DEPRESSION IN THE STRUCTURE OF SOMATOFORM DISORDERS IN CHILDREN, ITS SIGNIFICANCE, THE ROLE OF SEROTONIN AND TRYPTOPHANE IN THE EMERGENCE OF THESE DISORDERS

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The disorders of the autonomic nervous system are an actual problem of modern child and adolescent medicine due to the wide prevalence, polymorphism of clinical manifestations as well as the negative impact on the quality of children's life and adolescents [1].

The syndrome of autonomic dysfunction (SAD) is considered as polysystemic disorders that arise as a result of violation of the activity of over-segmental vegetative structures. In modern psychiatry SAD is often considered as «Somatoproformal dysfunction of the autonomic nervous system» (according to ICD-10, heading F45,3). This concept combines a group of psychogenic diseases that are characterized by pathological symptoms resembling a somatic disease but according to the results, there are no morphological manifestations are detected with them, although often there are nonspecific functional disorders [2].

Criteria for diagnosing of somatoform disorders were published for adults and there are used for children due to the lack of research base which are oriented on children [3].

Somatoform disorders (CD) are a class of mental disorders characterized by persistent physical symptoms and complaints, however, even in the presence of somatic disorders, they can not have adequate medical explanation [4, 5]. These symptoms lead to numerous appeals to the doctor, additional unnecessary research and manipulation and caused family and social disadaptation in children, violations in educational functioning causing significant psychosocial distress [6].

Such point of medical view unclear physical symptoms in children and adolescents form to 50% of appeals at the outpatient level. Children can hardly express their emotions and feelings through the language, so psychological stress can find expression in the form of somatic symptoms [3].

With the release of DSM-5 somatoform disorders have received a new name - "Somatic Symptom Disorder". "Somatic Symptom Disorder" is characterized by somatic symptoms that are either very unpleasant or result in significant functional impairment, as well as significant thoughts about the severity of symptoms, a high level of anxiety about symptoms and appropriate behavior in relation to these symptoms [7].

Comorbid psychiatric disorders can precede the development of somatic symptoms but often they occur during the onset of SD. Children of school age often have anxiety and depression [3].

Depression is a common mood disorder that is accompanied by a violation of behavioral and cognitive symptoms such as sleep and eating behavior, loss of interest, loss of pleasure (anhedonia), asthenia, feelings of guilt, helplessness, futility and general emotional instability [8].

Although there are numerous studies that tried to highlight the pathophysiology of depression, it still stays completely incomprehensible [9].

Several hypotheses have been proposed for the origin of depression but the monoamine hypothesis (with the involvement of serotonin, norepinephrine and dopamine) is still the most common since most currently available antidepressants affect the carriers of monoamines or their receptors [10].

Serotonin is one of the key monoamines involved in the pathogenesis of depression. Violation of its exchange in the central nervous system is associated with symptoms of depression such as mood swings, anxiety, panic attacks, anxiety, psychosomatic disorders, appetite and mental disorders. The hypothesis of the main role of serotonin in the development of depression was confirmed after the use of antidepressants which increased the level of monoamines in the central nervous system and reduced the depressive symptoms [9]. However the hypothesis about the special role of serotonin was also criticized for delayed onset of action and inadequate efficacy of selective serotonin reuptake inhibitors (SSRI) [10].

Unfortunately data about mechanisms of occurrence and factors of development of SD and depression, especially the role of monoamine in their occurrence and other pathogenesis chains in children are very limited and it requires further research.

The aim of the work - is to investigate the presence of depressive disorders and their manifestation in children with somatoform disorders from different organs and systems and to establish the role of disorders of serotonin and tryptophan metabolism in their occurrence.

Material and methods. Studies were performed on the clinical basis of the Department of Pediatrics, Obstetrics and Gynecology Faculty of Postgraduate Education, National Pyrogov Memorial Medical University in the gastroenterological, cardiological, nephrological and neurological departments of Khmelnytskyi regional children's hospital in Khmelnitskyi.

Following the informed consent of parents and children, 111 patients were diagnosed with SD, whose average age was 13,6±2,3 years (M±σ), of which boys were 37,8% (n=42) and girls – 62,2% (n=69). The patients were divided into two groups: with SD without depression, 56,8% (n=63) and with SD with depression – 43,2% (n=48). The control group included 33 children who had no emotional disorders, with an average age of 13.2±2.0 years (M±σ).

The selection of children and the diagnosis of SD were performed after general clinical examination and according to the criteria of SD ICD-10. The detecting of depression presence and its clinical symptoms in a selected group of children with somatoform disorders it was used the children's depression inventory of M. Kovacs, 1992. The method is intended for the study of children and adolescents of 6-17 years and allows assessing the affective and cognitive symptoms of depression, somatic complaints, social problems and behavioral problems. The overall normal index for CDI can range from 0 to 54, where 50 is a critical value after which the depth of symptoms increases [10]. The presence of depression was diagnosed in the presence of a T-score that was higher than the average (>60), which was translated the total amount of scores.

