

PROTEIN METABOLISM IN CHILDREN, SUFFERING FROM VITILIGO, DEPENDING ON MICROBIOCYNOSIS OF INTESTINE AND METHODS OF THIS CORRECTION

¹Sobirov U.Yu., ³Rixsiev U.Sh., ^{1,2}Mamadiev A.A., ^{2,3}Yuldashev M.A.

¹Republican Specialized Scientific and Practical Medical Center for Dermatovenereology and Cosmetology of the Ministry of Health of the Republic of Uzbekistan

²Jizzak Regional Regional Branch of the Republican Specialized Scientific and Practical Medical Center of Dermatovenereology and Cosmetology of the Ministry of Health of the Republic of Uzbekistan,

³Tashkent Pediatric Medical Institute

✓ Resume

Subjects of the inquiry: blood, faeces, saliva of 132 children suffered from vitiligo at the age from 1 to 16 years.

Aim of the inquiry. To study protein metabolism, microbiocynosis of intestine and disintoxicational function of liver in children suffered from vitiligo, depending on clinical forms of disease and to improve present methods of therapy.

Methods of inquiry: clinical, bacteriological, biochemical.

The results achieved and their novelty. For the first time in children with vitiligo aminoacid blood spectrum, depending on clinical forms of disease, was researched. At the same time with hyper-aminoacidemia changes of correlation between different aminoacids were revealed: reduce of phenylalanine/tyrosine, histidine/glutamine acid and serine/glycine. Coefficients raise of asparagin acid/alanin, glutamine acid/prolin shows to expressed metabolism disorder of aminoacids, intensified formation of ammonia in tissues and reduce of hepatocytes functional activity. Leucin/isoleucin coefficient is increased in 1,2 times that witnesses about disorder of protein synthesis. It was revealed that in all patients with vitiligo, not depending on intestine disbacteriosis, statistically reliable raise of above mentioned aminoacids and insignificant reduce of phenylalanine concentration, was marked. For the first time influences of blood aminoacid spectrum on activity and vitiligo process course were analysed, that gave possibility to approach purposefully to complex treatment, including therapeutic nutrition.

Practical value. Practical health care was suggested the carried out scheme of treatment of children suffering from vitiligo with inclusion of therapeutic nutrition (diet 4b), that will take to a raise of therapy efficiency.

Key words: vitiligo in children aminoacids, metabolism disorder, disbacteriosis of intestine, therapeutic nutrition, pathogenetic treatment.

БЕЛКОВЫЙ ОБМЕН У ДЕТЕЙ БОЛЬНЫХ ВИТИЛИГО, В ЗАВИСИМОСТИ ОТ МИКРОБИОЦЕНОЗА КИШЕЧНИКА И МЕТОДЫ ИХ КОРРЕКЦИИ

¹Собиров У.Ю., ³Рихсиев У.Ш., ^{1,2}Мамадиев А.А., ^{2,3}Юлдашев М.А.

¹Республиканский специализированный научно-практический медицинский центр дерматовенерологии и косметологии Министерства Здравоохранения Республики Узбекистан

²Джизакский областной региональный филиал республиканского специализированного научно-практического медицинского центра дерматовенерологии и косметологии министерства здравоохранения Республики Узбекистан,

³Ташкентский педиатрический медицинский институт

✓ Резюме

Объект исследования: Было обследовано 132 детей и подростков больных витилиго в возрасте от 1 года до 16 лет.

Цель работы: Изучить белковый обмен, микробиоценоз кишечника и дезинтоксикационную функцию печени у детей больных витилиго, в зависимости от клинических форм заболевания и усовершенствовать существующие методы терапии.

Методы исследования: Клинический, бактериологический, биохимический.

Полученные результаты и их новизна: У детей больных витилиго, было изучено аминокислотный спектр крови в зависимости от клинической формы заболевания. Наряду с гипераминоацидемией выявлено изменение соотношения между отдельными аминокислотами: снижение коэффициентов фенилаланин/тирозин, гистидин/глутаминовая кислота и серин/глицин. Увеличение коэффициентов аспарагиновая кислота/аланин, глутаминовая кислота/пролин указывает на выраженное нарушения метаболизма аминокислот усиленное образования аммиака в тканях и снижение функциональной активности гепатоцитов. Коэффициент лейцин/изолейцин повышается 1,2 раза, что свидетельствует о нарушении синтеза белков. Выявлено, что у всех больных витилиго независимо от степени дисбиоза кишечника отмечается статистически достоверное повышение вышеуказанных аминокислот и незначительное снижение концентрации фенилаланина. Проанализировано влияния аминокислотного спектра крови на активность и течение витилигиозного процесса, что дало возможность целенаправленно подходить к комплексному лечению с включением лечебного питания.

