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THE STATE OF BLOOD AMINO ACID SPECTRUM IN CHILDREN WITH VITILIGO

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

Vitiligo is currently considered as a multifactorial disease of the organism [2-10]. When studying the etiology and pathogenesis of vitiligo, much attention is paid to the study of metabolic processes in the body. Many have found in this dermatosis changes in mineral, carbohydrate, lipid, vitamin and other types of metabolism [2-10]. According to literature sources, amino acid metabolism in vitiligo patients is disturbed, but these data are controversial, in addition, they are obtained with the help of low-informative laboratory methods of research [3,5,9]. In this regard, the study of amino acids metabolism, which are the main structural elements of protein molecule, including melanocytes, melanin, is of certain interest. The biochemical essence of this phenomenon is still unclear. But about the reasons of melanogenesis disturbance in vitiligo there are controversial judgments of researchers [1,8]. If we take into account that the ancestor of melanin is tyrosine, and such amino acids as phenylalanine, arginine, histidine, methionine are directly related to melanin metabolism, then the study of amino acid spectrum of blood in vitiligo patients is of certain interest.

Materials and methods of the study

The amino acid spectrum of blood was studied using high-performance liquid chromatography (HPLC) according to the Kochen method. Free amino acids were isolated from biological fluids by precipitation with a 20% solution of TCUK. During precipitation of proteins with TCUK, acidic peptides remained in solution and were the last to leave the column during amino acid analysis. Therefore, they did not screen for the identification of free amino acids.

To solve the set goal, we analyzed 18 amino acids in serum of 36 children with vitiligo patients. Of them, 7 had limited, 14 - disseminated, 6 - generalized forms of vitiligo, and 5 had Seton's disease. The control group consisted of 12 healthy children of similar age.

Results

Analysis of the obtained data showed statistically reliable increase in concentration of all studied amino acids, except phenylalanine (Table 1). From the studied 18 amino acids, the biggest discrepancy was stated in the indices of cysteine, where its concentration in blood serum was 7.4 times more in comparison with the control group (in the control group 29.32±1.78; in the examined patients 218.0±11.27). Concentration of histidine, glutamic and asparagic acids was almost 3 times higher (318,41±18,53-922,5±14,48;79,75±3,68 233,31±5,63; 76,56±4,08-223,295±9,43 in patients and healthy subjects, respectively, at P<0,001). Significant increase was registered in the indices of isoleucine, valine, threonine, argenine, proline, lysine, where their quantity exceeded the corresponding indices of the control group in 2,1-2,5 times (P<0,001). In the same reliability (P<0,001), serine, leucine, tyrosine and tryptophan concentrations were increased in blood serum. The amounts of methionine and alanine in the examined patients were also statistically significantly (P<0.05) different from those of the control group (87.98± 3.21-97.5± 4.05; 110.4±5.58137.76±4.06, respectively). Among the 18 amino acids studied, only phenylalanine concentration was statistically significantly (P<0.05) lower than in healthy children (53.45±2.78; 45.51±2.85 in sick and healthy children, respectively).

Table 1

Amino acid spectrum of blood in children with vitiligo before treatment

Aminoacids	Control group (p-12)	Patients with vitiligo (п-36)	P	How many times increased or decreased
Methionine	87,98± 3,21	97,5± 4,05	P <0,001	<1,11
Glutamic acid	76,56±4,08	223,295±9,43	P <0,001	<2,92
Isoleucine	63,45±4,45	139,119±7,71	P <0,001	<2,2
Threonine	71,65±5,76	182,2211±4,55	P <0,001	<2,5
Serine	93,14±4,8	181,03±3,69	P <0,001	<1,9
Glycine	59,85±2,32	152,5±5,32	P <0,001	<2,6
Phenylalanine	53,45±2,78	45,51±2,85	P < 0,05	>0,85
Leucine	77,91±3,35	146,65±3,81	P <0,001	<1,88
Valine	103,76±6,08	229,08±4,97	P <0,001	<2,2
Alanine	110,4±5,58	137,76±4,06	P <0,05	<1,3
Argenine	303,32±12,45	781,39±11,87	P <0,001	<2,6
Proline	222,78±13,67	468,3±9,58	P <0,001	<2,1
Cysteine	29,32±1,78	218,0±11,27	P <0,001	<7,4
Asparg. acid	79,75±3,68	233,31±5,63	P <0,001	<2,9
Histidine	318,41±18,53	922,5±14,48	P <0,001	<2,9
Lysine	43,62±2,61	92,502±2,88	P <0,001	<2,1
Tyrosine	129,36±14,58	245,69±9,94	P <0,001	<1,9
Tryptophan	66,95±3,45	112,767±4,59	P <0,001	<1,7

Note: P- reliability in comparison with the data of the control group.