In all 111 children who had SD blood samples were taken to determine the serum concentrations of serotonin and tryptophan. The investigations were performed by biochemical method in the certified laboratory of Diagnostics Plus LLC, Kharkiv.

The tryptophan was examined by liquid chromatography using the Milchrom-6 microcolonial liquid chromatography.

The statistical analysis was performed using the Statistica

8.0.360, MedCalc.7.4.4.1. and Excel (2007). The hypothesis of normal distribution was checked using the criterion of Shapiro-Uilka. Quantitative attributes are given in the form M ± σ (arithmetic mean ± mean deviation). The probabilities of differences were estimated using Student's twin-t-criterion and constructing a 95% confidence interval (CI) for the mean difference, as well as methods of correlation and regression analysis with the construction of a CI for the correlation coefficient. The value at p<0,05 considered probably.

Results and discussion. In general in the study of the whole quantity of children (n=111) with SD 48 (43,2%) children have the overall score of the T-score in the questionnaire exceeded the upper limit of the average of 60 points, which made it possible to diagnose the presence of depression. The overall score of the T-score in this category of children was 69,6±8,7, which according to the interpretation of the CDI questionnaire significantly exceeds the average level in which it is possible to diagnose the minimum depressive disorder.

Also according to the questionnaire among the 48 children with depression in 14 (29,2%) it was possible to ascertain the presence of mild depressive disorders, depression of moderate severity was found in 27 (56,2%) children and severe depression - in 7 (14,6%) children.

Figure 1 shows the general structure of depressive disorders in children with SD.

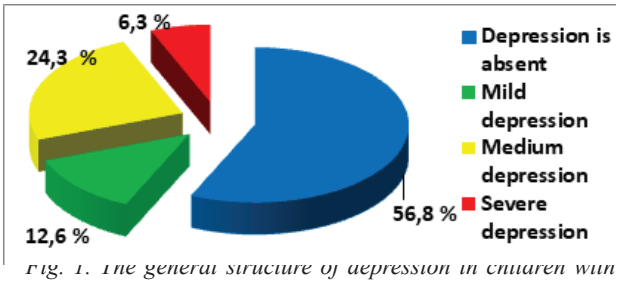

Fig. 1. The general structure of depression in children with SD according to the data of the questionnaire CDI

In the general structure of adolescents signs of severe depression were found in 7 (6,3%) persons whose data significantly exceeded the average and reached 75 and above points (at most 100), which is quite substantial and requires appropriate attention, since they are the most at risk on the development of suicidal behavior.

The average age of children with symptoms of depression was 13,8±2,2 years and did not differ significantly from the average age of all children with SD, which was 13,6±2,3 years.

Among patients with SD with depression there was a significant prevalence of girls - 34 (70,8%), boys - 14 (29,2%).Their ratio was 2.4:1 and indicated a greater tendency of women to develop depressive disorders and respectively to the more severe SD.

The general level of depressive symptoms although not reliably according to the T-score of the questionnaire was higher in girls (70,0±10,4 points), as compared to boys (66,4±5,6 points), which also indicates a higher the severity of depressive disorders in females.

Mostly depressive disorders occurred in children with SD which had manifestations from the gastrointestinal tract (GIT) (functional dyspepsia, chest disorder, abdominal pain, appetite disorder, aerophagia, irritable bowel syndrome) and urinary excretory system (dysuric manifestations, neurogenic bladder, urinary incontinence) which respectively were examined and treated in the gastroenterological and nephrology departments of the hospital. Thus, there are 39 children with SD depressive disorders occurred in 18 (46,1%) in the gastroenterology department and from 16 children with SD in 12 (75%) depression was detected in nephrology.

Less often depressive disorder met children with SD who had signs of the nervous system in the form pain syndromes (fibromyalgia, headache, joint pain), autonomic dysfunction with a tendency to hypotension or hypertension, syncope states, autonomic crises, as well as in children with SD who had signs of the cardiovascular system (CVS) (hyperventilation syndrome, tachycardia, extrasystolic arrhythmia, cardialgia) were treated in the cardiology department and neurological department. Thus, in the neurological department from 30 children with SD depressive disorders occurred in 10 (33,3%), in the cardiology department - from 26 children with SD in 8 (30,7%) depression was detected.

The most pronounced depressive symptomatology was found in children with SD from the gastrointestinal tract where the total score of the T-score on the CDI scale was 73,3±10,9 points, where the largest number of children with depression was of medium severity (66,7%) and severe depression (22,2%). The less pronounced depressive symptoms were found in children with SD from the CVS and nervous system, where the total score of the T-score on the CDI scale was 69,1±7,2 points, and 68,7±6,4 points, respectively. In children with SD from the CVS depressive symptoms of moderate severity occurred in 62,5% of cases, severe depression - in 12,5% of cases. In children with SD from the nervous system depressive symptoms of moderate severity were found in 50,0% of cases, severe depression - in 10,0% of cases.