Практическая значимость: Практическому здравоохранению предложена разработанная схема лечения детей, больных витилиго с включением лечебного питания (Диета 4В), что приведет к повышению эффективности терапии.

Ключевые слова: витилиго у детей, аминокислоты, нарушение обмена, дисбактериоз кишечника, лечебное питание, патогенетическое лечение.

ВИТИЛИГО КАСАЛЛИГИГА ЧАЛИНГАН БОЛАЛАРДА ОКСИЛ АЛМАШИНУВИНИНГ ИЧАК МИКРОБИОЦЕНОЗИГА БОГЛИҚЛИГИ ВА УНИ КОРРЕКЦИЯЛАШ УСЛУБЛАРИ

¹Собиров У.Ю., ³Рихсиев У.Ш., ^{1,2}Мамадиев А.А., ^{2,3}Юлдашев М.А.

¹Ўзбекистон Республикаси соғлиқни сақлаш вазирлиги Республика дерматология ва косметология ихтисослаштирилган илмий-амалий тиббиёт маркази

²Ўзбекистон Республикаси соғлиқни сақлаш вазирлиги Республика дерматология ва косметология ихтисослаштирилган илмий-амалий тиббиёт марказининг Жиззах вилояти минтақавий филиали,

³Тошкент педиатрия тиббиёт институти

✓ Резюме

Тадқиқот объеклари: витилиго касаллигига чалинган ва даволанган 1 ёшдан 16 ёшгача бўлган 132 бола текишилди.

Ишнинг мақсади. Витилиго билан оғриган болаларда оксил алмашинуви, ичак микробиоценози ва жигар дезинтоксикацион функциясини касалликнинг клиник шакллариغا боғлиқ ҳолда ўрганиш ва мавжуд даволаш услуларини такомиллаштириш.

Тадқиқот услулари: клиник, бактериологик, биохимик.

Олинган натижалар ва уларнинг янгилиги. Биринчи марта витилиго касаллигига чалинган болаларда касалликнинг клиник шаклига боғлиқ ҳолда қондаги аминокислоталар миқдори ўрганилди. Беморларда гипераминоацидемия билан бир қаторда алоҳида аминокислоталар ўртасидаги нисбатининг ўзгариши: фенилаланин/тирозин, гистидин/глутамин кислотаси ва серин/глицин коэффициентларининг камайиши аниқланди. Аспарагин кислота/аланин, глутамин кислота/пролин коэффициентларининг ошганлиги эса аминокислоталар алмашинувининг яққол бузилганлигидан, тўқималарда аммиакнинг жадал ҳосил бўлиши ва гепатоцитлар функционал фаолиятининг сусайганидан далолат беради лейцин/изолейцин нисбатининг 1,2 баробар органи эса оксиллар синтези бузилганлигидан далолат беради. Барча беморларда ичак дисбиози даражасидан катъий назар ўрганилган аминокислоталар миқдорининг ишончли равишида ошгани, фенилаланин миқдорининг эса бир оз камайгани аниқланди. Биринчи марта витилиго касаллигининг фаоллиги қондаги аминокислоталар миқдориغا боғлиқлиги ўрганилди, бу эса даволовчи оқатланиш тартиби киритилган даволаш комплексига мақсадли ёндоиши имконини беради.

Амалий аҳамияти. Соғлиқни сақлаш амалиётига витилиго касаллигига чалинган болаларни даволовчи оқатланиш (№4в-парҳез) билан биргаликда даволаш услуги тақдиф қилинди, бу эса даволаш самарадорлигини оширишга олиб келади.

Қилинган сўзлар: болаларда витилиго, аминокислоталар, модда алмашинувини бузилиши, ичак дисбактериози, даволовчи оқатланиш, патогенетик даво.

Relevance

The problem of vitiligo is currently one of the most important and difficult in dermatology, especially in central Asia, where the inadequate attitude of others to these patients still persists. Along with the successes achieved in the study of this disease, there are many controversial and unresolved issues regarding its etiology, pathogenesis and treatment.

