

How to Cite:

Abidov, K., Khaitov, K., & Abidov, A. (2022). Application of cholecalciferol in complex therapy of atopic dermatitis. *International Journal of Health Sciences*, 6(S1), 4011–4020.
<https://doi.org/10.53730/ijhs.v6nS1.5731>

Application of cholecalciferol in complex therapy of atopic dermatitis

Khasankhodja Abidov

Tashkent Pediatric Medical Institute, Tashkent, Uzbekistan
Email: kabidov@gmail.com

Kakhramon Khaitov

Tashkent Pediatric Medical Institute, Tashkent, Uzbekistan
Email: drkakhramon1972@tashpmi.uz

Alisher Abidov

Tashkent Pediatric Medical Institute, Tashkent, Uzbekistan
Email: abidali@mail.ru

Abstract---The efficacy of cholecalciferol in the complex treatment of children with AD taking into account the level of vitamin D has been studied. 84 children with AD at the age from 3 to 15 years were studied, of which 41 (48.8%) were boys and 43 (51.2%) were girls. According to the SCORAD index, it was revealed that 25 patients were mild - 15.3 ± 2.3 points, 35 patients - moderate - 35.3 ± 5.4 points and 24 - severe - 63.2 ± 7.2 points. As a result of the therapy, the greatest clinical efficacy was achieved in the group of patients who received vitamin D, in addition to traditional treatment.

Keywords---children, atopic dermatitis, vitamin D, SCORAD index, cholecalciferol.

Introduction

Today, the problem of vitamin D deficiency is one of the most urgent, since, according to the results of numerous studies, more than half of the world's population is deficient in vitamin D [20], and its optimal serum level should not be lower than 20 ng / ml [23]. In this regard, it is of interest to study the mechanisms of vitamin D metabolism, its effect on metabolic processes in the body, as well as the relationship between this vitamin deficiency and the development of various pathologies in children and adult patients [4].

Urbanization also affects vitamin D deficiency, as in cities, children have more vitamin D deficiency [16] than their peers in rural areas [18]. The most significant

International Journal of Health Sciences ISSN 2550-6978 E-ISSN 2550-696X © 2022.

Corresponding author: Abidov, K.; Email: kabidov@gmail.com

Manuscript submitted: 18 Jan 2022, Manuscript revised: 09 Feb 2022, Accepted for publication: 27 March 2022

vitamin D deficiency was noted in adolescent children [24]. Research results show that vitamin D deficiency affects the development of body allergization [6, 9] and atopic dermatitis (AD), the severity of which correlates with the level of vitamin D in the blood serum [2, 3].

AD is a multifactorial inflammatory skin disease characterized by itching, chronic recurrent course and age-related characteristics of the localization and morphology of lesions. The disease is one of the most common skin pathologies (from 20 to 40% in the structure of skin diseases), occurring in all countries, in both sexes. In recent years, there has been an increase in the incidence of AD throughout the world. The disease is more common in large cities (less often in rural areas) [12].

In typical cases, AD begins in early childhood, may continue or recur in adulthood, significantly disrupts the quality of life of the patient and his family members. In most cases it develops in individuals with a hereditary predisposition and is often combined with other forms of allergic pathology, such as bronchial asthma, allergic rhinitis, etc. [1, 11, 13].

Correction of vitamin D deficiency in children is one of the urgent tasks of modern medicine. In children of various ages with a low level of vitamin D, it correlated not only with the development of pathologies of the musculoskeletal system, but also with the earlier development and severe course of atopic dermatitis, which led to a decrease in the quality of life of patients [22].

According to the results of randomized, double-blind, placebo-controlled studies, the effectiveness of AD therapy by adding vitamin D to the complex treatment of the disease was evaluated. In a number of studies, scientists using various scales – SCORAD (Scoring of Atopic Dermatitis) [15], EASI scale (Eczema Area and Severity Index) [17] assessed the effect of vitamin D on the severity of atopic dermatitis. An analysis of the research results showed that, according to the SCORAD and EASI scales, the patients showed a significant improvement in the skin pathological process and a mild course of the disease after taking vitamin D. Another study showed that according to the results of assessments on the SCORAD and TIS scales (Three item severity score) and as a result of taking cholecalciferol, there was a significant improvement in the clinical picture of the disease in children with AD. [15].