Although in children with SD from the side of urinary system depressive disorders were frequent but depressive symptoms were the least pronounced. The total score of the T-score on the CDI scale in them was 65,4±5,4 points. Among them the most commonly diagnosed were mild depressive disorders (50,0%) and least severe depression (8,3%).

In children with SD from the GIT in contrast to SD from other systems depressive symptoms were characterized by a predominance of low mood, tendency to tearfulness, tiredness, increased anxiety, as evidenced by the high score of the T-score for subclass A of the CDI questionnaire (69,1±10,9 points), which was also higher in comparison with children on SD by the CVS (64,6±6,8 points), from the nervous system (67,5±10,2 points) and from the urinary tract systems (61,9±6,5 points) (95% CI, 0,01 - 14,4; p<0,05). Also, in children with SD from the GIT the clinical picture of depression was greatly complemented by such manifestations as a high level of fatigue, a sense of loneliness and anhedonia, as evidenced by the high score of the T-score for subculture D of the questionnaire CDI (68,0±6,8 points), which was also higher in comparison with children on SD by the CVS (66,8±6,2 points), from the nervous system (66,5±5,1 points) and from the urinary system (60,7±6,6 points) (95% CI, 2,17 – 14,4; p<0,07).

Anhedonia is one of the key symptoms of depression and is characterized by a decrease or loss of satisfaction and therefore important in terms of identifying it in children as an important clinical marker of depression.

In children with SD from the CVS and the nervous system, unlike SD from the side of other systems depressive symptoms were predominantly characterized by high levels of fatigue, a sense of loneliness and anhedonia, as evidenced by the highest score of the T-score for the s subscale D of the CDI question-

naire (66,8±6,2 and 66,5±5,1 points, respectively) compared to other subscales.

In children with SD from the urinary system unlike SD from other systems depressive symptoms were predominantly characterized by a negative assessment of their own insolvency, the presence of suicidal thoughts, as evidenced by a higher score of the T-score in the subscale E of the CDI questionnaire (60,9±8,5 points) compared with subclasses of patients with SD from the side of the CVS and the nervous system (56,7±11,5 and 57,0±8,6 points, respectively) and practically did not differ from the index in patients with SD from the side of the GIT (61,6±8,7 points).

The level of serotonin in serum in children with SD with depression was 1,03±0,37 μmol/L and was significantly lower in comparison with children with CD without depressive symptoms with serotonin levels of 1,30±0,27 μmol/L (95% CI, 0,15 – 0,39 μmol/L, p<0,0001). The level of serotonin in serum in children with SD with depression was also significantly lower in comparison with the control group of children without CD and depression, the level of which in them was 1,35±0,34 μmol/L (95% CI, 0,16 – 0,48 μmol/L, p<0,0002) (Fig. 2).

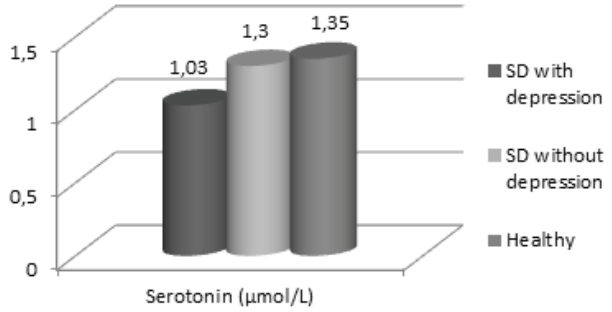

Fig. 2. The average serotonin level in blood serum of children with SD with depression and without depression.

Unlike serotonin, levels of tryptophan in the blood serum in children with SD with depression were 0,035±0,031 mmol/L and were higher but statistically insignificant compared to children with SD without depressive symptoms, which included tryptophan 0,026±0,026 mmol/L (p>0,05) and in comparison with the control group of children without SD and depression the level of which in them was 0,029±0,024 mmol/L (p>0,05) (Fig. 3).

To analyze the key clinical symptoms of depression that characterize subclasses of the CDI questionnaire, the lowest serotonin levels were associated with symptoms such as anhedonia and decreased and hypotymia (Table 1). The highest level of tryptophan was associated exclusively with the development of anhedonia.

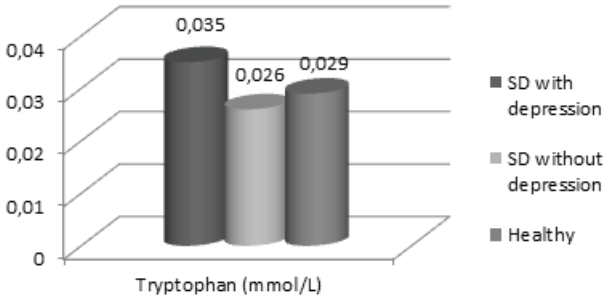

Fig. 3. Average tryptophan level in blood serum of children with SD with depression and without depression

Analyzing the concentrations of serotonin and tryptophan on the subscales of clinical manifestations of depression it can be noted that the trend of a dependent increase in the levels of tryptophan with a decrease in the concentration of serotonin can be noted.

