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FEATURES OF THE BIOELEMENT STATUS OF CHILDREN AND ADOLESCENTS LIVING IN OIL AND GAS REGIONS

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In the context of intensive development of gas industry, environmental safety issues are becoming increasingly important. The high rates of gas production and the growth of its chemical processing have turned gas industry enterprises into a powerful source of environmental pollution, which poses a real threat to public health, contributes to an increase in morbidity and ecologically caused pathological conditions. The aim of the study was to study the mineralization of bone tissue in children with different levels of physical development, to determine the options for physical development, which could be the criteria for classifying children into groups at increased risk of osteopenia and indications for in-depth laboratory and instrumental examination. 519 adolescents aged 14-17 years were examined, of which 349 lived in the oil and gas region and 170 were the control group. Anthropometry and biochemical blood examination were performed to determine the parameters of bone metabolism (osteocalcin, calcium, phosphorus, PTH, P1NP, b-Crosslaps). As a result, it was revealed that the physical development and indicators of bone metabolism in children of the oil and gas region are lower than in the control group. The indicator characterizing the ratio of P1NP/b-Crosslaps processes, bone remodeling was almost 2 times lower in children of the main group (p=0.039), which may indicate a relative prevalence of resorptive processes over synthetic in bone tissue in children of the oil and gas region.

Key words: bone metabolism, teenagers, bone mineral density, osteopenia

Aktobe region is the leader of oil and gas production in Western Kazakhstan. The high rates of gas and oil production, the growth of their chemical processing have turned oil and gas extraction into powerful sources of environmental pollution, which poses a real threat to the health of the population, especially children, and contributes to a delay in its physical development [1, 2].

The physical development of children and adolescents is the growth and formation of the child's body, including the rates, stages and critical periods of its maturation, inherited characteristics, individual variability, maturity and connection with factors of the internal and external environment [2, 3]. The indicators of physical development are anthropometric data, the rate of their change in the process of growth, harmony of development, the ratio of calendar and biological age, constitutional features [4, 5]. In recent decades, there has been a tendency to a degradation of the indicators of physical development, especially in oil and gas regions [6, 7]. As a result, pathological changes in the nervous system may develop, as well as in the musculoskeletal system.

From the modern point of view, bone is a dynamic living tissue with high sensitivity to various regulatory mechanisms, as well as to endo- and exo-influences [8]. The process of precipitation and accumulation of minerals, i.e., mineralization of bone tissue, mostly depends on the structure and functional state of the bone matrix. The maximum increase in bone mass is observed in puberty, which more than doubles at the age of 10-17 years [9, 10]. Intensive growth in childhood with simultaneous remodeling creates a very special position for bone tissue, in which it is especially sensitive to adverse environmental influences. Decreased bone density, i.e. osteopenia, makes bone structures vulnerable and can ultimately lead to a loss of more than 5% of bone mass, i.e. osteoporosis [11, 12].

Osteopenic syndrome (ICD code 10 M89.9) does not pose a threat to life, but it is dangerous with a quiet asymptomatic course, which does not manifest itself clinically until the onset of complications [13, 14]. It is characterized by a progressive decrease in bone tissue mass and a decrease in its strength due to microarchitectonic disturbances, and is one of the most significant medical and social diseases [15]. It has now been proven that the origins of the development of osteopenia/osteoporosis are in childhood, especially in adolescence [6]. The prevalence of osteopenia/osteoporosis among children is characterized by a significant range of data from 5% to 59%, due to the lack of special diagnostic equipment [16, 17]. There is not enough information in the literature on the bone mineral density in adolescents living in ecologically unfavorable conditions, including oil and gas producing

regions. The complex use of laboratory diagnostic methods allows characterizing objectively the dynamic features of the metabolic state of bone tissue.

Laboratory diagnosis of osteodeficiency in most cases is based on the determination of indicators, the study of markers of bone origin, which could be used to diagnose osteopenia/ osteoporosis, clarify its genesis [17, 18, 19].