During repeated examinations of children with AD with an initially low level of vitamin D, after the use of cholecalciferol for 3 months, an improvement in serum vitamin D parameters was noted with a simultaneous decrease in the SCORAD index, normalization of the cytokine status. Based on the results obtained, the authors come to the conclusion that the use of vitamin D in children with AD not only reduces clinical manifestations and provides an easier course of the disease, but also normalizes the parameters of immunity [5].

In the study by E. Galli, during the assessment by the SCORAD index, no statistically significant differences in the level of 25 (OH) D in the blood serum of children were found, depending on the severity of eczema manifestations.

Cholecalciferol administration did not affect the decrease in the SCORAD index [12].

Thus, the use of vitamin D in the prevention and treatment of skin pathology can be justified from the standpoint of the presence of confirmed cases of its positive effect on the clinical manifestations and the severity of the course of the disease, as well as data on the role of vitamin D deficiency in the immunopathogenesis of dermatological diseases. However, to date, the results of some studies are not so unambiguous regarding the clinical effect of the use of vitamin D in skin pathologies in children. In this regard, there is a need to further expand the study of the effectiveness of vitamin D use in children with various clinical forms of AD at different age periods. In this regard, the aim of the study was to study the effectiveness of cholecalciferol in the complex treatment of children with AD, taking into account the level of vitamin D.

Materials and Methods

Observations were carried out in 84 children with AD at the age of 3 to 15 years, of which 41 (48.8%) were boys and 43 (51.2%) were girls. The subjects were classified according to the following clinical forms of the disease based on the Working Classification of Atopic Dermatitis in Children, proposed by the Russian Association of Allergists and Clinical Immunologists (RAACI) in 2002, reflecting the specific clinical manifestations of dermatosis. Thus, the exudative form was established in 9 (10.7%) patients, erythematous-squamous - in 38 (45.2%), erythematous-squamous with lichenification - in 23 (27.4%), lichenoid - in 12 (14.3%) and pruriginous form - in 2 (2.4%) patients, respectively.

Studying the duration of the disease in our sample of patients showed that 37 (44.0%) patients had a disease duration of more than 3 years (Table 1), which indicates a late appeal of patients for medical help and a high probability of developing severe forms of the disease, when the skin process is widespread or diffuse in nature with prolonged exacerbations, rare and short-term remissions. It is natural that such a situation significantly complicates the course of the skin-pathological process itself and makes it difficult to carry out appropriate therapy.

Table 1
Distribution of patients by disease duration

Duration of the disease, n=84							
up to 1 year		from 1 to 3 years		from 3 to 6 years		from 6 to 14 years	
n	%	n	%	n	%	n	%
27	32,2%	20	23,8%	15	17,8%	22	26,2%

The study was conducted on the basis of the dermatological department of the clinic of the Tashkent Pediatric Medical Institute. To determine the severity of the course of the disease, the severity of the condition of patients with AD was assessed according to the SCORAD (Scoring of Atopic Dermatitis) index, which takes into account the prevalence of the skin process, the intensity of clinical manifestations and the patient's subjective sensations: $SCORAD = A / 5 + 7B / 2 + C$, where A - the sum of the points of the prevalence of skin lesions, B - the sum

of the points of the intensity of manifestations of AD symptoms, C - the sum of the points of subjective symptoms (pruritus, sleep disturbance) [14].

Determination of 25 (OH) D using enzyme-linked immunosorbent assay was carried out in order to identify the effect of the therapy on the condition of patients at various stages of treatment. According to the Russian Association of Endocrinologists, vitamin D deficiency is recommended to be defined as a concentration of 25 (OH) D <20 ng/ml, deficiency - a concentration of 25 (OH) D from 20 to 30 ng/ml, adequate levels as 30-100 ng/ml. Recommended target values of 25 (OH) D for correcting vitamin D deficiency are 30-60 ng/ml [7].