Currently, vitiligo is considered as a multifactorial disease of the body caused by a malnutrition of tissues and metabolism, and the appearance of white spots on the skin is only a consequence, the most noticeable external signal of an internal "failure" (Vaisov A.Sh., 2019; Koshevenko Yu.N., 2001; Abdullaev M.I. 2019; Mannanov A.M. et al., 2019). Disruption of metabolic processes, including protein, in the body is often caused by the pathology of the state of intestinal endoecology, due to dysbacteriosis, changes in immunity indicators, the functional state of the liver and hormonal imbalance. Due to the main function of protein, which serves as a plastic material for tissue regeneration, synthesis of enzymes, hormones, vitamins of immune bodies and other biological substances, it occupies a leading place in metabolism. Among the listed factors, amino acid metabolism in vitiligo patients is a relatively poorly studied, but an important problem of modern dermatology.

Purpose of the study: Based on the study of the peculiarities of protein metabolism in relation to intestinal microbiocenosis and detoxification function of the liver in children with vitiligo, depending on the clinical forms of the disease, to optimize the therapeutic regimens with an emphasis on diet therapy.

Object and subject of the study

132 children and adolescents with vitiligo aged from 1 to 16 years old were examined, being treated in the Jizzakh Regional Branch of the RSNPMTSDViK MH RUz (DORF RSNPMTSDViK MH RUz). The studies were carried out in the clinic and laboratories of the DORF RSNPMTSDViK of the Ministry of Health of the Republic of Uzbekistan, the microbiological laboratory of the TMA, in the protein laboratory of the Institute of Bioorganic Chemistry of the Academy of Sciences of the Republic of Uzbekistan.

The activity of the skin-pathological process in children with vitiligo was studied depending on the clinical form of the disease according to the VIDA index (Vitiligo Disease Activity), proposed by M. Njoo in 1999 and currently considered more perfect. Microbiological study of the microflora of the large intestine was carried out in the microbiological laboratory of the TMA. The analysis is based on the methodological recommendations of V.G. Petrovskaya. and Smolyanskaya A.Z. (1984).

Assessment of dysbacterial deviations in the intestine according to the degree of dysbiosis was carried out according to the classification of Kuvaev I.B., Ladodo K.S. (1991).

To study the activity of the monooxygenase enzyme system, the functional state of the liver was assessed using the antipyrine test, which is generally accepted for studying the monooxygenase activity of the liver. The study was carried out in the clinical diagnostic laboratory of the RSNPMTSDViK MH RUz Research Institute DiV. Determination of the amino acid spectrum of blood was carried out in the IBOC protein laboratory using high performance liquid chromatography (HPLC) and pre-column modification. The amount of free amino acids was determined by the Cohen method.

The patients' age ranged from 1 to 16 years inclusive. Depending on age, children were distributed as follows: children from 1 to 3 years old - 14 (10.6%), from 3 to 7 years old - 22 (16.7%), from 7 to 11 years old - 46 (34.8 %) and from 11 to 16 years old - 50 (37.9%) children (recommendations of A.A. Mazurin and I.M. Vorontsov, 1986). Among them there were 59 boys (44.7%), and 73 girls (55.3%). The number of patients increased in parallel with age and reached its peak at 11-16 years (37.9%). These data were consistent with the results of clinical observation of other authors (Koshevenko Yu.N., 1999, Zverkova F.I., 1992, Abdullaev M.I., 2019). The duration of the disease ranged from 10 days to 11 years. It was found that 3.7% of children had depigmented spots from birth. The first signs of the disease began in the first year of life in 7.6%, at the age from 1 to 3 years - in 7.1%, up to 7 years - in 35.0%, before 11 years - in 39.8% and up to 16 years old - in 6.8%. The disease most often began in the spring-summer season (63.5%).

In the anamnesis, 15.9% of patients had a hereditary burden of vitiligo: 5.8% for the maternal side and 10.1% for the paternal side. In 3 cases, vitiligo was diagnosed in both parents of the child, while the disease in 3 generations was observed in 2 cases. Noteworthy is the relatively large number of children who have a pathology of the digestive system as concomitant diseases (intestinal giardiasis - 47.0%, helminthiasis - 65.9%, colitis - 15.4%, chronic hepatitis - 7.4% and gastritis - 4.9%). Among other diseases, chronic foci of infection in the form of chronic tonsillitis (41.1%) and dental caries (35.2%) were most often diagnosed. In all cases, concomitant diseases, regardless of their nature, significantly aggravated the course of the skin-pathological process, which became more common and differed in resistance to the therapy.

When distributing according to the clinical forms of vitiligo in children, the working classification

developed by the staff of the Department of Dermatovenerology of TashPMI was used (Shadyev Kh.K. et al., 1993). Considering that the assessment of vitiligo activity is of great importance when choosing a method of therapy, the VIDA index on a 6-point scale was used to determine the activity of vitiligo (M. Njoo, 1999).