Identification, accounting and correction of factors that disrupt bone mineralization in children can significantly reduce the incidence of the musculoskeletal system in children, control growth processes and reduce the likelihood of developing osteoporosis in the future. At the same time, there are still no reliable, substantiated and easily determined criteria for classifying children into groups of increased and high risk of osteopenia and failure to achieve peak bone mass.

In this regard, the purpose of this study was to study the mineralization of bone tissue in children with different levels of physical development, to determine the options for physical development, which could be the criteria for assigning children to groups of increased risk of osteopenia and indications for in-depth laboratory and instrumental examination.

MATERIALS AND METHODS

519 adolescents aged 14-17 years were examined, of which 349 were included in the main group (186 boys and 163 girls) and 170 in the control (89 boys and 81 girls) groups.

The children of the main group lived in the village of Kenkiyak, Temir district of the Aktobe region of Kazakhstan, where an oil field has been developed since 1959. As a control group, children living in the village of Kobda, an environmentally friendly area, where there are no oil and gas enterprises, were examined.

Inclusion criteria: adolescent children living in the survey area for at least 10 years or more; with informed consent to conduct research and process personal data, in accordance with the requirements of the Ethical committee of West Kazakhstan Medical University named after Marat Ospanov.

The exclusion criteria: the presence of acute and chronic inflammatory diseases from the examination program; autoimmune, hereditary and mental diseases.

To determine physical development, body length was measured in centimeters using a stadiometer, weight – in kilograms using a floor scale.

The indicators of the harmony of physical development in terms of body length and weight were determined using centile scales of nomograms proposed and tested by N.A. Matveeva and Yu. G. Kuzmichev. This method was developed on the basis of the centile method recommended by the WHO in the form of an international standard as a screening test to identify children 5-17 years old with developmental disabilities.

The indiactors of physical development according to centile scales are presented in a system of two coordinates, where the vertical indicates the body length (cm), and the horizontal indicates the body weight (kg).

One-dimensional age centile scales are plotted in parallel to each coordinate axis,: on the right scales for body length, above - for body weight. In the center there is a nomogram for assessing the correspondence of body weight to its length. Numbers 1-8 on scales and nomograms indicate centile intervals. The average values of length and body weight, limited at the 4th and 5th centile intervals, are shaded; the medians (50^{th} centiles) are marked with a dotted line.

Body length was assessed using one-dimensional centile scales. For this, the value of the child's body length was found on the ordinate axis. From this point, the perpendicular was restored to its intersection with the age scale of body length located in the right margin of the figures.

The indicators that fell into the 4-5^{th} intervals were characterized as average, in the 3^{rd} – low, in the 2^{nd} – low, in the 1^{st} – very low, 6^{th} – increased, in the 7^{th} – high, in 8^{th} – very high.

Body weight was assessed using age centile scales located in the upper field of the figures and nomograms in which centile body weight intervals are presented per unit of body length (weight index/body length).

The assessment of body weight by age centile scales was carried out similarly to the assessment of body length.

According to the nomograms proposed for use, the physical development of children was regarded as harmonious if the body weight corresponded to the 4-5 interval; disharmonious – when assessed by the 2-3^{rd} or 6-7^{th} intervals; sharply disharmonious – when assessed by the 1^{st} or 8^{th} centile interval of the nomogram.

In this regard, 3 groups of physical development were distinguished: normal physical development, risk, with deviations in physical development.

The concept of «normal physical development» corresponds to an average, decreased or

increased body length (3-6th intervals of the scale) and a harmonious ratio of length/body weight (4-5th intervals of the nomogram).

The concept of «risk group» for physical development included children:

• with low, high and very high body length (2,7,8th scale intervals) with harmonious development;

• with disharmonious physical development due to deficiency or excess body weight (2-3rd or 6-7th intervals of nomograms) with a body length estimated within 2-8th intervals of the scale [20].