Along with hyperaminoacidemia, the change of ratios between separate amino acids was revealed: phenylalanine/tyrosine coefficients were reduced (in healthy people - 0,4; in vitiligo patients - 0,18), histidine/glutamic acid (in healthy people - 4,2; in vitiligo patients - 4,0) and serine/glycine (in healthy people - 1,6; in vitiligo patients - 1,2). Violation of coefficients asparagic acid/alanine (in healthy people - 0,7; in vitiligo patients - 1,7), glutamic acid/proline (in healthy people - 0,3; in vitiligo patients - 0,48) was established, that indicates the expressed violation of amino acids metabolism.

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

Taking into account the above-mentioned, we analyzed the obtained data of amino acid spectrum depending on the clinical forms of the disease (Table 2). As can be seen from the table, the greatest discrepancies in amino acids indices were found in patients with generalized form of the disease,

especially in tyrosine indices, which in comparison with the control group were increased almost 2 times (129,36±14,58; 245,9±10,75), in contrast to patients with limited form - 1,4 times (at P < 0,001). Indices of cysteine in patients with generalized form of vitiligo in comparison with the control group were 7,5 times higher, and in patients with localized form - 2,3 times higher. As can be seen from the data in Table 2, the same trend was observed in the indicators of argenin, histidine, tryptophan, glutamic acid, threonine, to a lesser extent methionine.

Table 2

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

№	Aminoacids	Control group (п-12)	Clinical forms of vitiligo			
			Limited (п-7)	Disseminated (п-14)	Generalized (п-6)	Disease Sutton's (п-5)
1	Methionine	87,98± 3,21	91,69±3,97	93,54±2,95	97,5±3,17*	89,20±2,44
2	Glutamic acid	76,56±4,08	102,7±5,42**	198,44±7,47**	223,3±5,74**	85,67±3,18
3	Isoleucine	63,45±4,45	84,48±3,71*	112,92±4,21**	139,2±8,15**	71,14±4,36
4	Threonine	71,65±5,76	94,42±5,24*	137,65±6,55**	182,2±7,36**	91,9±4,42*
5	Serine	93,14±4,8	116,02±6,68**	146,81±6,08**	181,1±7,44**	106,72±5,39*
6	Glycine	59,85±2,32	78,68±2,84*	129,04±3,67**	152,5±5,87**	63,54±3,27
7	Phenylalanine	53,45±2,78	51,05±1,89	47,7±2,88*	45,5±3,17*	52,06±2,88
8	Leucine	77,91±3,35	94,37±4,06*	123,26±6,24**	146,7±11,08**	88,36±2,16*
9	Valine	103,76±6,08	141,83±5,87**	188,43±6,13**	229,1±8,37**	122,87±4,48*
10	Alanine	110,4±5,58	114,85±6,47	124,07±5,38*	137,76±6,79**	115,05±5,11
11	Argenine	303,32±12,45	450,6±15,49**	579,51±12,6**	781,39±14,8**	378,45±13,58*
12	Proline	222,78±13,67	278,07±11,8**	336,89±11,29**	468,3±12,83**	244,62±8,39*
13	Cysteine	29,32±1,78	94,58±4,29**	168,77±6,53**	218±7,16**	58,09±3,37**
14	Asparg. acid	79,75±3,68	122,36±4,15**	183,49±7,74**	233,3±13,22**	106,38±5,22**
15	Histidine	318,41±18,53	448,71±15,4**	604,78±14,21**	922,5±17,06**	426,75±15,54**
16	Lysine	43,62±2,61	53,38±3,70*	74,22±2,06**	92,5±3,45**	48,8±1,96
17	Tyrosine	129,36±14,58	157,9±10,84*	214,43±8,89**	245,9±10,75**	142,07±12,41*
18	Tryptophan	66,95±3,45	78, 89±3,22*	96,68±3,93**	112,77±5,83**	71,62±4,85

Note: * marked reliability of the difference and indicators equal to P< 0.05; ** P< 0.001 when comparing with the control group.

Apparently, due to impaired melanogenesis, the formed above amino acids are not used and accumulate in the body.

In patients with the Setton form of the disease, the indicators of such amino acids as methionine, glutamic acid, isoleucine, glycine, phenylalanine, alanine, lysine, tryptophan differed little from those of the control group. The concentration of cysteine and histidine differed statistically more reliably (P<0.001), threonine, serine, leucine, valine, argenine, aspartic acid, and tyrosine differed less reliably. The revealed difference in the amino acid spectrum of blood in patients with Seton's disease in comparison with other forms of vitiligo once again confirms the data on the versatility of etiology and pathogenesis of these clinical forms of the disease.

When analyzing the indicators of amino acids in blood serum depending on the activity of vitiliginous process with the same clinical form of the disease, there was a large discrepancy between them.

In this connection, the state of amino acid spectrum of blood in vitiligo patients depending on the activity of skin pathologic process is of certain interest (Table 3).

