Spinal mobility in children with diabetes and factors, which influence it

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Aim of study: to evaluate spine mobility, as an integral marker of joint mobility, according to the duration of the disease and provision of vitamin D in children with diabetes.

Materials and research methods. Overall, 93 children from 11 to 17 years old with insulin-dependent diabetes were examined. According to the duration of the disease, all the children were divided into three groups: the first group consists of 26 children (average age 12.9 ± 0.4 years) with the duration of the disease less than a year, the second group consists of 33 patients (average age 13.8 ± 0.4 years) with the duration of the disease from one to five years, the third group consists of 34 patients (average age 14.3 ± 0.4 years) with the duration of the disease for more than five years. The control group consists of 30 conditionally healthy children that are representative by age and gender. Evaluation of joints motion was performed in all the children with the help of metrical tests. The content of vitamin D and periostin was identified in blood serum by the method of immunoenzyme assay.

Results. It was found that in children with diabetes mellitus, compared with the control group, there is a decrease in spine mobility. Starting from the second year of disease, it was noticed that there is gradual decrease of mobility of all parts of the spine. We observed a decrease in blood serum vitamin D levels, which progress with the enlargement of illness duration. In the first year of the disease, vitamin deficiency was only 10%. At that time, in group 2 in 50% of children, and in group 3 in 80% of children there was a decrease in vitamin D level (P < 0.05). Lack of vitamin D sufficiency was accompanied by a deterioration of the overall mobility of the spine. The lowest levels of vitamin D were found in children with high-risk glycemic control.

It was determined that the level of periostin tended to increase gradually with the progress of diabetes. Data analysis showed that children with high levels of periostin had low levels vitamin D in blood serum.

Conclusions. Children with diabetes are characterized by the deterioration in the functional state of the spine in the form of reduced mobility in all its regions, which progress with an increase in the duration of the disease. One of the mechanisms for the development of the revealed violations is poor compensation for diabetes and vitamin D deficiency.
There are more than 20 million people on the Earth with insulin-dependent diabetes, which is 10–15% of all patients with diabetes. Nevertheless, WHO experts prognose that the number of this patients will increase by 1.5 times until 2030 taking into consideration fast pace of this disease increase. The most important problem of insulin-dependent diabetes is revealing of early and late complications of different organs and systems, that cause worsening of life quality. The main reason for late complications is hyperglycemia [1]. That is why it is very important to treat diabetes correctly and on time. If during treatment it is not possible to achieve normoglycemia, syndromes of joints movement volume restriction and many others can be reversed.

Diabetic arthropathy is a common complication of diabetes and it often occurs, according to literature review in 0.08–13.00%, and in patients with a high risk of glycemic control, it increases to 29% [3]. Skeleto-muscular lesion appears in children even if the duration of the disease is not long, meantime adult patients have such changes after a much longer disease duration [1]. This happens due to age-related peculiarities of skeleton, gaining bone mass and growth spurt [4]. Decreasing of bone mass leads to disorder of mechanical strength, which causes accelerated bone friability. However, osteopenia in children usually goes covertly and it is not diagnosed throughout a long time [3].

Recently, syndrome of joints movement volume restriction in patients with diabetes is vividly studied, long-existing hyperglycemia takes the leading position in mechanisms of its development, as well as specific complications of this disease [5]. It is known that vitamin D is needed for normal bone mineralization and maintenance of calcium and phosphorus in the blood serum. In the late 80s, it was found that in osteoblasts and osteocytes there are both vitamin D receptors (VDR) and 1.25 (OH)2D [6]. VD directly participates in bone tissue metabolism, acting with VDR on osteoclasts, chondrocytes, osteoblasts [7]. In addition to the effect of VD on the bone system, the role of VD hypovitaminosis on the pathogenesis of metabolic disorders, including diabetes, is possible [8]. In support of this fact, VDR were found in β-cells of the pancreas, in adipose tissue and skeletal muscles involved in glucose homeostasis [9].