The group with disabilities in physical development corresponded to:

1. Very low body length (1st scale interval) at any body weight

2. Sharply disharmonious development due to body weight deficiency (1st interval of the nomogram) at any body length

3. Sharply disharmonious development due to excess body weight (8th interval of the nomogram) at any body length [21].

After the distribution of children into groups of physical development, a laboratory examination was carried out in 132 adolescents (main group 89, control group 43), the program of which included: determination of calcium, inorganic phosphorus, PTH, calcitonin, osteocalcin in blood serum. In order to assess the features of bone tissue remodeling, P1NP and β-Crosslaps were determined in blood serum.

The material of the study in both groups of observation was venous blood, which was placed in a sterile centrifuge tube without anticoagulants. The samples were frozen at a temperature of –75 °C. All samples were analyzed in duplicate in accordance with the requirements of the analysis.

To determine the concentration of P1NP, the method of electrochemiluminescence immunoassay, Cobas e601 (Roche) was used; β-Crosslaps – by immunoassay, Osteocalcin-electrochemiluminescence immunoassay «sandwich» 2-site immunoassay, specific for intact osteocalcin (1 – 49) and a fragment (1 – 43); Ca-colorimetric photometric method, P-colorimetric with ammonium molybdate; calcitonin – solid phase chemiluminescent enzyme immunoassay.
Statistical data processing was carried out using:

1) descriptive statistics of quantitative data in groups,

2) comparison of groups on a personal computer using MS Excel, EpiData database,

3) the licensed statistical program SAS 9.2.

The following indicators were calculated: mean, median, mode, standard error of the mean, standard deviation. A p level value <0.05 was considered statistically significant.

RESULTS AND DISCUSSION

The level and harmony of physical status according to the results of a comprehensive assessment of health status were determined in 519 adolescents in grades 7-11 (boys – 275, girls – 244). Of these, 349 (boys – 186, girls – 163) are schoolchildren of the main group (Kenkiyak) and 170 (boys – 89, girls – 81) adolescents in the control group (Kobdy).

The results of the examination for the level and harmony of physical development are presented in table 1.

The presented data indicate that normal physical development in the main group took place only in 48.4% of children, the remaining 51.6% were underweight or deficient in weight and height, 4% were overweight. All of them were classified as disharmonious development. At the same time, in 16 children, despite the fact that weight and height parameters corresponded to age norms, development was also disharmonious. In general, 43.8% of children had normal, harmonious development, 56.2% – disharmonious. Among children with disharmonious development, children with a lack of weight predominated, mainly boys (table 3).

In the comparison group, 68.8% of children had normal physical development, the remaining 31.2% were underweight or deficient in weight and height, and 4.7% were overweight. All these children were classified as disharmonious development, while only 4 children (2.4%), despite the fact that weight and height parameters corresponded to age norms, development was also disharmonious. On the whole, 66.5% of children had normal, harmonious development, 33.5% – disharmonious.

Thus, in the main group of children living in the oil and gas region, their physical development is much worse than in the control group. 56.2% had a disharmonious development.

In recent years, more and more attention has been paid to laboratory research methods that allow a quick and accurate assessment of bone metabolism.

It has been proven that biochemical markers allow early diagnosis of signs of bone loss and thereby predict the risk of fractures; the in formativeness of markers was revealed for assessing the effectiveness of various methods of preventing osteoporosis. The reference values of the indicators can differ significantly depending on

many factors: the method and equipment used, ethnicity, age, sex, anthropometric, behavioral and other parameters of the patient, etc. [22].

Table 3 shows the indicators of bone tissue metabolism in children living in the oil and gas region and in the control group (table 3).

Osteocalcin (OC) is synthesized by osteoblasts and is the most abundant non-collagenous protein in the bone matrix, specific to bone tissue and dentin. OC is considered as one of the most informative biochemical markers of bone formation and the rate of "bone turnover".

The study revealed that the concentration of osteocalcin in the blood of children from the oil and gas region, when compared with the control group, was significantly reduced ($p < 0.05$) (fig. 1).