In the examined patients, localized (31.8%) and disseminated (56.1%) forms of vitiligo prevailed. According to the VIDA index, in 33.3% of patients, the activity of the skin-pathological process was in the stationary stage, in the remaining 66.7% - in the progressive stage. In patients with disseminated form of vitiligo, the activity of the skin-pathological process in 24.3% was in the stationary stage, in the remaining 75.7% - in the progressive one.

In 7 patients, whose age was over 11 years old, a generalized form of vitiligo was established. Among them, 3 (42.9%) of the skin-pathological process was characterized by a rapidly progressive course. In all patients, the degree of activity of the skin-pathological process was high (3-4 points). 9 (6.8%) children had Setton's disease. Vitiliginous spots were often localized on the smooth skin of the back, neck, chest around pigmented nevi. It is noteworthy that this form was found in children over 3 years of age.

In 36 children with vitiligo in the blood serum, the content of 18 amino acids was determined. Analysis of the data obtained showed a statistically significant increase in the concentration of all studied amino acids except phenylalanine. Of the 18 amino acids studied, the largest discrepancy was found in the indicators of cysteine, where its concentration in the blood serum is 7.4 times higher than the indicators of the control group (in the control group 29.32 ± 1.78 , and in the examined patients 218.0 ± 11.27). The concentration

of histidine, glutamic and aspartic acids was almost 3 times higher ($318.41 \pm 18.53 - 922.5 \pm 14.48$; $79.75 \pm 3.68 - 233.31 \pm 5.63$; $76.56 \pm 4.08 - 223.295 \pm 9.43$, respectively, in sick and healthy) ($P < 0.001$). A significant increase was noted in the indices of isoleucine, valine, trionine, arginine, proline, lysine, where their number exceeded the corresponding indices of the control group by 2.1-2.5 times ($P < 0.001$). The concentration of serine, leucine, tyrosine and tryptophan is significantly increased in the blood serum ($P < 0.001$). The amount of methionine and alanine in the examined patients statistically significantly differed from those in the control group ($87.98 \pm 3.21 - 97.5 \pm 4.05$; $110.4 \pm 5.58 - 137.76 \pm 4.06$, respectively) ($P < 0.05$). Among the studied 18 amino acids, only the concentration of phenylalanine was statistically significantly lower than the indicators of healthy children (53.45 ± 2.78 ; 45.51 ± 2.85 , respectively, in sick and healthy children) ($P < 0.05$).

When analyzing the data obtained, depending on the clinical form of vitiligo, it was found that the greatest hyperaminoacidemia was observed in patients with the generalized form of the disease, and the smallest in patients with Setton's and limited forms of the disease (Fig. 1).

Along with hyperaminoacidemia, a change in the ratio between individual amino acids was revealed: a decrease in the phenylalanine / tyrosine, histidine / glutamic acid, and serine / glycine ratios. An increase in the ratios of aspartic acid / alanine, glutamic acid / proline indicates a pronounced violation of amino acid metabolism, increased formation of ammonia in tissues and a decrease in the functional activity of hepatocytes. The leucine / isoleucine ratio increases by 1.2 times, which indicates a violation of the synthesis of plasma proteins that provide homeostasis of the body.

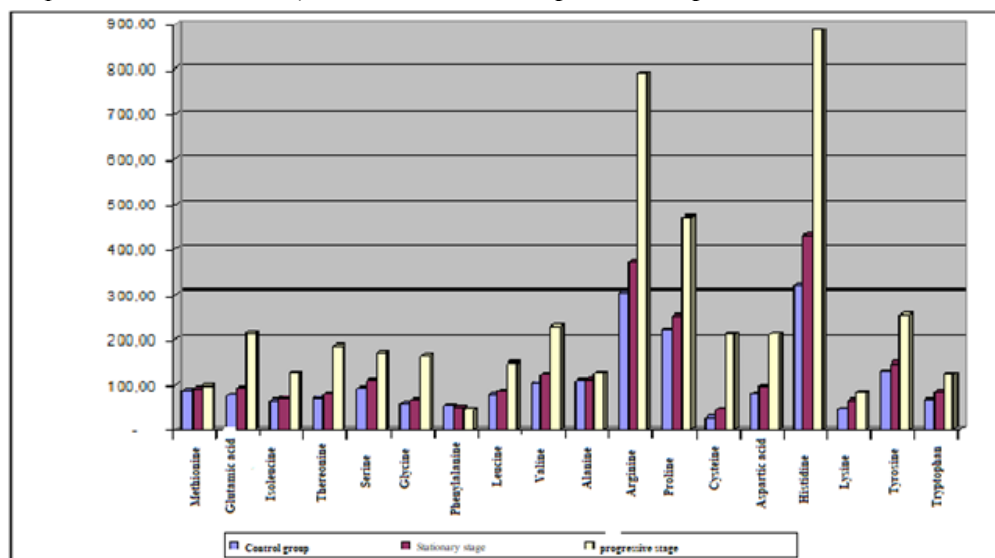


Fig. 1. Amino acid spectrum of blood in children with vitiligo depending on the clinical form of the disease