It is proved that extracellular protein – periostin also takes part in the metabolism of bone tissue. It regulates the collection and adhesion of bone marrow osteoblasts for bone regeneration. An experiment was conducted on mice with lacked periostin. Defects such as stunted growth, short bones, impaired regeneration and bone density were discovered [10]. However, to date, there are only a few works in which the relationship of periostin and vitamin D and their changes in various pathologies were studied [11]. Nevertheless, until now the question about the whole spectrum of changes in skeleto-muscular system in children with insulin-dependent diabetes is open. That is why there is a strong need for searching of early diagnostic criteria for changes in skeleto-muscular system, especially at early age, when pathological processes can be reversed.
Aim
To evaluate spine mobility, as an integral marker of joint mobility, according to the duration of the disease and provision of vitamin D in children with diabetes.

Materials and research methods
The research was held on the base of Endocrinology Department of Communal Enterprise “Zaporizhzhia regional clinical children hospital” of Zaporizhzhia regional council. Overall, 93 children from 11 to 17 years old with insulin-dependent diabetes were examined. According to the duration of the disease, all children were divided into three groups: the first group consists of 26 children (average age 12.9 ± 0.4 years) with the duration of the disease less than a year, the second group consists of 33 patients (average age 13.8 ± 0.4 years) with the duration of the disease from one to five years, the third group consists of 34 patients (average age 14.3 ± 0.4 years) with the duration of the disease for more than five years. The control group consists of 30 conditionally healthy children that are representative by age and gender.

Evaluation of joints motion was performed in all the children with the help of metrical tests [12,13]:
1) Definition of mobility of cervical region of the spine. 8 centimeters is measured up from VII cervical vertebra, where the mark is made. Then one asks a child to lean head down as much as possible. Then this distance is marked as well. This distance increases for 2–3 centimeters in healthy children.
2) Chin-sternum test. While leaning the head down, a person's chin must touch the sternum. If there is a lesion of cervical region of spine, then some space is left between chin and sternum.
3) Otto test – mobility evaluation of thoracic region of spine. 30 centimeters is measured down from VII cervical vertebra, where the mark is made. Then the distance between these two points is measured, while a child is leaning forward as much as possible. Healthy children have the increase of this distance for 3–4 centimeters.
4) Restriction of chest excursion is used for determination of costovertebral joints mobility. Chest circumference is measured on the level of the IV rib while a child inhales deeply and then exhales. The difference between index of chest circumference is usually 4.0–4.5 centimeters.
5) Schober's test – mobility evaluation of lumbar region of spine. 10 centimeters is measured up from V lumbar vertebra, where the mark is made. While leaning forward as much as possible this distance increases for 3–4 centimeters.
6) Thomayer test – evaluation of general mobility of the whole spine. It is conducted by measuring distance in centimeters from middle finger of outstretched hands to the floor. This distance equals 0 in healthy children.

The content of vitamin D in blood serum was determined by EIA method using commercial kits: 250H Vitamin D Total ELISA (DI Asource ImmunoAssays S.A., Belgium).

The group of patients with diabetes mellitus whose vitamin D level was determined consisted of 30 children, the control group consisted of 10 children. During Vitamin D assessment 5 threshold levels of serum hydroxycal-ciferol concentration were allocated: absolutely toxic level – more than 200 ng/ml; level with a possible manifestation of toxicity – 100–200 ng/ml; adequate level – 30–100 ng/ml; insufficiency – 21–29 ng/ml and deficiency – less than 20 ng/ml [14].

The group of patients with diabetes mellitus whose peristin level was determined consisted of 62 patients, the control group consisted of 20 patients. The content of peristin in blood serum was determined by EIA method using commercial kits HUMAN PERIOSTIN/OSF-2 ELISA KIT (Aviscera Bioscience Inc., USA)

All the results were analyzed using the set of statistic programs Statistica 13.0 (StatSoft Inc. № JPZ8041382130ARCN10-J). Parametrical methods that helped to evaluate arithmetic mean (M), standard deviation (σ) and mean error (m) were applied for normally arranged rates. Check of normality was held with the Shapiro–Wilks test of asymmetry. The method of correlation analysis was used to calculate the Pearson correlation coefficient in the normal distribution of features and the Spearman rank correlation coefficient in their absence.