PTH is a powerful regulator of Ca homeostasis, a stimulator of bone resorption. It slows down the excretion of Ca in the urine and indirectly promotes its absorption in the intestine. Its effect on the P level is characterized by the opposite effect. The effects of PTH are opposite to the action of calcitonin - it reduces the level of calcium, bone resorption, and reduces the reabsorption of Ca and P in the kidneys. PTH indicators of the study group compared with the control group are presented (figure 2).

Figure 2 shows that PTH values are reduced compared to the comparison group.

Calcium and phosphorus are microelements, their main role in maintaining the structural basis of the body. The optimal ratio of calcium to phosphorus intake is 2: 1. The blood calcium and phosphorus levels in the compared regions do not differ significantly.

Calcitonin is a single-chain polypeptide hormone of 32 amino acids. The N-terminal disulfide bridge between the cysteine residues at positions 1 and 7 creates a ring structure of 7 amino acids, and there is also a C-terminal amidated proline [23]. The physiological effects of calcitonin are known to occur via receptor-mediated processes, and interactions involving the N-terminal ring and the C-terminal end appear to be involved in receptor binding and signal transduction [23, 24]. Also, there were no significant differences in the studied regions.

It is known that the intensive production of bone mass in childhood is provided by increasing the synthesis of bone matrix. A reflection of this process is the level of the total aminoterminal propeptide of the first type of procollagen-P1NP, which is formed during the formation of bone tissue by osteoblasts and fibroblasts from which collagen type 1 is subsequently formed, and is a marker of bone tissue formation. As a result of the study, it was found that in children of the oil and gas region, the serum P1NP level is lower than in children of the control group ($p=0.0156$) (fig. 3).

The study group of adolescents also showed a decrease in the level of β-Crosslaps (a degradation product of type 1 collagen, which makes up more than 90% of the organic matrix of the bone), compared with the control group, which indicates a violation of mineral metabolism due to the prevalence of resorptive processes ($p = 0.039$) in bone tissue (fig. 4)

Thus, the optimization of the diagnosis of osteodeficiency, along with instrumental studies, undoubtedly requires an additional assessment of the state of bone metabolism [17].

CONCLUSION

1. Physical development of children in the oil and gas region is lower compared to the control group. The children are significantly more often have disharmonious physical development in the form of a deficiency in body weight and a decrease in average growth rates.

2. Indicators of bone metabolism, such as: osteocalcin, PTH in children of the oil and gas region, are reduced, when compared with the control group.

3. The levels of calcium and phosphorus in the blood serum in the comparative aspect are not changed.

4. The indicator characterizing the ratio of the processes P1NP / -Crosslaps, bone remodeling was almost 2 times lower in children of the main group ($p = 0.039$). It may indicate a relative prevalence of resorptive processes over synthetic in bone tissue in children of the oil and gas region, especially groups of 16-18 years old, which indicates a weakening of the activity of bone tissue remodeling, which may be due to impaired regulation of mineral metabolism.

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Table 1 – The level and harmony of physical development of adolescents in the main group

Sex/n	Normal harmonious abs./ comp.	Normal disharmonious abs./comp.	Hyposomy abs./comp.	Hypersomy abs./comp.	Distrophy abs./ comp.
Boys n-186	73-39,2%	10-5,4%	20-10,8%	7-3,8%	76-40,8%
Girls n-163	80-49,1%	6-3,7%	12-7,4%	7-4,3%	58-35,5%
Overall n-349	153-43,8%	16-4,6%	32-9,2%	14-4%	134-38,4%

Table 2 – The level and harmony of physical development of adolescents in the control group

Sex/ n	Normal harmonious abs./ comp.	Normal disharmonious abs./comp.	Hyposomy abs./comp.	Hypersomy abs./comp.	Distrophy abs./comp.
Boys n-89	65-73,0%	1-1,1%	9-10,1%	4-4,5%	10-11,2%
Girls n-81	48-59,2%	3-3,7%	13-16,1%	4-4,3%	13-16,0%
Overall n-170	113-66,5%	4-2,4%	22-12,9%	8-4,7%	23-13,5%

