplementation in the treatment of patients [13]. Sadeghian et al. demonstrated the effect of external Zn supplementation on the reduction in the PASI [28]. In contrast, Elhaddad et al. and Butnaru et al. validate the increase in Zn concentration in psoriatic patients serum [12, 29].

NICKEL, CHROME, CADMIUM, ARSENIC

It is also worth paying attention to elements less frequently discussed in the literature, such as Ni, Cr, Cd, and As. Studies on Ni show its increase in serum, blood, urine, and hair in ill patients. However, the results of these studies are limited

TABLE 5. Overview of nickel, chrome, and cadmium in blood compartments in psoriatic patients

First author and year of publication	Trace elements	Compartment	Measuring method	Association with psoriasis	Number of psoriatic patients	Country
Smith et al., 1994 [30]	Ni	serum	ETAAS	↑ ($p < 0.05$)	16	USA
Afridi et al., 2011 [26]	Ni Cr Cd	blood	ETAAS	↑ ($p < 0.001$) ↑ ($p < 0.001$) ↑ ($p < 0.001$)	418	Pakistan
Liaw et al., 2017 [31]	Cd	serum	ETAAS	↑ ($p < 0.005$)	150	USA
Kolachi et al., 2012 [32]	As	blood	ETAAS	↑ ($p = 0.01–0.001$)	418	Pakistan

ETAAS – electro thermal atomic absorption

to only 2 populations (Tab. 5) [26, 30]. Concentrations of Cr, Cd, and As were also found to be increased in the serum, blood, urine, and hair of psoriasis patients in the cited analyses [26, 31, 32]. In the case of Cd, it has been observed that excessive exposure to this element may exacerbate the course of the disease and increase the frequency of remission. Moreover, its serum concentration correlates with the advancement of psoriasis. Therefore, patients should avoid factors that increase Cd concentration in the body, such as smoking [31]. For each of the above-mentioned elements, the dominant factor contributing to their increased concentration in the body is ubiquitous environmental pollution. Reducing it or improving protection against them could potentially decrease the incidence of psoriasis in the future.

CONCLUSIONS AND FUTURE DIRECTIONS

The concentration of Cu in the blood is quite clearly related to psoriasis. We have enough reports to conclude that it is related to the severity of the disease, namely, it increases the PASI. As for Se and Zn, the majority of reports suggest decreased levels of these microelements in patients with psoriasis. This reduction lessens the antioxidant capacity of their bodies and thus contributes to disease progression. The data regarding Fe are so inconsistent that it is difficult to draw any clear conclusions. The rest of the elements, such as Ni, Cd, Cr, and As also seem to be an interesting topic for research, but there is too little data to find an answer to the question of whether they are clearly related to the disease. An important problem regarding the different levels of micronutrients is also the ubiquitous environmental pollutants, the influence of which on the incidence of psoriasis should be thoroughly investigated. The pathogenesis of psoriasis depends on plenty of factors. The most clinically important ones, which determine the methods of managing the disease, are currently well elucidated and documented. The concentration of trace elements cannot be included among them yet. Contemporary research indicates that their influence, in comparison with the aforementioned factors, is rather marginal.

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