Genij Ortopedii. 2023;29(3):299-306.

Original article

https://doi.org/10.18019/1028-4427-2023-29-3-299-306

Predicting scoliosis progression in children and adolescents measuring serotonin blood level

Marina E. Winderlich[1]✉, Natalya B. Shchekolova[2]

[1]Mari State University, Yoshkar-Ola, Republic of Mari El, Russian Federation
[2]Perm State of Medicine University named after Academician E.A. Wagner, Perm, Russian Federation

Corresponding author: Marina E. Winderlich, vinderlikh@yandex.ru

Abstract

Introduction Idiopathic scoliosis is associated with severe spinal deformity, and prediction of scoliosis progression is important in the early stages for prevention and treatment. **The objective** was to identify the relationship between the serotonin blood level in children and adolescents aged 4 to 15 years and progressing scoliosis grades I-II over a five-year period. **Material and methods** Eighty-six children and adolescents with impaired posture and scoliosis were assigned to 3 groups according to clinical and radiological data and the serotonin level, the course of scoliosis, and the parameters were measured during 5 years. **Results** A significant increase in the medians, interquartile intervals of serotonin levels and the curve angle was observed in the group of progressive scoliosis with higher rates seen in girls. Significant differences in the serotonin serum level were observed in the groups. Correlation analysis showed a weak relationship between the serotonin level and the curve evaluated radiologically in patients with non-progressive scoliosis with an increase in the relationship to moderate in the progression group at 5 years. The analysis of the diagnostic efficiency of the serotonin blood level in patients with different course of scoliosis revealed the good quality of the prognostic test. **Discussion** The serotonin serum level had a statistically significant relationship with the progression of the curve examined radiologically. **Conclusion** A laboratory marker indicating progression of the curvature in children and adolescents with idiopathic scoliosis was identified. The marker included an increased serotonin blood level of greater than 270 ng/ml. The marker appeared to be practical because it could 1) be measured in the blood of children and adolescents; 2) show the dynamics in the increased serotonin level correlating with radiographic findings of the spine; and 3) indicate to the neurohumoral state of a growing body with the pathology under study. The serotonin blood level can be a marker of progressive scoliosis. The findings have been protected by an invention patent.

Keywords: serotonin, scoliosis, Adam's test, progression, radiography, diagnosis

For citation: Winderlich M.E., Shchekolova N.B. Predicting scoliosis progression in children and adolescents measuring serotonin blood level. *Genij Ortopedii*. 2023;29(3):299-306. doi: 10.18019/1028-4427-2023-29-3-299-306

INTRODUCTION

There has been an increase in the number of musculoskeletal diseases in children and adolescents in the last decade [1]. Idiopathic scoliosis is the most common type of spinal deformity confronting orthopedic surgeons. Idiopathic scoliosis is a a three-dimensional deviation of the spinal axis encountered in children and adolescents of school age ranging from 1 % to 39 % in the population and from 22.0 % to 37.0 % among all chronic diseases in childhood making the condition a medical and social problem [2-12].

Parents may ignore the first symptoms of progressing scoliosis in children aged 7 to 14 years who develop asymmetric posture, unilateral deformity of the ribs, back and heart pain, and seek help from a pediatric orthopaedic surgeon for severe scoliotic deformity types II-III to be treated with braces [13] or surgically. Idiopathic scoliosis is a socially significant problem for young patients with spinal deformity-related appearance concerns affecting patient's thoughts, self-esteem, self-image, emotional well-being and ability to function daily [13]. Even though a large number of genetic, hormonal, neurohumoral, central, neuromyogenic, neurodysplastic hypotheses have been put forward the etiology and pathogenesis of idiopathic scoliosis are poorly understood [14]. The pathogenetic mechanisms of scoliosis are associated with the formation of the musculoskeletal and nervous systems, the environmental effect on cellular metabolism and bone tissue composition [15], and with the neurohumoral status of a growing body. There are changes in the pediatric metabolism observed in the era of excessive exposure to digital technologies with impaired transfer of biologically active amines of serotonin, melatonin [16], dopamine resulting in neurological pathology, visual and nutritional disorders [17]. There is a growing interest in studying the role of neurotransmitters in the formation of scoliosis and other neuroorthopedic diseases among researchers [18]. The effect of serotonin on pregnancy and the fetus has been established with delayed formation of pathology and congenital malformations. The serotonin level was examined in premature babies and newborns with hypoxic ischemic injury to CNS (HII CNS). A pathological course of pregnancy, the method of delivery and serotonin imbalance in newborns