To correct vitamin D deficiency in children, drugs are used as a mandatory component of therapy. In the treatment of vitamin D deficiency / insufficiency, preference is given to the D3 form (cholecalciferol), which is comparatively more effective in achieving and maintaining target serum 25 (OH) D values. Cholecalciferol-D3 is a "native" form of vitamin D. It does not have initial activity, which explains its low toxicity, a wide therapeutic range and the possibility of using it in high doses.

One of the most effective representatives of this group is the water-soluble micellized form of vitamin D (Aquadetrim®, Medana Pharma TERPOL Group J.S., Co., Poland). The release form is an aqueous solution of 150,000 IU in a 10 ml dropper bottle (15,000 IU (375 µg) in 1 ml). 1 drop of the drug contains 500 IU of vitamin D3. This vitamin D preparation can be used with food or on an empty stomach, ensures the absorption of vitamin D regardless of diseases of the gastrointestinal tract, diet and biosynthesis of bile acids and does not require additional fat content in food for absorption. The benefits of an aqueous solution of vitamin D are:

- better absorption from the gastrointestinal tract (the aqueous solution is absorbed 5 times faster, and the concentration in the liver is 7 times higher);
- longer effect when using an aqueous solution (lasts up to 3 months, and an oil solution - up to 1-1.5 months);
- high activity, rapid onset of clinical effect (5-7 days after administration);
- convenience of dosage and safety of the dosage form [10].

Extensive clinical experience of using Aquadetrim and many experimental and clinical studies have demonstrated its high efficacy and safety. To fulfill our goals, we divided our patients into 2 groups: the control group (n = 31) - patients with AD with a 25 (OH) D level of 21.1 ng / ml, who received traditional therapy (levocetirizine, 5 mg per day, externally mometasone furoate 1 mg (glucocorticosteroid in the form of a lotion, cream or ointment) 2 times a day in a thin layer, ceramide - containing emollient, sodium thiosulfate 30% - 2-5 ml IV slowly No. 10 daily, enterosorbent containing 355 mg of hydrolyzed lignin and 120 mg lactulose); the main group (n = 53) - patients with AD with a 25 (OH) D level of 16.7 ng / ml, who underwent complex therapy using traditional methods of treatment and cholecalciferol. The results of clinical studies and meta-analyses demonstrate that in order to achieve the optimal level of 25 (OH) D in the blood in children (> 30 ng / ml), the drug should be taken in a dosage of 2000-5000 IU of

vitamin D per day [8]. The selection of the optimal dose of vitamin D to correct deficiency in each case was made individually, depending on age and body weight. The course of treatment in groups was carried out for 30 days. Evaluation of the effectiveness of treatment was carried out based on the registration of the SCORAD index and the level of 25 (OH) D.

Results and Discussions

During carrying out an objective assessment of the severity of the patient's condition according to the SCORAD index, we found that 25 patients were mild - 15.3 ± 2.3 points, 35 patients - moderate - 35.3 ± 5.4 points and 24 patients - severe - 63.2 ± 7.2 points. In all patients, the skin process corresponded to the clinical picture of AD and was predominantly widespread, represented by erythematous-squamous and / or papular rashes with severe infiltration and lichenification, multiple excoriation covered with hemorrhagic crusts and severe dryness of the skin (Fig. 1).