Results
Carried out analyses shows that the longer the duration of diabetes is, the worse functional condition of spine children have (Table 1).

For example, in the group of children who have diabetes for less than a year, there were only solitary cases of decrease of spine functional condition. Moreover, average parameters of spine mobility did not statistically differ from data of control group. Despite that, starting from the second year of disease, it was noticed that there is gradual decrease of mobility of all regions of the spine. The individual analyses showed that patients from the second group suffered primarily from lesion of cervical region of spine, decrease of spine mobility was noticed in one third of patients (Table 2). It was noted
Table 1. Mobility conditions of spine in children with diabetes, depending on the duration of the disease according to data of metrical tests (M ± m)

<table>
<thead>
<tr>
<th>Metrical tests</th>
<th>1 group, n = 26</th>
<th>2 group, n = 33</th>
<th>3 group, n = 34</th>
<th>Control group, n = 30</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mobility of cervical region of spine, cm</td>
<td>2.37 ± 0.12</td>
<td>1.95 ± 0.11</td>
<td>1.65 ± 0.10</td>
<td>2.33 ± 0.09</td>
</tr>
<tr>
<td>Chin-sternum test, cm</td>
<td>0.12 ± 0.06</td>
<td>0.44 ± 0.12</td>
<td>0.96 ± 0.13</td>
<td>0.10 ± 0.07</td>
</tr>
<tr>
<td>Otto test, cm</td>
<td>3.25 ± 0.12</td>
<td>2.91 ± 0.10</td>
<td>2.68 ± 0.10</td>
<td>3.13 ± 0.13</td>
</tr>
<tr>
<td>Schober’s test, cm</td>
<td>3.42 ± 0.11</td>
<td>3.17 ± 0.10</td>
<td>2.79 ± 0.10</td>
<td>3.53 ± 0.11</td>
</tr>
<tr>
<td>Chest excursion, cm</td>
<td>4.56 ± 0.13</td>
<td>4.23 ± 0.15</td>
<td>3.69 ± 0.10</td>
<td>4.67 ± 0.12</td>
</tr>
<tr>
<td>Thomayer test, cm</td>
<td>0.15 ± 0.11</td>
<td>0.82 ± 0.24</td>
<td>2.66 ± 0.30</td>
<td>0.20 ± 0.09</td>
</tr>
</tbody>
</table>

Table 2. Registration frequency of spinal movement disorders in children with diabetes, according to metrical tests, depending on duration of the disease (n, %)

<table>
<thead>
<tr>
<th>Metrical tests</th>
<th>1 group, n = 26</th>
<th>2 group, n = 33</th>
<th>3 group, n = 34</th>
<th>Control group, n = 30</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mobility of cervical region of spine, cm</td>
<td>2</td>
<td>10</td>
<td>17</td>
<td>2</td>
</tr>
<tr>
<td>Chin-sternum test, cm</td>
<td>2</td>
<td>11</td>
<td>23</td>
<td>2</td>
</tr>
<tr>
<td>Otto test, cm</td>
<td>2</td>
<td>8</td>
<td>16</td>
<td>3</td>
</tr>
<tr>
<td>Schober’s test, cm</td>
<td>2</td>
<td>9</td>
<td>17</td>
<td>1</td>
</tr>
<tr>
<td>Chest excursion, cm</td>
<td>1</td>
<td>4</td>
<td>11</td>
<td>1</td>
</tr>
<tr>
<td>Thomayer test, cm</td>
<td>2</td>
<td>11</td>
<td>27</td>
<td>2</td>
</tr>
</tbody>
</table>

Table 3. Mobility conditions of spine in children with diabetes, according to the status of glycaemic control (M ± m)