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with HII CNS have a negative impact on the ontogenesis of the child's nervous system [18]. This is manifested by impaired motor activity of children in the form of depression or excitation of the central nervous system indicating the regulatory effect of serotonin on motor neurons and elements of the central movement patterns located in the brain stem and the spinal cord [19].

The effect of melatonin on the tone of postural muscles has been shown resulting in scoliosis in experimentally pinealectomized chickens and progression of idiopathic adolescent scoliosis with melatonin deficiency [20]. Suppression of the SPRY4 gene in mesenchymal stem cells of the bone marrow was revealed in adolescents with scoliosis characterized by a decrease in osteogenic differentiation of stem cells into osteoblasts, and melatonin used for treatment of the patients enhanced osteogenic differentiation [21]. The tryptophan, precursor of melatonin, obtained from the blood, is converted into 5-hydroxytryptophan effected by tryptophan hydroxylase, and then into serotonin effected by decarboxylase. Serotonin is converted into melatonin effected by N-acetyltransferase and 5-hydroxyindole-O-methyltransferase. The therapeutic value of serotonin has been proven by intraperitoneal injection of 5-hydroxy-tryptophan, a precursor of serotonin, to pinealectomized chickens. Scoliosis developed in 100 % of the chickens in the control group, and 30 % of the chickens treated with 5-hydroxytryptophan were healthy [22].

Conventional radiography, MRI, CT, EEG, EMG and laboratory methods are used to predict progression of scoliosis [23-33], but they may not be available for various reasons. There is research on early diagnosis and prediction progression of scoliosis in children and adolescents to prevent severe spinal deformities requiring surgical treatment. The above effects of serotonin on the central nervous system suggested that changes in the serotonin level cause progression of the curvature in children and adolescents.

The objective was to identify the relationship between the serotonin blood level in children and adolescents aged 4 to 15 years and progression of scoliosis grades I-II over a five-year period.

MATERIAL AND METHODS

The study involved 86 children and adolescents aged 4 to 15 years with impaired posture and scoliotic deformity grades I-II. There were 38 male and 48 female patients. Clinical, biochemical and radiological examination was performed with informed consent signed by a parent. Patients of the treatment group were divided into groups: aged 3-7 years (n = 12; 14 %), 8-12 years (n = 55; 63.9 %), 13-15 years (n = 19; 22.1 %). The control group included 20 healthy children and adolescents aged 4 to 15 years with no signs of posture disorder and scoliosis including 12 females (60 %) and 8 males (40 %).