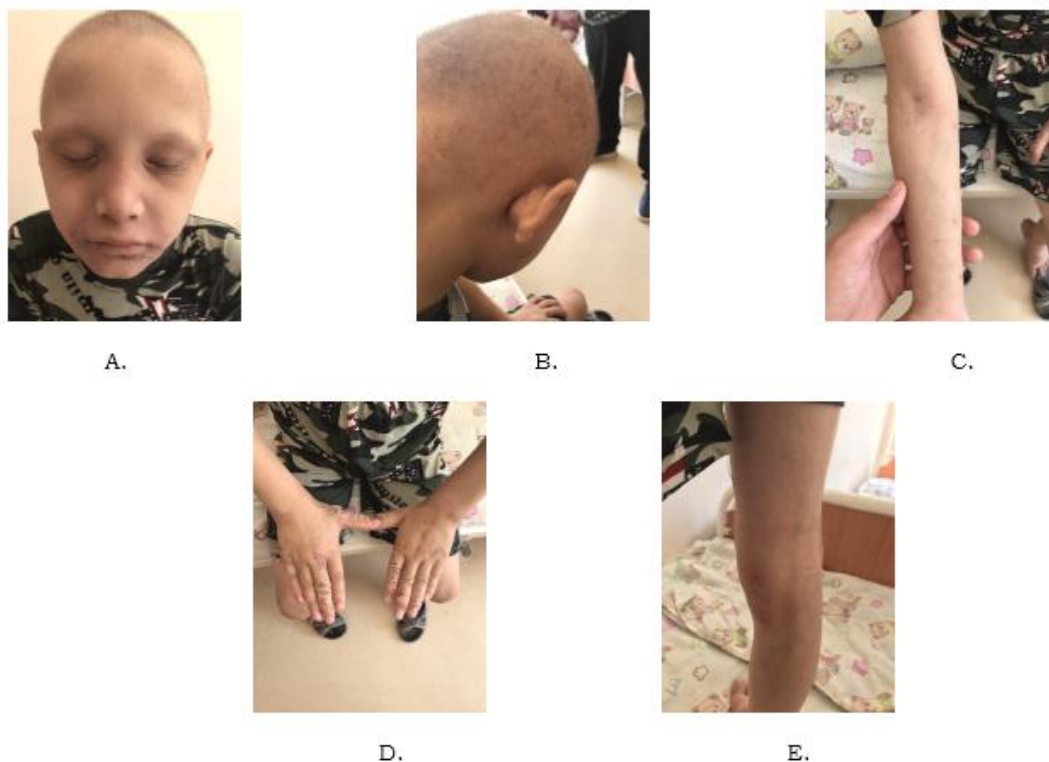


Figure 1. Patient U. Age - 7 years old, diagnosed with “L-20. Atopic dermatitis, erythematous-squamous form with lichenification” with a SCORAD index of 65.75 points and severe manifestations of atopic dermatitis. The pathological skin process is represented by erythematous-squamous foci with lichenification. There are papular elements with the formation of perifollicular and lichenoid papules localized on the skin of the face, upper and lower extremities, in the area of the forearms, wrists, as well as elbow and popliteal folds, ankle joints and feet. In the

area of the rash, there is pronounced dryness of the skin, peeling, slight erythema and infiltration, accompanied by the formation of erosions and excoriation due to intense itching. The main elements are epidermal-dermal papules that are very itchy, sometimes draining. Many secondary elements are revealed: erythema, papules, desquamation, excoriation on the skin of the face (Fig. 1A), upper (Fig. 1C, 1D) and lower (Fig. 1E) limbs. The patient had the diagnostic criteria J.M. Hanifin and G. Rajka: Denier-Morgan infraorbital folds, hyperpigmentation of the skin of the periorbital region and angular cheilitis (Fig.1A), typical morphology and localization: in children, the lesion on the face (Fig.1A) and in the flexion parts of the limbs (Fig.1C), localization of the skin process on the hands (Fig.1D), frequent lesions with cracks and crusts in the folds behind the ear (Fig.1B).

We divided patients by 25 (OH) D level into 2 groups: control group (n = 31), patients with AD with 25 (OH) D level - 21.1 ± 0.4 ng / ml and severity indicators according to SCORAD index - 27.9 ± 2.9 points; and the main group (n = 53), patients with AD with 25 (OH) D level - 16.7 ± 0.4 ng / ml and severity indicators according to the SCORAD index - 42.8 ± 3.8 points (Table 2).

Table 2
Dynamics of indicators in patients with AD during treatment

	main group, n=53		control group, n=31	
	before treatment	after treatment	before treatment	after treatment
SCORAD	42,8±3,8	12,2±1,9*	27,9±2,9	15,5±2,2°
25(OH)D ng/ml	16,7±0,4	30,3±0,5*•	21,1±0,4	21,1±0,4

Note: * - $p \leq 0.001$ in the main group before and after treatment; ° - $p \leq 0.05$ in the control group before and after treatment

Table 2 shows that as a result of the therapy, clinical efficacy was achieved in both groups of patients. However, there was a significant difference in the dynamics of the SCORAD index and the 25 (OH) D level. It was found that after 1 month of treatment, there was a significant decrease in the clinical symptoms of AD in the control group according to the SCORAD index by 44.4%, and in the main group - by 71.5% ($p \leq 0.001$) (Fig. 2). As a result of therapy, a statistically significant decrease in the severity of the course of the disease was noted with the formation of clinical remission in more than 75% of patients in both groups.