<table>
<thead>
<tr>
<th>Metrical tests</th>
<th>Glycemic control</th>
<th>Control group, n = 30</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mobility of cervical region of spine, cm</td>
<td>2.28 ± 0.10</td>
<td>2.33 ± 0.09</td>
</tr>
<tr>
<td>Chin-sternum test, cm</td>
<td>0.06 ± 0.06</td>
<td>0.10 ± 0.07</td>
</tr>
<tr>
<td>Otto test, cm</td>
<td>3.11 ± 0.14</td>
<td>3.13 ± 0.13</td>
</tr>
<tr>
<td>Schober’s test, cm</td>
<td>3.42 ± 0.11</td>
<td>3.53 ± 0.11</td>
</tr>
<tr>
<td>Chest excursion, cm</td>
<td>4.56 ± 0.13</td>
<td>4.87 ± 0.12</td>
</tr>
<tr>
<td>Thomayer test, cm</td>
<td>0.76 ± 0.21</td>
<td>0.20 ± 0.09</td>
</tr>
</tbody>
</table>

Table 4. The amount of vitamin D and periostin in blood serum of children with diabetes according to the duration of the disease (Me (Q25–Q75))

<table>
<thead>
<tr>
<th>Score</th>
<th>1 group</th>
<th>2 group</th>
<th>3 group</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin D, ng/ml</td>
<td>32 (30–35) n = 10</td>
<td>29 (28–34) n = 10</td>
<td>29.5 (29–31) n = 10</td>
<td>31.5 (30–33) n = 10</td>
</tr>
<tr>
<td>Periostin, ng/ml</td>
<td>37.2 (22.7–114.7) n = 20</td>
<td>44 (16–145) n = 21</td>
<td>60 (36.5–128.0) n = 21</td>
<td>2.5 (1.3–33.5) n = 20</td>
</tr>
</tbody>
</table>

We noticed significant decrease of mobility of thoracic and lumbar regions of spine in patients from the third group comparing to other researched groups (P < 0.05). Registered changes were reflected in general spine mobility, and its restriction was noticed in 27 (79.4 %) patients from the third group.

Considering impact of hyperglycemia on the development of diabetic arthropathy we analyzed the spine mobility in children with diabetes, according to the status of glycaemic control (Table 3).

The analysis showed that there was no violation of the state of spinal mobility with ideal and optimal glycemic control in patients with diabetes. At the same time lack of compensation for the disease was accompanied by decrease of mobility of all regions of the spine. The most significant deviations from normative indicators were determined in patients with glycemic control with a high...
We observed a decrease in blood serum vitamin D levels, which is progressing with the increase of illness duration. The variation diagram of vitamin D amount in blood serum in investigated groups is given in Fig. 1.

As it is shown in Fig. 1, there was wide variation in levels of vitamin D (26.0–42.0 ng/ml) in blood serum of children with diabetes. The highest variability in the content of vitamin D in the blood serum was detected in the group of patients with a duration of diabetes up to 1 year, concentration fluctuated within 28.0–42.0 ng/ml. The range of 25(OH)D values of the control group was 28.0–35.0 ng/ml. The individual analyses showed that in the first year of the disease, vitamin D deficiency was only 10 %. At that time, in group 2 in 50 % of children, and in group 3 in 80 % of children there was a decrease in vitamin D level (P < 0.05).

We have analyzed the relationship between the state of general spinal mobility and the level of vitamin D provision (Fig. 2). As a result, the data obtained showed that in children with diabetes mellitus, an insufficient level of vitamin D provision was accompanied by a deterioration in the state of general spinal mobility (Fig. 2).