Inclusion criteria included clinical symptoms of impaired posture and scoliosis with asymmetric shoulder girdle, angles of the shoulder blades and triangles of the waist, deviation of the vertebrae from the midline, oblique pelvis, positive Adams test in children and adolescents. An orthopaedic examination, AP standing view of the thoracolumbar spine, serum serotonin level measured by enzyme-linked immunosorbent assay using the ELISA Fast Track kit (reference values of serum serotonin 70-270 ng/ml) were performed at the beginning of the study and every 12 months during 5 years. The serum serotonin level was measured in children and adolescents with scoliosis and compared with radiological findings of the spine. Statistical processing was performed using Statistica 12 and Excel software package. Normality was assessed using the Shapiro-Wilk test. The results of the study are shown in tables as median (Me) and an interquartile range [Q1 - Q3] within the standard range of 25-75 %, arithmetic mean and standard deviation (Xi ± SD). The Friedman test was used to compare serotonin level within the same group (control, non-progressing, feebly progressing, progressing scoliosis) in different years. If Friedman's test was significant, a pairwise comparison of the results between years was performed using the Wilcoxon W-test, the significance level was determined considering the Bonferroni correction. Correlation analysis was used to explore the relationship between two variables using the nonparametric Spearman correlation coefficient rs. The threshold level of statistical significance was accepted at $p < 0.05$. The sensitivity, specificity, accuracy, predictive value of positive and negative results were determined to assess the quality of the binary test for measurements of serum serotonin in groups of healthy children and patients with different course of scoliosis. Sensitivity was associated with the number of patients with idiopathic scoliosis, correctly confirmed by a test for measuring blood serotonin above the reference values and calculated with the formula: $Se = A / (A + C)$, where A was true positive (patients, test "+"), C was false negative (patients, test "-"). Specificity was associated with the number of healthy children who had a normal serum serotonin level, and calculated with the formula: $Sp = D / (B + D)$, where B was false positive (healthy, "+" test), D was true negative (healthy, test"-").

RESULTS

The average serotonin levels were within the reference measurements in the control group of healthy children and adolescents without postural disorders and scoliosis for 5 years (Table 1).

Table 1

The content of the serum serotonin in children and adolescents aged 4-15 years old in the control group

Serum serotonin, ng/ml	Control Group (healthy)	
C1 (1)	Me [Q1 - Q3]	120.0 [113.5 - 133.5]
C2 (2)		138.0 [131.0 - 147.5]
C3 (3)		136.0 [121.0 - 165.0]
Wilcoxon test, p	$p^{1-2} = 0.002$; $p^{1-3} = 0.013$; $p^{2-3} = 0.56$	

Note: C1, serotonin level measured in the 1st year (ng/ml); C2, serotonin level measured after 3 years (ng/ml); C3, serotonin level measured after 5 years (ng/ml); p^{1-2}, p^{1-3}, p^{2-3}, level of significance of differences between groups in the 1st, 3rd, 5th year of the study at $p < 0.017$.

Serotonin blood levels in the of healthy children and adolescents increased by 13.3 % over a five-year period and were within the reference values. This fact could be explained by the predominance of girls aged 9-11 years with the hormonal changes and active skeletal growth. The Wilcoxon test was used considering the Bonferroni correction to determine a statistically significant difference between the serum serotonin level at time points. There were significant differences in the serotonin level in control patients at 1 year and at 3 years, at 1 year and 5 years. The children and adolescents of the treatment group were divided by age and gender into 3 groups according to clinical and radiological findings and the course of scoliosis: non-progressive, slow progressive and progressive (Table 2). The course of scoliosis was confirmed by serum serotonin level at five years. The Pearson's Chi-square test was used to determine a statistically significant difference in sex distribution in groups according to the course of scoliosis. When analyzing the results, a homogeneous distribution by gender was revealed in the groups of non-progressive and slow progressive scoliosis ($p = 0.686$), the distribution was heterogeneous ($p = 0.01$) in the group of progressive scoliosis due to the predominant number of girls (77.4 %) over boys (22.6 %) and had differences with the other two groups. Distribution of patients by age was performed with the Kruskal-Wallis test in groups; homogeneity of distribution was demonstrated in the groups with idiopathic scoliosis (Table 2).

Of 86 children and adolescents of the treatment group with impaired posture and scoliosis degree I-II, 19 (22.1 %) were in the group of non-progressive scoliosis and had average serum serotonin levels of 192.6 ± 12.6 ng/ml and an average angle of curvature measuring 7.0 ± 1.2° at a short term, at 5 years, the average levels of serotonin in the blood increased by 29.9 % (274.9 ± 10.8 ng/ml), and the angle of curvature increased by 36.9 % (11.1 ± 1.6°). An increase of the curvature by 5° at 6-12 months is one of radiological signs of the progression of scoliosis. Patients with grade I scoliosis had serotonin levels within the normal range at 1 year followed by an increase in the level to 300 ng/ml with no radiological signs of progression of scoliosis deformity in AP view. The group of slow course of scoliosis consisted of 36 people (41.9 %) with a predominance of school children aged 8-12 years (72.2 %).

