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The role of Vitamin D in the prevention and treatment of inflammatory skin diseases – atopic dermatitis and psoriasis - literature review

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Summary:

Vitamin D is an important substance that has a pleiotropic range of action in the human body. Its important role is to influence the cells of the immune system and regulate the body's inflammatory response. Many physiological processes at the immune level have been discovered to prove this. Vitamin D deficiency is common and results mainly from limited sun exposure at certain latitudes or from insufficient dietary supply. This likely increases the risk of many diseases, including autoimmune diseases. Numerous evidence shows that also in skin

diseases such as AD or psoriasis, the level of calcitriol is of great importance, and its supplementation in the prevention and treatment of these diseases promotes frequent remissions and improves the clinical condition of patients. Therapy with high doses of vitamin D analogues can be effective and safe. The exact knowledge of the properties of this vitamin probably allows for its real and effective use in the treatment of skin diseases. However, numerous large-scale studies are still needed to more accurately determine the dosage, effects of this therapy and to use this preparation with certainty and the highest possible effectiveness in everyday medical practice.

Key words: vitamin D, vitamin D deficiency, vitamin D supplementation, atopic dermatitis, AD, psoriasis

INTRODUCTION AND PURPOSE

Vitamin D, otherwise known as calcitriol, is one of the most important substances needed by humans. The body can obtain it through synthesis as a result of exposure to the sun, especially UVB radiation, or by supplying it in the daily diet or in preparations from the pharmacy [1].

Vitamin D has a pleiotropic effect on the entire body. The basic and best known mechanism of its action is the regulation of calcium and phosphate metabolism in the body [2]. A large body of evidence in studies proves that the receptors characteristic of vitamin D are not only found in bones. They have also been found in other tissues of the body, including in the kidneys or liver. In addition, the immune, nervous and muscular systems also have relatively many of them [3]. Vitamin D is also integrally related to the skin, not only because of its synthesis there, but also by influencing a number of processes related to the physiology of skin cells. It has an impact on the immune functions that are associated with inflammation and hence disease processes that take place on this basis and have skin manifestations.

The aim of this study is to summarize the current knowledge on the use of vitamin D analogues in skin diseases as protective agents and as an additional treatment option next to traditional therapeutic regimens.

DESCRIPTION OF THE STATE OF KNOWLEDGE

It is well known that vitamin D has a very broad systemic effect, including anti-inflammatory and immunomodulatory effects [4, 5]. Currently, it is considered that it even acts as a hormone rather than a vitamin.

In the process of vitamin D production, human skin is a very important organ, because it is synthesized here, but it is also the target site for its biologically active form. Therefore, human

skin plays a key role in the metabolism of vitamin D. Vitamin D, in turn, is an important factor influencing many physiological functions of the skin. It participates in the proliferation of keratinocytes, their differentiation and apoptosis [6], has an immunoregulatory function, directly influencing the function of lymphocytes and the secretion of cytokines [7].

Vitamin D also plays a very significant role in skin homeostasis, mainly by acting as a barrier [8]. The active forms of vitamin D have a modulating effect on the skin's resistance, which makes them indispensable factors needed for the proper functioning of the immune system [9].

Due to numerous relationships with skin physiology and a number of functions, especially immunomodulating, vitamin D is considered as a therapeutic option in many skin pathologies [10], especially in those with inflammatory causes, such as atopic dermatitis, psoriasis, vitiligo and many others.

Vitamin D in atopic dermatitis

Atopic dermatitis (AD) is a chronic, recurrent skin disease that manifests itself by symptoms such as itching, inflammation and dry skin. They concern specific parts of the body, rarely covering large areas. Various factors contribute to the development of AD, of which genetics and the interaction of immunology play a large role. The influence of the environment is also significant. The interactions of these variables primarily disrupt the skin barrier - it is broken at the epithelial site. It is the leading cause of symptoms in AD patients. At the same time, there are disturbances in the skin's immune system, increased serum IgE levels, which are a characteristic feature of these patients [11].

Vitamin D₃ influences the skin barrier through various mechanisms. It modulates the structural proteins of the dermis - it affects, inter alia, glycoseramides. They are mainly responsible for maintaining proper skin hydration. In addition, it regulates innate immunity, producing peptides such as AMP peptides, defensins [12]. Additionally, it can be mentioned that vitamin D has an inhibitory effect on the production of many factors and cells that are actively involved in the onset of inflammation, which is also associated with the progression of skin symptoms. This vitamin reduces the activity of dendritic cells, inhibits the release of pro-inflammatory cytokines and IgE [13]. Good evidence for the above-mentioned interactions are vitamin D receptor polymorphisms. The occurrence of these genetic polymorphisms for vitamin D has an impact on the development of AD [14].