As shown in Fig. 2, in patients whose vitamin D content was in the range of 30–100 ng/ml, the Thomayer test did not differ from the data obtained in the children of the control group, and was 1.0 [0.0; 3.0] cm (P > 0.05) in both groups. At the same time, children who were found to be deficient in vitamin D had a worsening of the overall mobility of the spine and showed a statistically significant increase in the Thomayer test to 5.0 [3.0; 6.0] cm (P < 0.05). Thus, the total mobility of the spine depended on the level of vitamin D, which was confirmed by the inverse correlation between its content in the serum and Thomayer test (r = -0.38, P < 0.05). There was an inverse correlation between the content of vitamin D in the blood serum and glycated hemoglobin (r = -0.41, P < 0.05). Low values of vitamin D were inherent in children with glycemic control with a high risk for life.

The next stage of our work was the study of the content of periostin in the blood serum of children with diabetes mellitus (Table 4). Analysis of the data showed that the level of periostin in the blood serum of children with diabetes mellitus had a wide variation of values (8.0–225.0 ng/ml), but was statistically higher than its level in the control group (P < 0.05) regardless of the duration of the disease. It was conduct data analysis of the serum periostin content in patients with diabetes mellitus depending on the duration of the disease. A gradual increase with the progression of diabetes with the highest values in children with longer duration of diabetes was established (Fig. 3).

Given that both vitamin D and periostin are involved in bone metabolism [15], we examined the content of the latter in children with diabetes mellitus, depending on the level of vitamin D provision (Fig. 4). Visual analysis diagram of variation showed that children with low vitamin D supply had high serum periostin content and it was 140.00 [45.75; 177.75] ng/ml. At the same time, in children with diabetes with normal supply of vitamin D, the median concentration of serum periostin was 44.0 [27.0; 64.0] ng/ml (P < 0.05). However, it did not reach the control values (2.5 [1.3; 33.5] ng/ml, P < 0.05).
The obtained data were confirmed by the inverse correlation relationship of medium strength ($r = -0.36$, $P < 0.05$) between the level of periostin and the vitamin D content in the blood serum of children with diabetes mellitus.

**Discussion**

All data obtained has shown that a violation of the functional capabilities of the spine was observed, which was manifested by a decrease in mobility in all its regions in children with diabetes. The revealed changes were progressing in the dynamics of the disease and occurred against the background of lack of diabetes compensation, insufficiency of vitamin D and an increase in blood serum periostin.

It is known that bone is a dynamic system in which the remodeling processes continuously occur: formation and resorption of bone tissue. Provision of vitamin D influences the process of resorption. In case of insufficiency or deficiency of vitamin D there is a violation of bone homeostasis. In addition, it is believed that vitamin D affects glucose homeostasis by acting directly on β-cells and indirectly through calcium regulation, since insulin secretion depends on calcium [16]. Our findings also indicate an existing relationship between vitamin D and the state of glycemic control in patients with diabetes. Our findings are consistent with other studies, which demonstrated a significant improvement in glycemic control in the treatment of vitamin D deficiency in children and teenagers with diabetes [17].

Another marker of bone metabolism is periostin. It is expressed in bone by osteocytes and plays a key role in the regulation of osteoblast function and bone formation [15]. Our results show that periostin can be a marker of changes in the osteoarticular system and can be used as a diagnostic tool in the development of diabetic arthropathy. The results of our study show that one of the mechanisms for increasing level of periostin in diabetes mellitus is lack of vitamin D. Together, this leads to a violation of the functional state of the joints, in particular the spine.

**Conclusions**

1. Children with diabetes are characterized by a deterioration in the functional state of the spine in the form of reduced mobility in all its regions, which progresses with an increase in the disease duration. One of the mechanisms for the development of the revealed violations is poor compensation for diabetes and vitamin D deficiency.

2. The results of our study prove that it is necessary to determine the level of vitamin D in children with diabetes mellitus. It requires timely correction of the deficit in order to improve glycemic control and the prevention of violations of the bones and joints.

**Prospects for further research.** In the future, it is planned to study the condition of the joints of the upper and lower limbs in children with diabetes mellitus, and to determine the pathogenetic factors that influence the development of their changes.

**Funding**
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**Conflicts of interest:** authors have no conflict of interest to declare.
References