The blood serotonin level was higher in the group than the reference values at 1 year with an average value of 321.5 ± 18.9 ng/ml and the mean angle of curvature was 10.0 ± 2.3°; there was an increase in the average serotonin level by 28.3 % (412.9 ± 15.5 ng/ml) with an increase in the average curvature by 46.2 % (18.6 ± 2.2°) at 5 years. The group of progressive scoliosis consisted of 31 individuals (36 %) who showed the average level of serum serotonin of 559.0 ± 79.8 ng/ml at 1 year, and there was an increase of 37.1 % (888.0 ± 104.6 ng/ml) with an increase in the angle of scoliosis by 53.3 % (28.9 ± 5°) at 5 years. There were 77.4 % (n = 24) of girls in the group of progressive scoliosis and had higher parameters than boys. Serum serotonin and spinal deformity angle were assessed by comparing the median and quartile values of the parameters on radiographs in healthy individuals and patients with different course of scoliosis (Table 3).

Table 2

Distribution of patients of the treatment group into subgroups by age and sex according to clinical and radiological data fndings

Type of scoliosis	Number		Age, years	the Kruskal-Wallis test	Gender		The Pearson's Chi-square test
	abs.	%	Me [Q1 - Q3]	p	female	male	p
non-progressive	19	22.1	9.0 [6.0 - 13.0]	0.2	9 (47.4 %)	10 (52.6 %)	0.686
slow progressive	36	41.9	10.5 [9.0 - 11.5]	0.51	15 (41.7 %)	21 (58.3 %)	
progressive	31	36.0	11.0 [9.0 - 12.0]	0.75	24 (77.4 %)	7 (22.6 %)	0.01
Total	86	100			48 (55.8 %)	38 (44.2 %)	

Table 3

Dynamics in absolute parameters of serum serotonin and the curvature angle on radiographs of patients with idiopathic scoliosis and control patients

Parameter	Groups of patients				The Wilcoxon test, p
	control (healthy) (1)	non-progressive scoliosis (2)	Slow progressive scoliosis (3)	progressive scoliosis (4)	
	Me [Q1 - Q3], n = 20	Me [Q1 - Q3], n = 19	Me [Q1 - Q3], n = 36	Me [Q1 - Q3], n = 31	
C1, ng/ml	120.0 [113.5 - 133.5]	194.0 [185.0 - 203.0]	319.0 [306.0 - 328.0]	559.0 [511.0 - 616.0]	$p^{1-2} = 0.0001$ $p^{1-3} = 0.00009$ $p^{1-4} = 0.00009$ $p^{2-3} = 0.0001$ $p^{2-4} = 0.0001$ $p^{3-4} < 0.00001$
C2, ng/ml	138.0 [131.0 - 147.5]	218.0 [205.0 - 235.0]	379.0 [355.5 - 407.5]	692.5 [648.0 - 734.0]	
C3, ng/ml	136.0 [121.0 - 165.0]	283 [269.0 - 287.0]	415.5 [405.0 - 419.0]	897.0 [831.0 - 972.0]	
P1, °	–	7.0 [6.0 - 8.0]	10.0 [8.3 - 12.0]	13.0 [11.0 - 16.0]	$p^{2-3} = 0.0018$ $p^{2-4} = 0.0001$ $p^{3-4} < 0.0001$
P2, °	–	9.7 [7.5 - 10.3]	14.3 [11.7 - 14.6]	20.3 [17.3 - 23.0]	$p^{2-3} = 0.0003$ $p^{2-4} = 0.0001$ $p^{3-4} < 0.00001$
P3, °	–	11.0 [10.3 - 12.5]	18.6 [17.3 - 19.5]	28.5 [25.5 - 32.5]	$p^{2-3} = 0.0001$ $p^{2-4} = 0.0001$ $p^{3-4} < 0.00001$