The level of serotonin in children with SD from the urinary system and depression was lower than in children without depression (0,75±0,46 and 1,23±0,22 μmol/L, respectively, p>0,05), in that time as the level of tryptophan was higher in children with depression compared with children without depression (0,036±0,025 and 0,016±0,010 mmol/L, respectively, p>0,05). The level of serotonin in children with SD from the urinary system and depression was the lowest compared with patients with SD with manifestations from other systems and depression (for patients with SD from the GIT 95% CI, 0,09 – 0,63 μmol/L, p<0,01; for patients with SD from the side of the nervous system - 95% CI, 0,02 – 0,70 μmol/L, p<0,03; for patients with SD from the side of the CVS - 95% CI, -0,007 – 0,80 μmol/L, p>0,05).

The concentration of serotonin in children with SD from the side of the CVS and depression, SD from the side of the GIT and depression it is not reliable but was lower than in children without depression (1,15±0,36 and 1,30±0,25 μmol/L, respectively, and 1,11±0,27 and 1,24±0,22 μmol/L, respectively, p>0,05), while the level of tryptophan was higher in children with depression to compare with children with SD from the side of the CVS without depression (0,045±0,040 and 0,032±0,035 mmol/L, respectively, p>0,05) and for patients with SD from the GIT (0,029±0,025 and 0,022±0,023 mmol/L, respectively, p>0,05).

Serotonin levels in children with SD from the nervous system and depression were significantly lower in children without depression (1,11±0,25 and 1,38±0,34 μmol/L, respectively) (95% CI, 0,02% - 0,52 μmol/L, p<0,03), while the level of tryptophan was higher in children with depression to compare with children without depression (0,036±0,037 and 0,028±0,023 mmol/L, respectively, p>0,05).

Table 1. Levels of serotonin and tryptophan depending on the clinical manifestations of depression in SD according to the data of the CDI questionnaire

	Serotonin, μmol/L			**Tryptophan, mmol/L**		
	n	**M±σ**	**p**	**n**	**M±σ**	**p**
Hypotymia	35	1,08±0,31	<0,02	31	0,030±0,029	>0,05
Normal mood	76	1,24±0,36		73	0,030±0,030	
Anhedonia	46	1,05±0,42	<0,0003	42	0,038±0,034	<0,02
Without anhedonia	65	1,29±0,25		62	0,025±0,025	
Hypotymia	32	1,11±0,38	>0,05	27	0,035±0,031	>0,05
Normal self-esteem	79	1,22±0,33		77	0,028±0,028	

The level of serotonin in boys was slightly lower to compare with girls 1,00±0,29 μmol/L and 1,04±0,40 μmol/L respectively, while the level of tryptophan in boys was relatively higher – 0,043±0,037 mmol/L and 0,031±0,027 mmol/L respectively, but these differences were statistically insignificant.

Taking into account the obtained data indicating the possible relationship between serotonin and tryptophan concentrations in SD children with depression, as a possible chain of pathogenesis of its development, correlation and regression analyzes were used to establish this relationship.

Figure 4 shows a linear regression diagram that indicates a direct feedback between serotonin serum concentrations and its tryptophan precursor.

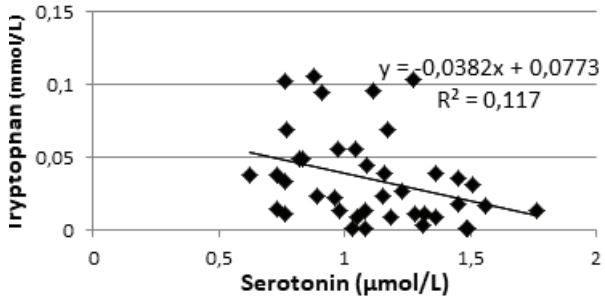

Fig. 4. Relationship between serotonin blood serum concentration and its precursor - tryptophan in children with SD with depression

The analysis of the diagram showed the features of the relationship between serotonin and tryptophan. The regression equation y = -0,03817 x +0,07729 (the forecast error for the y = bx + a equation is 0,0391 ± 0,0101, where 95% CI, 0,0229 to 0,0492) indicates the feedback between serotonin and tryptophan (95% CI, for the coefficient b, -0,0725 to -0,00379, 95% CI, for the coefficient a, 0,038 to 0,117, p<0,05). The determination coefficient R^2 = 0,117 = 0,117 indicates that in 11,7% of the cases of changes in serotonin concentration the level of tryptophan is changed. The calculated coefficient of correlation r is -0,342 (95% CI for r, -0,65 to -0,034, p<0,05) and indicates that the relationship between serotonin and tryptophan is moderate and reversible.