The influence of plasma vitamin D concentration and its supplementation on the occurrence of AD disease is an interesting topic that has been discussed in many studies. Links have been found between where a given population lives (at different latitudes) and the levels of vitamin D in the body. It is related to a specific exposure to the sun in certain areas of the Earth - low exposure to radiation has a direct impact on a lower level of vitamin D synthesis [15] then people with vitamin D deficiency, including children, in whom vitamin deficiencies are more often observed, have a greater risk of developing inflammatory diseases, including atopic eczema [16, 17]. Similarly, it has been found that winter is the time of more frequent clinical

exacerbations of AD symptoms in patients [15]. However, when vitamin supplementation was attempted for about 3 months in these patients, adequate clinical improvement was noticed [11]. Moreover, after 1 month of supplementing the deficiencies, there was a significant improvement in the skin microbiome, less frequent skin colonization by *S. aureus* [18].

Some studies, however, show a different position on the matter, showing that there is no link between low vitamin D levels in patients and a higher risk of developing the disease [19].

There is no known and confirmed optimal level of vitamin D, which would bring clear clinical effects in the prevention or treatment of patients with atopic eczema. Consequently, a great deal of further research is needed on this topic.

Vitamin D in psoriasis

Psoriasis is a chronic autoimmune, multifactorial skin disease. The pathology of this condition is not fully understood, but the processes influencing the development of this disease mainly include genetic factors and immunological dysregulation [20]. It is a disease in which the proliferation of keratinocytes is disturbed in an uncontrolled process. Also in the pathology of this disease, abnormal differentiation of these cells takes place [21].

Vitamin D deficiencies play a leading role in the scalp. They have been found in many psoriasis patients, and their association with the development of this disease has been confirmed frequently. Some studies show that oral calcitriol supplementation resulted in an improvement in the clinical condition, measured using the PASI questionnaire, even up to about 80% of the studied patients [22, 23]. However, there are also reports to the contrary [24].

Vitamin D analogues are used to treat psoriasis. It is an addition to the first line of therapy, next to the commonly used glucocorticosteroids, especially in mild disease [25]. They are characterized by a good profile, due to their high safety and good effectiveness in the treatment of patients [26]. Moreover, it was found that the combination of the two methods is much more effective than when steroids and calcitriol preparations are used alone. The vitamin reduces the negative side effects of steroid treatment (it reduces the thinning effect, skin atrophy), and these in turn reduce skin irritation caused by calcitriol [27]. UVA / UVB phototherapy, which is also one of the basic treatment methods like glucocorticosteroids, may also positively correlate with calcitriol. It is believed that it may be conducive to increasing its concentration in the serum of patients when both methods are used simultaneously [28].

Vitamin D receptors, as mentioned above, are present on skin cells - keratinocytes, which explains the beneficial therapeutic effect in treating patients with psoriasis. Apart from keratinocytes, these receptors can also be found in lymphocytes present in infiltrated areas of the skin [29]. Despite the discovery of a weak relationship between VDR gene polymorphisms

and the development of clinical symptoms in patients with psoriasis, this fact can be treated as a probable argument why vitamin D is a beneficial option for these patients [30]. With the mediation of this gene, it affects the process of inhibiting the proliferation of skin cells and their differentiation. It introduces changes in proteins, cytokines and interleukins such as IL-17, which all interact together to contribute to the overall anti-inflammatory response. This is very significant in achieving disease regression [31, 32].

Vitamin D suppresses and regulates the inflammatory response in psoriasis. It improves the function of the epidermis. However, research on the certainty of its therapeutic effect in the form of oral supplementation in psoriasis is still ambiguous and insufficient.

CONCLUSIONS:

Vitamin D has a broad systemic effect. It is important for the regulation of many physiological processes in the body, including those in the skin. It takes part in the immunomodulation of inflammation, which plays a significant role in the course of autoimmune and autoinflammatory diseases, including skin diseases such as AD, psoriasis and others. Moreover, its deficiencies in these patients are more often noticeable. Numerous links were found, confirmed by scientific research, regarding both positive and negative coloring about the relationship between maintaining an adequate concentration of calcitriol in the plasma and the influence on the course of these diseases. However, these reports may be at risk of error due to many variables that make unambiguous interpretation difficult. You need to be aware of the differences related to the patient's diet, the different levels of sun exposure during certain periods of the year, or geography-related variables.

Therefore, many large-scale studies are still needed to summarize and reach a common and unequivocal position on the exact efficacy, long-term effects and safety profile of the use of vitamin D preparations in the treatment of diseases such as AD, psoriasis.

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