Note: C1, serotonin level at 1 year (ng/ml); C2, serotonin level at 3 years (ng/ml); C3, serotonin level at 5 years (ng/ml); P1 is the angle of curvature on the radiograph at 1 year (°); P2 is the angle of curvature on the radiograph at 3 years (°); P3, the angle of curvature on the radiograph at 5 years (°); p is the level of significant differences in groups of patients (Wilcoxon test); p^{1-2}, p^{1-3}, p^{1-4}, p^{2-3}, p^{2-4}, p^{3-4}, level of significant differences between groups.

Patients with progressive scoliosis showed a significant increase in the median and interquartile intervals of the serotonin level and the angle of the spinal deformity comparing baseline and long-term measurements. This indicated the relationship between the serotonin serum level and the progression of scoliosis. The Wilcoxon test was used to calculate significant differences in the measurements at time points between groups of healthy patients and patients with different course of scoliosis. Table 3 revealed significant differences in the values of serum serotonin between the groups throughout the study. Correlation analysis revealed a weak positive and negative correlation between serum serotonin levels and spinal deformity in patients with non-progressive scoliosis throughout the study and at baseline in patients with slow progressive scoliosis (Table 4). That meant that one variable (serotonin) increased with a slight increase in another variable (radiography) during the study period. The parameters of blood serotonin level and the angle of spinal deformity had a moderate positive statistically significant correlation in patients with a slow course of scoliosis at 3 and 5 years. There was an increase in correlations with a tight relationship between these two parameters in patients with progressive scoliosis (Table 4). That indicated interconnection between serotonin and spinal deformity.

The diagnostic efficiency of the method for predicting progression of scoliosis using the serum serotonin level was evaluated with the calculation of the main criteria: sensitivity, specificity, diagnostic efficiency, predictive value of positive and negative results in groups with different course of scoliosis (Table 5).

Table 4

Linear correlation between serotonin levels in patients with different course of idiopathic scoliosis

Course of scoliosis	Correlation coefficient, r		
	C1-P1	C2-P2	C3-P3
Non-pregressive, n = 19	0.137 (p = 0.576)	-0.360 (p = 0.129)	0.091 (p = 0.71)
Slow pregressive, n = 36	0.158 (p = 0.356)	0.394 (p = 0.017)	0.467(p = 0.004)
Pregressive, n = 31	0.572 (p = 0.0008)	0.570 (p = 0.0008)	0.484 (p = 0.006)

C1, serotonin level at 1 year (ng/ml); C2, serotonin level at 3 years (ng/ml); C3, serotonin level at 5 years (ng/ml); P1 is the angle of curvature on the radiograph at 1 year (°); P2 is the angle of curvature on the radiograph at 3 years (°); P3, the angle of curvature on the radiograph at 5 years (°); p is the level of significant differences in groups of patients

Table 5

Diagnostic criteria for predicting progression of scoliosis in groups of children and adolescents with scoliotic deformity

Groups	DS	DSp	DA	PPV	NPV	AUC	TV
Non-progressive scoliosis	84	80	89	94	86	0.894	0.851
Slow progressive scoliosis	83	80	88	97	76	0.961	0.430
Progressive scoliosis	87	80	90	96	83	0.992	0.598

Note: DS, diagnostic sensitivity (%); DSp, diagnostic specificity (%); DA, diagnostic accuracy (%); PPV, positive predictive value (%); NPV, negative predictive value (%); AUC is the area under the ROC curve; TV, threshold value.