However, it should be noted that such dependence was practically not observed in children with SD without depression (Fig. 5).

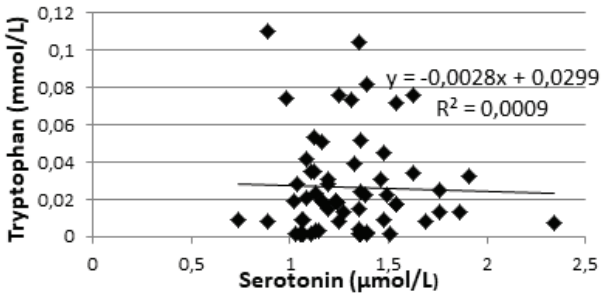

Fig. 5. Relationship between the serum concentration of serotonin and its precursor - tryptophan in children with SD without depression.

The analysis of the diagram and the regression equation is y = -0,00281 x + 0,02989 (the forecast error for the y = bx + a equation is 0,0271 ± 0,00996, where 95% CI, 0,0171 to 0,037) indicates the inverse. The relationship between serotonin and tryptophan (95% CI, for the coefficient b, -0,0273 to 0,0217, 95% CI, for the coefficient a, -0,00268 to 0,0625, p>0,05). Determination coefficient R^2 = -0,02932 = 0,000856 shows that in 0,09% of cases of changes in serotonin concentration the level of tryptophan is changed. The calculated coefficient of correlation r is -0,029 (95% CI for r, -0,284 to 0,225, p> 0,05) and indicates that the relationship between serotonin and tryptophan is reversible but very weak.

The monoamine hypothesis was accepted as the most widespread hypothesis about the main mechanism of development of depressive disorder for a long period because of its simplicity and understandability. In fact, it is believed that most currently used antidepressants are based on the monoamine hypothesis. However, an important problem with the monoamine hypothesis was the following: it cannot explain the delay in responding to antidepressants. In addition, many patients with depression remain refractory to the action of antidepressants [12, 13].

In view of this, we were asked to determine the role of serotonin and its precursor tryptophan in the development of depressive disorders in sick children in the SD, as well as the development of individual SD without depression.

The obtained data can indicate the important role of serotonin in the development of depressive symptoms in children with SD with a significant decrease in its concentration during the disease - up to 1,03 ± 0,37 μmol/L against 1,30 ± 0,27 μmol/L in patients with SD without depression (95% CI, 0,15 – 0,39 μmol/L, p<0,0001), while minimal role in the development of the SD itself since its levels did not differ significantly from the control group of children without SD and depression.

Tryptophan is an indispensable amino acid that is required for the biosynthesis of proteins in vivo. In the body tryptophan is metabolized in biologically active metabolites including serotonin, melatonin, kinurenin and vitamin niacin [14]. The transformation of tryptophan into serotonin on the periphery is controlled by tryptophan hydroxylase-1 (TRH1) and in the central nervous system, tryptophan hydroxylase-2 (TRH2). It is believed that low concentrations or disturbances of tryptophan metabolism can be one of the factors of the development of depressive disorders. [15]. However, the evidence base for such data is rather limited and ambiguous and requires further observations.

In our study we noticed a certain trend of changes in the level of tryptophan, namely when serotonin levels were reduced in children with SD with depression, there was a moderately dependent increase in the level of tryptophan (0,035 ± 0,031 mmol/L in patients with depression against 0,026 ± 0,026 mmol/L in patients without depression).

The use of correlation and regression analysis (Figure 4) confirmed a significant reciprocal and moderate correlation between the serotonin level and the level of tryptophan in children with SD with depression (r = -0,342; 95% CI for r, -0,65 to -0,034, p<0,05), that is with decreasing serotonin concentration the level of tryptophan increases. However, it should be noted that this dependence was practically not observed in children with SD without depression (r = -0,029; 95% CI for r, -0,284 to 0,225, p>0,05) (Fig. 5). The obtained data can indicate involvement in the pathogenesis of depression in children with SD in the chain of tryptophan-serotonin, in violation of the transformation of tryptophan into serotonin (it is possible that due to the decrease in activity or the synthesis of tryptophan hydroxylase), due to which it is likely that there is a corresponding dependence on their change concentrations.

The presence of more severe depression and its high frequency in patients with SD from the gastrointestinal tract can probably be explained by close ontogenetic communication between the gastrointestinal tract and the brain during fetal formation.

During the analyzing of the key clinical symptoms of depression that characterize subclasses of the CDI questionnaire, the lowest serotonin levels were associated with symptoms such as anhedonia and decreased and hypotymia (Table 1). The highest level of tryptophan was associated exclusively with the development of anhedonia.