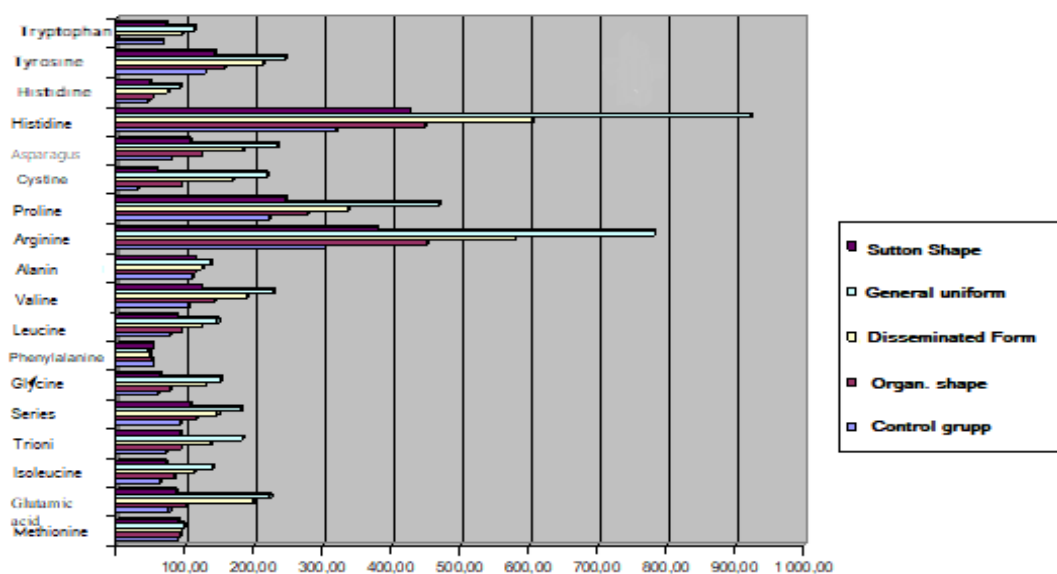
When comparing the percentage of amino acids in sick children with vitiligo compared with healthy children, a certain pattern of changes in the amino acid spectrum was found: against the background of a decrease in phenylalanine, there was a sharp increase in cysteine, histidine, aspartic acid, glycine, and less in methionine, lysine, tyrosine, tryptophan and serine. It should be noted that this nature of changes in children with vitiligo does not differ from those in secondary metabolic disorders caused by chronic diseases of the digestive system.

An increase in the serum level of cysteine, tryptophan, tyrosine and a decrease in phenylalanine in children with vitiligo are pathogenetically associated with the main process, since, as mentioned above, melanogenesis is interrelated with the exchange of these amino acids.

An increase in alanine, glutamic acid, glycine in the blood is possible as a result of secondary disorders in the exchange of aromatic amino acids.

The study of the amino acid spectrum of blood in children with vitiligo, depending on the activity of the skin-pathological process, once again confirmed the pathognomoncity of the revealed disaminoacidemia in the examined patients, since the highest concentrations of these amino acids and a violation of their ratio were found in the progressive stage of vitiligo, regardless of the clinical form of the disease (Fig. .2).

In patients in the stationary stage, hyperaminoacidemia is also observed, but the indicators are less reliable than in those patients whose skin process is in a progressive stage.



Rice. 2. Amino acid spectrum of blood depending on the activity of the skin-pathological process

A comprehensive examination of children suffering from vitiligo confirmed a close relationship between the degree of intestinal dysbiosis, clinical forms of the disease and the activity of the vitiliginous process. With the generalized form of vitiligo, significantly more often ($P < 0.001$) than with the widespread and limited ($P < 0.05$), there is a decrease in the total number of anaerobes, bifidobacteria and lactobacilli. A decrease in the number of lactose-positive *Escherichia coli* was revealed, moreover, it was more pronounced in children with a generalized form of the disease. In vitiligo patients, the number of lactose-negative

Escherichia coli was 2 times higher than in healthy children.