A high sensitivity of the test for measuring serotonin was revealed in patients with progressive scoliosis (87 %) with the correct diagnosis made according to the test results in 96 % of patients with a diagnostic accuracy of 90 %. The positive predictive value was higher in the group of patients with slow progressive scoliosis (97 %), showing a greater tendency of disease progression with an increase in serum serotonin levels. The AUC area under the ROC curve and threshold values were calculated to determine the predictive effectiveness of the serotonin test in groups. Table 5 revealed very good AUC values in the group of patients with non-progressive scoliosis (0.894) and excellent AUC values in patients with slow progressive (0.961) and progressive deformity (0.992) that indicated a good quality of the prognostic test for measuring serum serotonin. The relationship between an increase in the level of serum serotonin and the progression of scoliotic deformity was revealed, and a patent for the invention No. 2771873 dated May 13, 2022 was obtained [34]. Scoliosis had a non-progressive course in children and adolescents with scoliotic deformity and a serum serotonin value of up to 300 ng/ml, slow progressive course with a serotonin value of 300 to 420 ng/ml, and there was a higher risk of progression of scoliotic deformity with a value of more than 420 ng/ml. There is a clinical example showing the above.

Clinical instance A 10-year-old girl M. was diagnosed with asymmetric shoulder girdle, shoulder blade angles, waist triangles; deviation of the vertebrae in the thoracic spine from the midline to the left, the Adams test being positive in the thoracic spine on the left. Radiograph of the spine showed the curvature in the thoracic spine to the left of 5 degrees and torsion of 0 (Fig. 1). Serum serotonin content was 325 ng/ml. Left-sided thoracolumbar scoliosis grade 1 with a slow progressive course was identified. The patient was followed-up and treated as outpatient twice a year using physiotherapy, massage, swimming, exercise therapy during 3 years. Serum serotonin measured 496 ng/ml at the age of 11. Radiograph showed the angle of curvature in the thoracic spine to the left of 15 degrees and torsion of 0 (Fig. 2). She was diagnosed with left-sided scoliosis of the thoracic spine grade II and progressive curvature. Physical examination showed asymmetry of the shoulder girdle, shoulder blade angles, waist triangles; Adams test being positive in the thoracic spine on the left at the age of 12. Radiograph showed the curvature in the thoracic spine to the left of 21 degrees, torsion 1 and oblique pelvis (Fig. 3). The content of serum serotonin in patient M. was 538 ng/ml. She was diagnosed with left-sided scoliosis of the thoracic spine grade II and progressive course.