In the study of Kumar A. et al. (2016), low levels of platelet serotonin were found in individuals who attempted suicide. Also low levels of serotonin have been associated with impulsivity in men [16]. Reduction of serotonin in blood plasma in depressive disorder was observed in the study by Holck A. et al. (2019), it has also been noted that successful treatment with selective serotonin reuptake inhibitors is associated with a greater decrease in circulating serotonin in the blood [17].

Although in our study the presence of depression was associated with a decrease of the serotonin concentration in the blood, its severity did not have any dependence on serotonin concentration, including the concentration of tryptophan. Probably the severity of depression and its various clinical manifestations can also depend on other mediator systems of the brain (norepinephrine, dopamine) and their enzyme systems.

The high prevalence of depression among children with CD (43,2%) indicates its importance in the course of the disease, its clinical manifestations and possibly prognosis. The question of the relationship between depression and CD remains important. In most patients with psycho-somatic disorders, depression is a clinically significant pantry-poor disorder. It is important to emphasize that within the mentioned comorbidity it is possible to: 1) develop depression as a result of the patient's personal reaction to the existing somatic disease (Somatogenic depression); or 2) somatization of the primary depressive disorder in the form of one or another variant of "somatoform disorder", somatoform pain disorder (somatized depression) [18].

In accordance with the received data we, it can be argued that depression, as the root cause of the disease (which can be indicative of low levels of serotonin) can lie in a specific category of children in the SD but it is difficult to clinically determine this and this claim requires a more extensive study. At the same time there are patients with SD who do not have clinical manifestations of depression but have somatic symptoms. Probably SD can be a multifactorial pathology in the presence of various pathogenetic subtypes but with similar somatic symptoms. This can depend on the effectiveness of treatment, a different response to psychotropic drugs and the prognosis of the disease.

Conclusions. 1. The presence of depressive symptoms was found in 43,2% of children with SD, in the majority of which it was moderate (56,2%), whereas severe depression was found in 14,6% of adolescent children indicating its widespread prevalence in this quantity of children.

2. Among patients with SD with depression a significant predominance of girls (70,8%) over boys (29,2%) was 2,4:1, indicating a greater tendency of women to develop depressive disorders and accordingly to the more severe flow of SD.

3. The most pronounced depressive symptomatology was found in children with SD from the gastrointestinal tract, which can indicate the preservation and importance of close ontogenetic communication of the brain from the gastrointestinal tract and its primary inclusion in the mechanisms of development of depression and its clinical manifestations.

4. The clinical picture of depression in children on SD from different systems has certain differences. In children with SD from the gastrointestinal tract characterized by a predominance of depressive symptoms of depressed mood, a tendency to tearfulness, melancholy, increased levels of anxiety. In SD from the side of CVS and nervous system depressive symptoms usually manifested high levels of fatigue, loneliness and feeling the presence of anhedonia. SD depressive symptoms of the urinary system characterized mainly negative assessment of their own failure, the presence of suicidal thoughts.

5. Serotonin levels in serum in children with SD with depression were significantly lower in comparison with children without SD with depression (95% CI, 0,15 – 0,39 μmol/L, $p<0,0001$) and in comparison with children without SD (95% CI, 0,16 - 0,48 mmol/L, $p<0,0002$) indicating its important role in the development of depression but not in the development of the SD itself. Low serotonin levels were also associated with clinical manifestations of depression as a decreased and hypotymia (95% CI, 0,02 – 0,30 mmol/L, $p<0,02$) and anhedonia (95% CI, 0,11 - 0,36 μmol/L, $p<0,0003$).

6. A reliable reverse and moderate correlation between serotonin level and tryptophan levels was found in children with SD with depression ($r = -0,342$; 95% CI for r, -0,65 to -0,034, $p<0,05$), which can indicate a violation of the chain of tryptophan-serotonin and its involvement in the development of depressive disorders in children in the SD.

7. In children with SD depression requires timely diagnosis (using appropriate scales) and special attention since such children should be at risk for the development of suicidal behavior and other mental disorders, more severe and prolonged course of the disease need timely care and specific treatment.

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SUMMARY

DEPRESSION IN THE STRUCTURE OF SOMATOFORM DISORDERS IN CHILDREN, ITS SIGNIFICANCE, THE ROLE OF SEROTONIN AND TRYPTOPHANE IN THE EMERGENCE OF THESE DISORDERS

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The aim of the study - is to investigate the presence of depressive disorders and their manifestation in children with somatoform disorders (SD) from different organs and systems and to establish the role of disorders of serotonin and tryptophan metabolism in their occurrence.

111 children were diagnosed with SD. The average age of children was 13,6±2,3 years, among them boys were 42 (37,8%) and girls – 69 (62,2%). The patients were divided into two groups: children with SD without depression 63 (56,8%) and children with SD with depression 48 (43,2%). For diagnosing of depression it was used a questionnaire for childhood depression of M. Kovacs. The determination of blood serum concentration of serotonin was carried out by biochemical method, tryptophan – by chromatographic.