Subsequently, taking into account the importance of intestinal microflora in the digestion of protein products entering the intestine, as well as their participation in the formation and utilization of amino acids in the intestinal lumen, we analyzed the state of the amino acid spectrum of blood in children with vitiligo, depending on the degree of intestinal dysbiosis.

All patients with vitiligo, regardless of the degree of intestinal dysbiosis, showed a statistically significant increase in the above amino acids and a slight decrease

in the concentration of phenylalanine, but the greatest difference was observed in patients with grade III and IV intestinal dysbiosis. Analysis of amino acid parameters in blood serum indicates that with an increase in the severity of intestinal dysbiosis, the concentration of the studied amino acids, except for phenylalanine, increases in parallel. The noted change is especially characteristic of such amino acids as tyrosine, lysine, leucine, serine, isoleucine and glutamic acid. The amount of cysteine, histidine, aspartic acid, proline, arginine, alanine, valine, glycine and tyrosine is slightly reduced than in vitiligo patients with grade III intestinal dysbiosis. Apparently, this is due to a decrease or disappearance of the amount of bifidoflora, which is important in the breakdown and utilization of protein products entering the gastrointestinal tract, as well as chronic inflammation of the intestinal epithelium under the influence of dysbiosis and a violation of its resorption function.

The analysis and comparison of the obtained data, depending on the degree of intestinal dysbiosis, indicates the relationship between intestinal dysbiosis and the amino acid spectrum of the blood, which dictates the need for biocorrection in children with vitiligo.

Taking into account the importance of the liver in protein metabolism, we studied the amino acid composition of blood serum in children with vitiligo, depending on the antitoxic function of the liver.

According to the assigned tasks, the patients were divided into two groups, depending on the antitoxic function of the liver. The first group consisted of 22 patients with reduced antitoxic liver function, where an increase in the blood concentration of such amino acids as glutamic acid, isoleucine, glycine, cysteine, aspartic acid, to a lesser extent serine, histidine and tyrosine, was 2-2.5 times. If we take into account the participation of the liver in the exchange of these amino acids, then one of the main reasons for the decrease in the functional activity of hepatocytes in patients with vitiligo can be considered hyperaminoacidemia. A decrease in the intensity of neutralization leads to a sharp increase in the content of amino acids and ammonium salts in the blood and the development of endogenous intoxication.

In patients with preserved antitoxic liver function, a similar change was noted, but with a less significant difference. The increase in free amino acids in the blood serum, apparently, is promoted by toxic liver damage.

The revealed changes in the blood amino acid spectrum in children with vitiligo do not differ from those in secondary metabolic disorders caused by chronic diseases of the digestive system. In this regard, after consultation with nutritionists, the sick children with vitiligo in order to correct the revealed disorders

of the intestine, liver and the amino acid spectrum of the blood, diet No. 4c was included in the complex of therapeutic measures. The treatment regimens developed by us for children with vitiligo using medical nutrition have shown clear advantages of this method in comparison with conventional (traditional) treatment. They were manifested, first of all, by the normalization of bacteriological and biochemical parameters in the course of treatment.

In the course of therapy, in patients receiving traditional treatment, the indicators of intestinal microflora slightly improved, but long-term results showed that these positive changes were unstable.

In patients who followed a diet in the complex of treatment (Diet No. 4c), the indices of almost all studied microorganisms approached the data of the control group. Long-term results of studies carried out after 3 months showed the relative stability of the obtained positive changes from the intestinal microflora during treatment in these groups of patients.

In the process of treating children with vitiligo, in parallel with intestinal eubiosis, the antitoxic function of the liver was also studied. In general, in patients receiving traditional treatment, there was a slight decrease in the half-life of antipyrine, which was 11.16–0.44 hours versus 12.32–0.78 hours before treatment. In patients who followed Diet 4 during treatment, the half-life of antipyrine decreased to 9.4–0.72 hours, equal to the data in the control group. It should be noted that this improvement was statistically different from the pre-treatment data in this group ($P < 0.001$). The same trend in the course of treatment was observed from the side of antipyrine clearance. After treatment, the clearance of antipyrine increased to 0.86 ± 0.06 ml / min \cdot kg. At the same time, these data did not statistically differ from the data of the control group, but the long-term results demonstratively show the advantage of adherence by vitiligo patients to Diet 4c, since the positive results obtained were persistent.