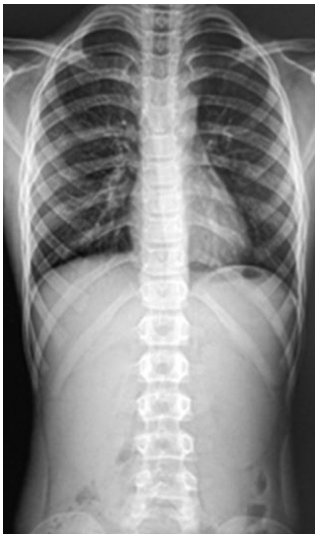

Fig. 1 AP view of the spine of a 10 yo patient M. at 1 year

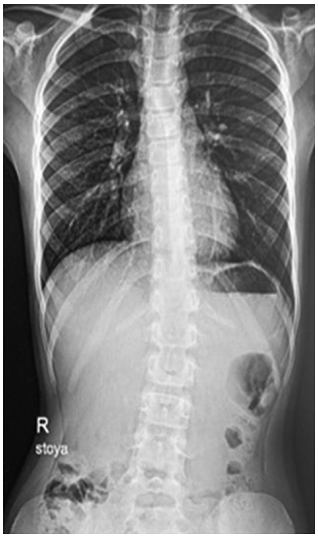

Fig. 2 AP view of the spine of a 11 yo patient M. at 2 years

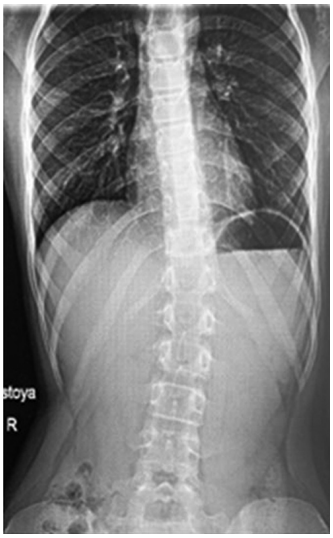

Fig. 3 AP view of the spine of a 12 yo patient M. at 3 years

The clinical example a patient with a slowly progressive course of scoliosis demonstrated the possibility of prediction of progressing scoliosis by increasing serotonin level in the early stages and monitoring the conservative treatment to prevent the development of severe spinal pathology.

DISCUSSION

Many foreign and Russian researchers report associations between the progression of scoliotic deformity and genetic polymorphism, with susceptibility genes being associated with structural anomalies of the connective tissue, impaired calcium metabolism, a defect in the signaling of hormones and growth factors in patients with idiopathic scoliosis [27, 31]. Instrumentation and laboratory methods are known to be used for predicting the progression of scoliosis using the clinical and radiological increase in Cobb angle by more than 5° per year with Risser stage 0-3 [14]. Quasiautomatic 3D reconstruction methods with biplanar X-rays low-dose biplanar radiography are used for automatic calculation of the scoliosis severity index and determination of the stability or progression of scoliotic deformity [32]. The course of scoliosis can be determined by osteoscintiogram according to the degree of absorption of the osteotropic radiopharmaceutical between the concave and convex sides of the vertebrae on both sides with a color assessment according to the table. The color asymmetry indicates the progression of scoliotic deformity [23]. There was association identified between severity or progression of scoliosis with the following characteristics: patient age < 13 years at diagnosis, female sex, premenarche status, initial Cobb angle severity (> 25o), decreased bone mineral density, skeletal immaturity, asymmetry of the electrical activity of the paraspinal muscles during electromyography, brain stem vestibular dysfunction, etc. [31].

Foreign researchers have identified single nucleotide polymorphisms of genes in patients with idiopathic scoliosis in various populations, for example, a sensitive locus in the MIR4300HG gene was found in Japanese patients with progressive spinal deformity. Studies in the Chinese population revealed an association between the estrogen receptor 1 gene, the tryptophan hydroxylase 1 (TPH1) gene, the neurotrophin 3 gene, the interleukin-17 receptor C gene, and the melatonin 1B receptor gene with the progressive course of idiopathic scoliosis [31], and the curvature progression was noted with calmodulin level in blood platelets from 1.46 to 10.67 ng/μg protein and Risser test 0-1 [24]. Impaired melatonin signaling in osteoblasts and peripheral blood mononuclear cells was found in operated patients with severe spinal deformity. The functional status of the Gai carrier protein was determined in peripheral blood mononuclear cells using cellular dielectric spectroscopy and the FG2 endophenotype, characterized by hypofunction of serine phosphorylation of Gai isoforms with impaired melatonin receptor signaling was detected in patients with a high risk of progression of scoliotic deformity [31].

A multigenetic predictive test ScoliScore AIS with quantitative and qualitative assessment of scoliosis progression has been developed. The algorithm converts TaqMan genotyping into scores from 1 to 200. Scores of 1 to 50 are classified as low risk, 51 to 180 as medium risk and 181 to 200 as high risk. Researchers have clinically proved that if there are low-risk results, there is a 99 percent chance that scoliosis will not progress to severe condition. Due to ethnic variations in the frequency of single nucleotide polymorphism markers, the test is only valid for white subjects and is not applicable to Hispanic, Asian or African American patients. The cost of the test is quite high and does not help predict the predisposition of the child to inherit the disease and the final result of the progression of the disease. The analysis of the above methods for predicting scoliosis revealed the limited predictive value of all the results obtained with a low level of evidence [31]. A 1.5 or more decrease in the sulfated glycosaminoglycans was determined in the urine of patients with an unfavorable course of idiopathic scoliosis with a 1.5-to-2 increase in the activity of lysosomal cathepsin D enzymes and a 1.5-to-10-time increase in the activity of α-galactosidase with respect to the norm [33].