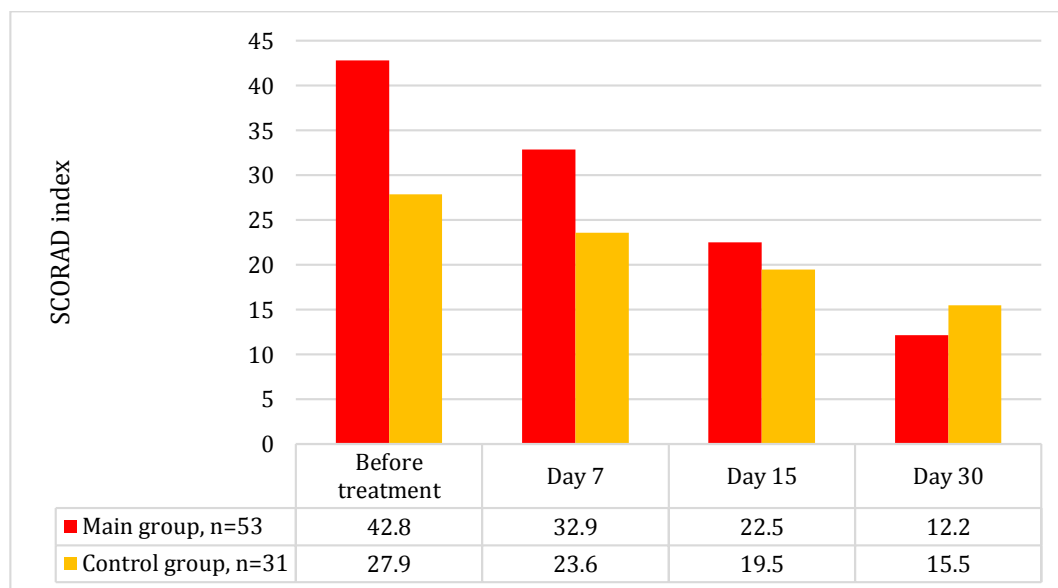


Figure 2. Dynamics of the mean values of the SCORAD index after treatment

The level of 25 (OH) D in the control group remained at the same values - 21.1 ng / ml - unchanged, while in the main group the level of 25 (OH) D increased to 30.3 ng / ml ($p \leq 0.001$). The normalization of the 25 (OH) D concentration in the blood serum of AD patients while taking cholecalciferol corresponded to the positive dynamics of the clinical symptoms of dermatosis. The patients showed a decrease in the area of the skin-pathological process, a quick restoration of the skin and a decrease in the number of eruptions and dry skin. In order to identify the features of the course of AD with an insufficient level of vitamin D, a comparative analysis of the severity and clinical forms of dermatosis was carried out (Table 3).

Table 3
Patient profile by severity and clinical forms of the disease

№	Sign	Group				
		main group, n=53		control group, n=31		
		n	%	n	%	
1	Severity	mild	11	20,7*	14	45,2
		moderate	23	43,4*	12	38,7
		severe	19	35,9*	5	16,1
		exudative	3	5,7	6	19,3
		erythematous-squamous	20	37,7	18	58,1
2	Clinical forms	erythematous-squamous with lichenification	18	33,9*	5	16,1
		lichenoid	10	18,9*	2	6,5
		pruriginous	2	3,8*	0	0

Note: * - in relation to the indicators of the control group $p < 0.05$

The study showed that patients in the control group with a vitamin D content in the blood serum of 21.1 ± 0.4 ng/ml had a milder course with a predominance of exudative (19.3%) and erythematous-squamous (58.1%) forms of AD. In the main group (with a vitamin D level of 16.7 ± 0.4), a more severe course was more often recorded with a predominance of the erythematous-squamous form with lichenification (33.9%), lichenoid (18.9%) and pruriginous (3.8%) forms of the disease.