Table 3

Amino acid spectrum of blood depending on the activity of skin pathologic process

Aminoacids	Control group (п-12) (I)	Activity of the skin pathologic process		P (between II and III group)
		Stationary (п-11) (II)	Progressive (п-21) (III)	
Methionine	87,98± 3,21	90,34±5,48*	99,08±6,05*	P< 0,001
Glutamic acid	76,56±4,08	92,44±6,12*	214,65±14,26**	P< 0,001
Isoleucine	63,45±4,45	71,89±3,29	126,04±6,63**	P< 0,001
Threonine	71,65±5,76	81,12±4,38*	188,25±9,31**	P< 0,001
Serine	93,14±4,8	111,32±12,36*	169,49±13,79**	P< 0,001
Glycine	59,85±2,32	66,87±3,75	162,06±8,83**	P< 0,001
Phenylalanine	53,45±2,78	48,9±2,14*	44,52±3,18*	P< 0,05
Leucine	77,91±3,35	87,47±4,26*	151,33±7,33**	P< 0,001
Valine	103,76±6,08	122,8±6,89**	230,41±12,51**	P< 0,001
Alanine	110,4±5,58	113,31±6,38	126,55±9,82**	P< 0,001
Argenine	303,32±12,45	371,32±16,19*	792,82±21,64**	P< 0,001
Proline	222,78±13,67	255,4±13,44*	471,06±18,47**	P< 0,001
Cysteine	29,32±1,78	44,76±2,51**	213,8±14,53**	P< 0,001
Asparg. acid	79,75±3,68	96,48±4,82*	212,32±6,85**	P< 0,001
Histidine	318,41±18,53	429,92±14,33**	884,7±24,77**	P< 0,001
Lysine	43,62±2,61	64,38±3,28**	83,81±3,91**	P< 0,001
Tyrosine	129,36±14,58	148,69±9,12*	256,39±13,48**	P< 0,001
Tryptophan	66,95±3,45	87,04±3,78**	123,58±5,12**	P< 0,001

Note: * marked reliability of the difference and indicators, even P< 0.05; ** P< 0.001 when comparing with the control group.

As can be seen from the data of Table 3, the highest values of amino acids in blood serum of the examined patients were found in the progressive stage of vitiligo, especially cysteine, glutamic acid, threonine, glycine, argenine, proline, tyrosine, aspartic acid, histidine. The amount of phenylalanine was reduced (P<0.05) in both groups of patients regardless of the stage of the disease. In children with vitiligo in the progressive stage of the disease, the indicators of 17 amino acids out of 18 studied, statistically significantly (P<0,001) differed not only from the data of healthy children, but also from the indicators of vitiligo patients, the activity of the skin process which was in the stationary stage.

The obtained data once again confirmed the pathognomics of the revealed disaminoacidemia in vitiligo patients, as the highest concentrations of these amino acids and violation of their ratio were found in the progressive stage of vitiligo regardless of the clinical form of the disease. In patients in stationary stage the observed hyperaminoacidemia is less reliable than in patients in progressive stage.

Discussion

Thus, in children with vitiligo patients the metabolism of the studied amino acids is disturbed,

more often it is manifested by increased concentration in blood serum of cysteine - 7.4 times, histidine, glutamic and asparagic acids - almost 3 times, isoleucine, valine, threonine, argenine, proline, lysine - 2.1-2.5 times, the concentration of serine, leucine, tyrosine and tryptophan was increased in the same reliability ($P<0.001$). The concentration of phenylalanine was found to be decreased ($P<0.05$). Increased serum levels of cysteine, tryptophan, tyrosine and decreased phenylalanine in children with vitiligo are pathogenetically, in all likelihood, associated with the underlying process, since, as indicated above, melanogenesis and the course of vitiligo are interrelated with the metabolism of these amino acids. The increase of alanine, glutamic acid and glycine in blood is probably secondary, as a consequence of disturbance of aromatic amino acid metabolism.

The revealed changes in the ratio between individual amino acids in vitiligo patients indicate a pronounced disorder of amino acid metabolism, increased ammonia formation in tissues and decreased functional activity of hepatocytes. Increase of1. leucine/isoleucine coefficient indicates a violation of synthesis of plasma proteins providing homeostasis of the organism. It should be noted that this character of changes in children with vitiligo does not differ from2. those in secondary metabolic disorders caused by chronic diseases of digestive organs.

The revealed regularity, i.e. increase in blood serum concentration of cysteine, histidine, tyrosine, tryptophan and to a lesser extent methionine (these amino acids participate in the process of melanogenesis and are part of melanin) with increasing prevalence of skin pathological process, indicates a violation of amino acid metabolism in children with vitiligo. Apparently, due to impaired melanogenesis, the above amino acids formed are not utilized and accumulate in the body.

The observed highest hyperaminoacidemia in the progressive stage of the disease is probably associated with increased breakdown of melanocytes and melanin, and the release of amino acids (cystine, argenine, tyrosine, tryptophan, methionine, histidine).

Hyperaminoacidemia and violation of the ratio between individual amino acids in the organism of children with vitiligo, especially in its widespread forms, indicates the importance of violation of this type of metabolism in the pathogenesis of vitiligo and opens new opportunities for research work in this direction.

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