Apparently, the observance of Diet 4c by patients with vitiligo during treatment leads to the restoration of intestinal microflora, as well as a decrease in the load on the liver: firstly, due to a decrease in the products of putrefactive decay in the intestinal lumen and the formation of toxic products of intestinal origin, and secondly, significant reducing the degree of hyperaminoacidemia.

Taking into account the importance of intestinal microflora and diet in the formation and utilization of proteins, the amino acid spectrum of blood has been studied in the course of treatment in various ways.

Analysis of the data obtained in patients who received traditional treatment in terms of the studied amino acids showed a positive trend, i.e. the amount of such amino acids as methionine, threonine, glycine, valine, arginine, proline, cysteine, histidine and

tryptophan statistically significantly decreased compared with the data before treatment, but remained quite high compared to the data of the control group.

In patients of the second group, where nutritional therapy was prescribed, the amount of studied amino acids decreased with greater reliability and the data approached the indicators of the control group. Analysis of the amino acid spectrum of blood after treatment in patients receiving the proposed therapy showed a clear advantage of this method of treatment, because the amount of methionine, isoleucine, glycine, phenylalanine, alanine did not statistically differ from the data of the control group, the indices of the remaining amino acids decreased significantly. In addition, the impaired ratio between individual amino acids began to normalize, which is one of the main indicators of the restoration of impaired metabolism.

Based on the data obtained, it can be concluded that traditional methods of treatment have little effect on the amino acid spectrum of the blood and on the ratio of individual amino acids.

In patients with traditional therapy who followed Diet No. 4b during treatment, the indices of all the amino acids studied approached the indices of the control group and significantly differed from the indices before treatment, and the amino acid ratio began to recover, which indicates the normalization of impaired protein metabolism.

Thus, the analysis of the material obtained indicates that in the course of treatment, adherence to the appropriate diet (Diet No. 4c) has a normalizing effect on the parameters of intestinal microbiocenosis, the amino acid spectrum of the blood and improves the antitoxic function of the liver. The results obtained confirm the literature data on the relationship and interdependence between the studied organs, systems and amino acid metabolism.

Positive dynamics on the part of the skin-pathological process testifies to the advantage of the proposed method of treatment.

After the 3rd course of treatment, in patients receiving traditional therapy, clinical recovery occurred in 3 (7.9%) patients, significant improvement in 16 (42%), improvement in 15 (39%) patients, while among patients in the course of treatment those who followed Diet No. 4c clinically recovered in almost 5 (10%) patients, a significant improvement was observed in 26 (50%), and an improvement in 18 (34%) patients.

Thus, analyzing the above data, we can conclude that the developed, modified methods of therapy (with therapeutic nutrition) for children with vitiligo, taking into account the revealed hyperaminoacidemia, intestinal dysbiosis and antitoxic liver function, have a beneficial effect not only on the indicators of these

systems, but also lead to the normalization of the ratio of the studied amino acids. Apparently, the listed interrelated and interdependent processes between these systems lead to a decrease in the degree of impaired metabolic processes in the body of children with vitiligo, including pigmented ones.

Conclusion

1. In children with vitiligo, due to a violation of the utilization of amino acids, their concentration in the blood serum is increased, especially cysteine, histidine, tyrosine, tryptophan and methionine (these amino acids are involved in the process of melanogenesis and are part of melanin). The concentration of these amino acids in parallel increases with an increase in the prevalence of the skin-pathological process, and the highest rates are recorded in the progressive stage of the disease, when there is an enhanced breakdown of melanocytes and melanin with the release of these amino acids.

2. The existing dysbacteriosis further aggravates the hyperaminoacidemia observed in children with vitiligo, since the highest amino acid indicators were found in patients with grade III and especially grade IV dysbiosis.

3. Simultaneously recorded changes in the intestinal microflora, antitoxic liver function and indicators of the amino acid spectrum of blood indicate the existing relationship and interdependence and affect all links of the studied systems. And although the cause-and-effect relationship is rather complex, our results indicate that the presence of dysbiotic changes in the composition of the intestinal microflora, antitoxic liver function and hyperaminoacidemia create favorable conditions for the development and course of vitiligo in children.

4. The developed treatment regimens for children with vitiligo, taking into account the functional state of the intestine, the antitoxic function of the liver, the amino acid spectrum of the blood and adherence to medical nutrition (Diet No. 4c) in the course of treatment, showed clear advantages over conventional (traditional) treatment. They were manifested, first of all, by a reduction in the period of stabilization of the skin-pathological process, an increase in the number of patients with a positive effect (93.6% of them, 9.6% with a clinical cure) and the normalization of bacteriological, immunological and biochemical parameters during treatment.