The depression was diagnosed in 48 (43,2%) children of which it was mild - in 14 (29,2%), moderate - in 27 (56,2%) and severe depression - in 7 (14,6%) children. Depression was more common in girls - 34 (70,8%), in relation to boys 2,4:1. The serotonin level in children with depression was 1,03 ± 0,37 μmol/L, and it was lower to compare with children without depression (1,30 ± 0,27 μmol/L) (95% CI, 0,15 – 0,39 μmol/L, p<0,0001). The level of tryptophan in children with depression was 0,035 ± 0,031 mmol/L and it was higher to compare with children without depression (0,026 ± 0,026 mmol/L) (p>0,05). Low levels of serotonin were associated with a negative mood (95% CI, 0,02 - 0,30 μmol/L, p<0,02), anhedonia (95% CI, 0,11 - 0,36 μmol/L, p<0,0003). It was found the moderate and inverse correlation between serotonin and tryptophan in SD in children with depression (r = -0,342; 95% CI for r, -0,65 to -0,034, p<0,05).

A low serotonin level was associated with depression and it was not associated with SD without depression. With a decrease in serotonin concentration the level of tryptophan increases which can indicate about the violation of the chain of tryptophan-serotonin and its involvement in the development of depression in SD.

Keywords: somatoform disorder, depression, serotonin, tryptophan, children.

РЕЗЮМЕ

ДЕПРЕССИЯ В СТРУКТУРЕ СОМАТОФОРМНЫХ РАССТРОЙСТВ У ДЕТЕЙ, ЕЕ ЗНАЧЕНИЕ, РОЛЬ СЕРОТОНИНА И ТРИПТОФАНА В ВОЗНИКНОВЕНИИ ЭТИХ НАРУШЕНИЙ

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Цель исследования - определить наличие депрессивных нарушений и их проявления у детей с соматоформными расстройствами и установить роль нарушения обмена серотонина и триптофана в их возникновении.

Обследовано 111 детей с диагнозом соматоформные расстройства (СР), средний возраст - 13,6±2,3 лет, из них 42 (37,8%) мальчика и 69 (62,2%) девочек. Дети разделены на две группы: I группа с СР без депрессии – 63 (56,8%) и II группа - с СР в сочетании с депрессией – 48 (43,2%). Для установления диагноза депрессии использован опросник детской депрессии M. Kovacs. Определение в сыворотке крови концентрации серотонина проводили биохимическим методом, триптофана – хроматографическим.

У 48 (43,2%) детей диагностирована депрессия, из них легкая форма выявлена у 14 (29,2%), средней тяжести - у 27 (56,2%) и тяжелая - у 7 (14,6%) детей. Депрессия чаще встречалась у девочек - 34 (70,8%), в соотношении с мальчиками 2,4:1. Уровень серотонина у детей с депрессией составил 1,03±0,37 мкмоль/л и был ниже в сравнении с детьми без депрессии (1,30±0,27 мкмоль/л, 95% ДИ, 0,15-0,39 мкмоль/л), p<0,0001. Показатель уровня триптофана у детей с депрессией составил 0,035±0,031 ммоль/л и был выше в сравнении с детьми без депрессии (0,026±0,026 ммоль/л), p>0,05. Низкий уровень серотонина ассоциирован с негативным настроением (95% ДИ, 0,02 - 0,30 мкмоль/л, p<0,02), ангедонией (95% ДИ, 0,11 - 0,36 мкмоль/л, p<0,0003). Выявлена умеренная и обратная корреляционная связь между серотонином и триптофаном при СР с депрессией (r = -0,342; 95% ДИ для r, -0,65 до -0,034, p<0,05).

Низкий уровень серотонина ассоциирован с СР с депрессией, и не ассоциирован с СР без депрессии. При уменьшении концентрации серотонина уровень триптофана увеличивается, что, по всей вероятности, свидетельствует о нарушении в цепи триптофан-серотонин и его вовлечении в развитие депрессии при СР.

რეზიუმე

დეპრესია სომატოფორმული დარღვევების სტრუქტურაში ბავშვებში, მისი მნიშვნელობა, სეროტონინის და ტრიპტოფანის როლი ამ დარღვევათა აღმოცენებაში

ლ.პიპა, ი.ლისიცა, რ.სვისტილნიკი, ს.რიმშა, ვ.კერნიჩნი

ვინიცას ნ.პიროგოვის სახელობის ეროვნული სამედიცინო უნივერსიტეტი, უკრაინა

კვლევის მიზანს წარმოადგენდა დეპრესიული დარღვევების არსებობის და მათი გამოვლინებების განსაზღვრა ბავშვებში სომატოფორმული დარღვევებით და სეროტონინისა და ტრიპტოფანის როლის დადგენა მათ განვითარებაში.