Proponents of the humoral theory of scoliosis predicted a progressive curve at a cortisol level ranging from 230 nm/l to 400 nm/l, a slowly progressive type, up to 500 nm/l and a non-progressive curve with greater than 500 nm/l [26, 27]. An increase in the level of hormones in the blood of a patient with scoliotic deformity predicts early activation of pituitary gonadotropins and progression of the severity of dysplastic scoliosis [28, 29]. The progression of scoliotic deformity can be predicted with the level of blood calcitonin > 4.14 pg/ml, somatotropin > 4.45 ng/ml, and with parathyrin < 18.64 ng/ml [30]. The analysis of laboratory diagnostic methods also showed the limitations of the clinical use as diagnostic criteria for predicting the progression of scoliosis for various reasons, including budgets of patients and medical institutions. The results of our study have a statistically significant relationship between the serum serotonin level and the progression of scoliosis, facilitating prediction of the course of scoliosis before the onset of the first clinical symptoms in children of any

age. Understanding the mechanisms of the pathogenesis of idiopathic scoliosis is important for identifying the patterns and progression of spinal deformities. The findings obtained in the course of the research should contribute to the development of new methods for the early diagnosis of scoliosis to allow timely prevention and treatment of children with idiopathic scoliosis at the initial stages of spinal deformity.

CONCLUSION

1. Most laboratory methods for predicting progression of scoliosis have limited use in clinical practice due to the high cost of equipment and reagents. Although spinal radiography is the most accessible instrumentation diagnostic method, it allows no prediction of idiopathic scoliosis prior to the first symptoms.

2. A correlation between the serotonin level and the angle of spinal deformity on the radiograph has been determined in the course of the study increasing with the progression of the disease and indicating the relationship of the parameters. Evaluation of the diagnostic efficiency of the method for predicting the progression of scoliosis by the serotonin level revealed the good quality of the prognostic model, and serotonin level can be used as a marker for early diagnosis and the course of scoliosis in children and adolescents.

3. Higher serum serotonin levels were observed during "growth spurts" and puberty, in girls, in particular, indicating the relationship between the child's hormonal status and the neurotransmitter system and confirming the neurohumoral theory of scoliosis formation.

4. We can suggest that measurement of the blood serotonin level allows prediction of the development and progression of scoliosis in children and adolescents in the early stages, timely influence on the skeletal growth between 4 and 15 years, adequate treatment to slow down the progressing of the curve and improve the patient's quality of life.

Conflict of interest *The authors declare no conflict of interest.*

Funding *This research received no external funding.*

Ethical expertise *The study was conducted in accordance with the ethical standards of the Declaration of Helsinki of the World Medical Association "Ethical principles for conducting scientific medical research involving humans", as amended in 2013, in compliance with the principles of research safety, awareness, voluntariness, and confidentiality.*

Informed consent *All patients or their legal representatives signed an informed consent to participate in the study and publish data without identification.*

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The article was submitted 27.09.2022; approved after reviewing 09.03.2023; accepted for publication 20.04.2023.

Information about the authors:

1. Marina E. Vinderlikh – Candidate of Medical Sciences, Associate Professor, vinderlikh@yandex.ru, https://orcid.org/0000-0002-9855-548X;
2. Natalya B. Shchekolova – Doctor of Medical Sciences, Professor, Professor of the Department, nb_sh @ mail.ru, https://orcid.org/0000-0002-3911-4545.

Contribution of the authors:

Winderlich M.E. – validation, formal analysis, conducting the research process, data processing, writing the initial version, visualization.
Shchekolova N.B. – conceptualization, methodology, validation, control, project management, writing - reviewing and editing, visualization.