Vitamin D has the following components: vitamin D3 - cholecalciferol and vitamin D2 - ergocalciferol. Vitamin D2 enters the body with food - foods containing this vitamin. Vitamin D3 is synthesized in the skin (the malpighian layer of the epidermis) by exposure to ultraviolet radiation from sunlight from 7-dehydrocholesterol. In the process of hydroxylation, vitamin D3 into 2 active forms: in the liver, under the action of 25-hydroxylase, 25-hydroxyvitamin D (25 (OH) D), or calcidiol, is formed, and in the kidneys, under the action of 1 α -hydroxylase, biologically active 1,25-dihydroxyvitamin D is synthesized (1,25 (OH) 2D3), or calcitriol. It is known that 1,25 (OH) 2D3 can be synthesized not only in the kidneys, but also in the cells of the pancreas, stomach, large intestine, epidermis, vascular endothelium, as well as in macrophages and placenta, which indicates the para- and autocrine function of cholecalciferol [21].

There is evidence that vitamin D3 plays an important role in strengthening the barrier function of the skin. It participates in the structuring of proteins of the stratum corneum of the skin, regulates glyceramides, which provide hydration of the protective lipid barrier that keeps the skin hydrated [1]. In addition, vitamin D reduces the release of pro-inflammatory cytokines and inhibits the release of IgE [6, 9, 19]. The above actions of vitamin D are possible and provide anti-inflammatory and regenerative effects on the skin, providing a therapeutic effect in AD.

Conclusion

Thus, the use of vitamin D (cholecalciferol) in the complex therapy of atopic dermatitis leads to the normalization of the level of 25 (OH) D in the blood of patients, has a positive clinical effect on the values of the SCORAD index and thereby reduces the length of hospital stay. Considering the above, it is necessary to continue further study of the relationship between vitamin D deficiency and AD and to develop complex therapy regimens for this pathology in children.

Acknowledgments

The authors thank Department of Pediatric Dermatology, Clinic of Tashkent Pediatric Medical Institute, Tashkent, Uzbekistan for their support in the data collection.

References

1. Gutsulyak, S. A. (2019). Atopic dermatitis in children: textbook. Irkutsk: ISMU, 72.
2. Dvoryankova, E., Piruzyan, A., Smolkina, O., & Korsunskaya, I. M. (2020). Effect of vitamin D on the course of atopic dermatitis. *Effective pharmacotherapy*, 16(9), 40-43.
3. Zhiltsova, E. E., & Chakhoyan, L. R. (2018). The role of immunological disorders in the development of atopic dermatitis. *Research'n Practical Medicine Journal*, 5(1).
4. Zakharova, I. N., Yablochkova, S. V., & Dmitrieva, Yu. A. (2013). Known and unknown effects of vitamin D. *Issues of modern pediatrics*, 12(2), 20-25.
5. Naletov, A., Shapchenko, T., & Karpenko, D. (2019). The role of vitamin D in the prevention and treatment of allergic diseases in children. *Medical and social problems of the family*, 24(1), 74-80.
6. Pigarova, E. A., Pleshcheev, A. V., & Dzeranova, L. K. (2015). The effect of vitamin D on the immune system. *Immunology*, 36(1), 62-66.
7. Pigarova, E. A., Rozhinskaya, L. Ya., Belaya, Zh. E., Dzeranova, L. K., Karonova, T. L., Ilyin, A. V., ... & Dedov, I. I. (2016). Clinical guidelines of the Russian Association of Endocrinologists for the diagnosis, treatment and prevention of vitamin D deficiency in adults. *Problems of Endocrinology*, 62(4), 60-84. <https://doi.org/10.14341/probl201662460-84>
8. Pludowski, P., Karczmarewicz, E., Bayer, M., Carter, G., Chlebna-Sokół, D., Czech-Kowalska, J., ... & Żmijewski, M. A. (2013). Practical guidelines for the supplementation of vitamin D and the treatment of deficits in Central Europe—recommended vitamin D intakes in the general population and groups at risk of vitamin D deficiency. *Endokrynologia Polska*, 64(4), 319-327.
9. Snopov, S. A. (2014). Mechanisms of action of vitamin D on the immune system. *Medical Immunology*, 16(6), 499-530.
10. Tatarova, N. A., & Airapetyan, M. S. (2020). Vitamin D deficiency and iron deficiency anemia in women in the transitional menopausal period. *Clinical case. Gynecology*, 22(5), 87-90. <https://doi.org/10.26442/20795696.2020.5.200446>
11. Khaitov, K. N., & Abidov, H. A. (2017). Skin pathologies in the aspect of allerge diseases. In *Theoretical and practical problems of the development of modern science* (pp. 47-48).
12. Khaitov, K. N., Abidov, H. A., & Kim, Z. A. (2019). Frequency of allergodermatosis. In *Actual problems of modern science in the 21st century* (pp. 45-50).
13. Khaitov, K., Abidov, H., & Fakhriev, J. (2018). Dermatoses and their significance. In *Modern trends in the development of education, science and technology* (pp. 140-142).
14. Yanchevskaya, E. Yu., Bashkina, O. A., & Makrem, B. M. (2016). Analysis of assessments of the severity of atopic dermatitis in children. *Russian Journal of Skin and Venereal Diseases*, 19(6), 334-339. <http://dx.doi.org/10.18821/1560-9588-2016-19-6-334-339>
15. Amestejani, M., Salehi, B. S., Vasigh, M., Sobhkhiz, A., Karami, M., Alinia, H., ... & Behzadi, A. H. (2012). Vitamin D supplementation in the treatment