გამოკვლეულია 111 ბავშვი დიაგნოზით სომატოფორმული დარღვევები, საშუალო ასაკი - 13,6±2,3 წელი, მათგან 42 (37,8%) - ვაჟი, 69 (62,2%) - გოგონა. ბავშვები დაიყო ორ ჯგუფად: I ჯგუფი - სომატოფორმული დარღვევები დეპრესიის გარეშე (63; 56,8%), II ჯგუფი - სომატოფორმული დარღვევები დეპრესიის თანხლებით (48; 43,2%). დეპრესიის დიაგნოსტიკისათვის გამოიყენებული იყო M. Kovacs-ის ბავშვთა დეპრესიის კითხვარი. სისხლის შრატში სეროტონინის კონცენტრაცია განისაზღვრა ბიოქიმიური, ხოლო ტრიპტოფანის – ქრომატოგრაფიული მეთოდით.

48 (43,2%) ბავშვს დაუდგინდა დეპრესია, მათგან მსუბუქი ფორმა - 14-ს (29,2%), საშუალო სიმძიმის - 27-ს (56,2%), მძიმე - 7-ს (14,6%). დეპრესია უფრო ხშირად აღინიშნებოდა გოგონებში (34; 70,8%), ვაჟებთან თანაფარდობით - 2,4:1.

სეროტონინის დონემ დეპრესიის მქონე ბავშვებში შეადგინა 1,03±0,37 მკმოლ/ლ და უფრო დაბალი იყო, ვიდრე ბავშვებში დეპრესიის გარეშე (0,15-0,39 მკმოლ/ლ, p<0,0001).

ტრიპტოფანის დონემ დეპრესიის მქონე ბავშვებში შეადგინა 0,035±0,035 მკმოლ/ლ და უფრო მაღალი იყო, ვიდრე ბავშვებში დეპრესიის გარეშე (0,026±0,026 მკმოლ/ლ, p>0,05). სეროტონინის დაბალი დონე ასოცირდებოდა ნეგატიურ განწყობასთან (95% ДО, 0,02 - 0,30 მკმოლ/ლ, p<0,02), და ანჰედონიასთან (95% ДО, 0,11-0,36 მკმოლ/ლ, p<0,0003). გამოვლინდა ზომიერი და უკუკორელაციური კავშირი სეროტონინსა და ტრიპტოფანს შორის სომატოფორმული დარღვევების და დეპრესიის დროს (r=-0,342; 95% ДО r, -0,65-დან -0,034, p<0,05).

სეროტონინის დაბალი დონე ასოცირდება სომატოფორმული დარღვევებისა და დეპრესიის ერთდროულ არსებობასთან, და არ ასოცირდება სომატოფორმულ დარღვევებთან დეპრესიის გარეშე. სეროტონინის კონცენტრაციის შემცირებისას ტრიპტოფანის დონე იზრდება, რაც, სავარაუდოდ, მიუთითებს დარღვევებზე ტრიპტოფან-სეროტონინის ჯაჭვში და მის ჩართვაში დეპრესიის განვითარებაში სომატოფორმული დარღვევების დროს.

ВОЗРАСТНАЯ ДИНАМИКА ДЕВИАНТНОГО ПОВЕДЕНИЯ ПОДРОСТКОВ

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Увеличение числа отклонений социального, физического и психического развития подрастающего поколения обусловлено условиями развития современного общества. Нестандартное, отклоняющееся от нормы поведение именуется девиантным. Основной оценкой девиантного поведения человека является анализ его взаимодействия с реальностью, поскольку главенствующий принцип нормы – адаптивность – исходит из приспособления по отношению к чему-то и кому-то, т. е. реальному окружению индивида. [11]. Различают поведение, отклоняющееся от норм психического здоровья, подразумевающее наличие явной или скрытой психопатологии и поведение антисоциальное, нарушающее какие-то социальные и культурные нормы, в том числе правовые [5]. Наиболее распространенными формами девиантного поведения среди подростков в возрасте 14-16 лет являются: табакокурение, школьные прогулы, сквернословие, агрессивное и грубое поведение в конфликтной ситуации со сверстниками и учителями, употребление алкогольных напитков, побеги из дома и бродяжничество, хулиганские действия и поступки, воровство в кругу семьи, употребление наркотиков, игровая зависимость, интернет-зависимость [10,12]. Среди студентов первого курса медицинского колледжа с признаками дезадаптации, высокий уровень склонности к рискованному поведению выявлен у 12,5%, средний уровень (адекватное ситуации поведение) у 72,5%, низкий уровень (не склонные к рискованному поведению) у 15% [14]. Различные адаптогенные воздействия, опосредованные индивидуально-психологическими особенностями личности, предъявляют качественно различные требования и обусловливают, в большей или меньшей степени, специфичные регуляторно-приспособительные реакции. Направление, механизмы, интенсивность и продолжительность данных реакций характеризуются сложной динамикой, претерпевают изменения в течение адаптационного цикла в соответствии со сложной системой внутренних и внешних факторов [8]. Как одну из медико-социальных