LIST OF REFERENCES:

1. Arifov S.S., Davletova L.S. The prevalence of vitiligo in various regions of Uzbekistan // Dermatol News. and venerol. - 2002. - 2. -S. 20-23. (in Russian).

2. 2. Arifov S.S. Some medico-social aspects of vitiligo / S.S. Arifov, B.B. Shukurov // *Ukrainian Bulletin of Dermatology, Venereology and Cosmetology*. - 2011. - No. 1. - S. 71-74. (in Russian).
3. Vaisov A.Sh., Arifov S.S., Khasanov D.S. The value of the monooxygenase enzyme system in the pathogenesis and clinical course of vitiligo // *News of Dermatol and Venerol*. - 1998. - 1. -S. 11-12. 48 (in Russian).
4. 4. Gereykanova L.G., Lomonosov K.M., Bashlakova K.A. Oxidative stress in the pathogenesis of vitiligo and methods of its correction // *Russian Journal of Skin and Venereal Diseases*. - 2016. - T. 19, No. 1. - S. 45-48. (in Russian).
5. Babeshko O.A., Lomonosov K. M., Gilyadova N. I. Rol' citokinov v patogeneze vitiligo // *Rossiyskij zhurnal kozhnyh i venericheskikh boleznej*. 2012. № 3. S.37–41 (in Russian).
6. Lomonosov K. M. Okislitel'nyj stress i antioksidantnaya terapiya pri razlichnyh zabolevaniyah kozhi // *Rossiyskij zhurnal kozhnyh i venericheskikh boleznej*. 2009. № 2. S.27–30 (in Russian).
7. Esmat S., Hegazy R. A., Shalaby S. et al. Phototherapy and Combination Therapies for Vitiligo // *Dermatol. Clin*. 2017. Vol. 35. № 2. P.171–192. doi: 10.1016/j.det.2016.11.008
8. Шарафутдинова Л. А., Ломоносов К. М. Современные аспекты топической терапии витилиго // *Российский журнал кожных и венерических болезней*. 2014. № 5. С.40–45 [Sharafutdinova L.A., Lomonosov K. M. Sovremennye aspekty topicheskoy terapii vitiligo // *Rossiyskij zhurnal kozhnyh i venericheskikh boleznej*. 2014. № 5. S.40–45 (in Russian)].
9. Толстов Д. А., Богдан В. Г. Комбинированный тромбоцитарно-фибриновый комплекс и обогащенная тромбоцитами плазма в комплексном лечении трофических язв венозной этиологии // *Хирургия. Восточная Европа*. 2014. № 3. С.45–56 [Tolstov D.A., Bogdan V. G. Kombinirovannyj trombocitarno-fibrinovyj kompleks i obogashchennaya trombocitami plazma v kompleksnom lechenii troficheskikh yazv venoznoj ehtiologii // *Hirurgiya. Vostochnaya Evropa*. 2014. № 3. S.45–56 (in Russian)].
10. Knezevic N. N., Candido K. D., Desai R., Kaye A. D. Is Platelet-Rich Plasma a Future Therapy in Pain Management? // *Med. Clin. North. Am*. 2016. Vol. 100. № 1. P.199–217. doi: 10.1111/jocd.12194
11. Marques L. F., Stessuk T., Camargo I. C. et al. Platelet-rich plasma (PRP): methodological aspects and clinical applications // *Platelets*. 2015. Vol. 26. № 2. P.101–113. doi: 10.3109/09537104.2014.881991
12. Van den Boorn J. G., Jakobs C., Hagen C. et al. Inflammasome-Dependent Induction of Adaptive NK Cell Memory // *Immunity*. 2016. Vol. 44. № 6. P.1406–1421. doi: 10.1016/j.immuni.2016.05.008
13. Ibrahim Z. A., El-Ashmawy A.A., El-Tatawy R.A., Sallam F. A. The effect of platelet-rich plasma on the outcome of short-term narrowband-ultraviolet B phototherapy in the treatment of vitiligo: a pilot study // *J. Cosmet. Dermatol*. 2016. Vol. 15. № 2. P.108–116. doi: 10.1111/jocd.12194
14. Abdelghani R., Ahmed N. A., Darwish H. M. Combined treatment with fractional carbon dioxide laser, autologous platelet-rich plasma, and narrow band ultraviolet B for vitiligo in different body sites: A prospective, randomized comparative trial // *J. Cosmet. Dermatol*. Epub 2017 Aug 20. doi: 10.1111/jocd.12397

Entered 09.05. 2021