- of atopic dermatitis: a clinical trial study. *Journal of Drugs in Dermatology*, 11(3).
16. Bose, S., Breysse, P. N., McCormack, M. C., Hansel, N. N., Rusher, R. R., Matsui, E., ... & Diette, G. B. (2013). Outdoor exposure and vitamin D levels in urban children with asthma. *Nutrition journal*, 12(1), 1-7.
 17. Camargo Jr, C. A., Ganmaa, D., Sidbury, R., Erdenedelger, K., Radnaakhand, N., & Khandsuren, B. (2014). Randomized trial of vitamin D supplementation for winter-related atopic dermatitis in children. *Journal of Allergy and Clinical Immunology*, 134(4), 831-835.
 18. Fang-Mercado, L. C., Urrego-Álvarez, J. R., Merlano-Barón, A. E., Meza-Torres, C., Hernández-Bonfante, L., López-Kleine, L., & Marrugo-Cano, J. (2017). Influence of lifestyle, diet and vitamin D on atopy in a population of Afro-descendant Colombian children. *Revista alergía México*, 64(3), 277-290.
 19. Khaitov, K. N., Abidov, A. M., Abidov, K. A., & Karimov, B. B. (2021). A modern view on pathogenetic therapy of atopic dermatitis in children. *New day in medicine*, (1), 217-227.
 20. Nabeta, H. W., Kasolo, J., Kiggundu, R. K., Kiragga, A. N., & Kiguli, S. (2015). Serum vitamin D status in children with protein-energy malnutrition admitted to a national referral hospital in Uganda. *BMC research notes*, 8(1), 1-8.
 21. Plum, L. A., & DeLuca, H. F. (2009). The functional metabolism and molecular biology of vitamin D action. *Clinical Reviews in bone and mineral metabolism*, 7(1), 20-41.
 22. Powe, C. E., Evans, M. K., Wenger, J., Zonderman, A. B., Berg, A. H., Nalls, M., ... & Thadhani, R. (2013). Vitamin D-binding protein and vitamin D status of black Americans and white Americans. *New England Journal of Medicine*, 369(21), 1991-2000.
 23. Rathi, N., & Rathi, A. (2011). Vitamin D and child health in the 21st century. *Indian pediatrics*, 48(8), 619-625.
 24. Maguire, J. L., Russell, M. L., Smieja, M., Walter, S. D., & Loeb, M. (2017). Prevalence and predictors of low serum 25-hydroxyvitamin D levels in rural Canadian children. *Paediatrics & Child Health*, 22(3), 125-129.