Table 3 – Indicators of bone tissue metabolism in children living in the oil and gas region and in the control group

Laboratory indicator	Control group	Oil and gas region
Osteocalcin,ng/ml	73,19± 37,154	65,445±37,984
Parathyroid hormone, pg/ml	3,17± 0,999	3,444±1,159
Calcium	2,37±0,2647	2,327±0,0714
calcitonin, pg/ml	2,20 ± 1,720	2,345±1,493
Phosphorus	9-15,4%	11-25,6%
Beta-Cross laps,ng/l	1,46± 0,684	1,426± 0,871
P1NP, ng/ml	541,38± 34,216	516,071± 35,795

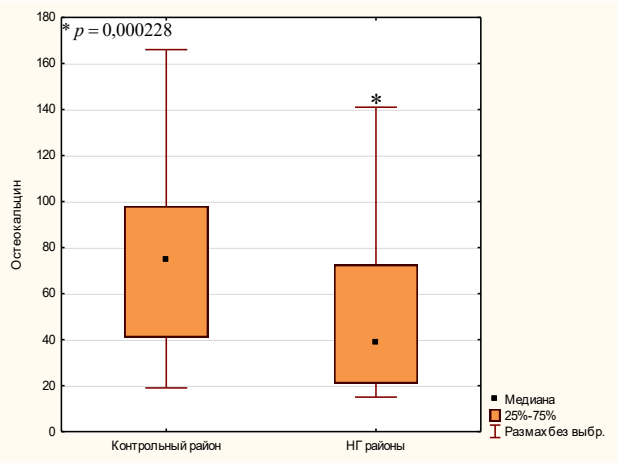

Figure 1 – Osteocalcin concentration in the blood of children from the oil and gas region in comparison with the control group

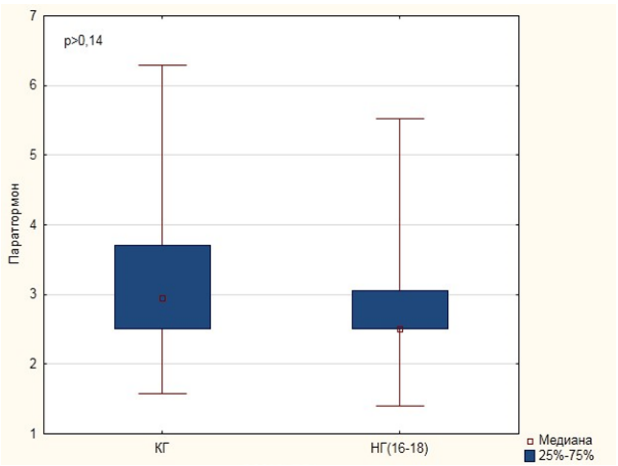

Figure 2 – Parathyroid hormone indicators in the main and control groupsф

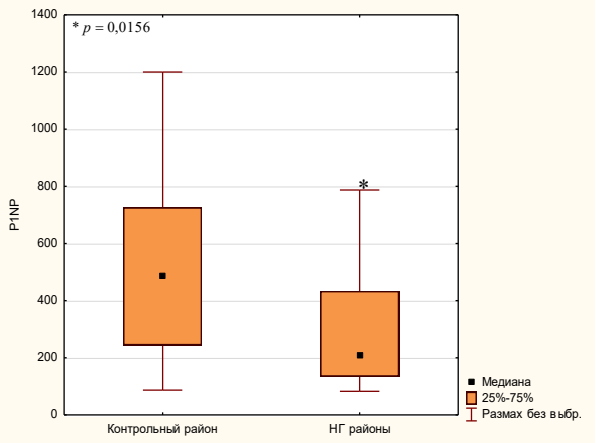

Figure 2 – Parathyroid hormone indicators in the main and control groups

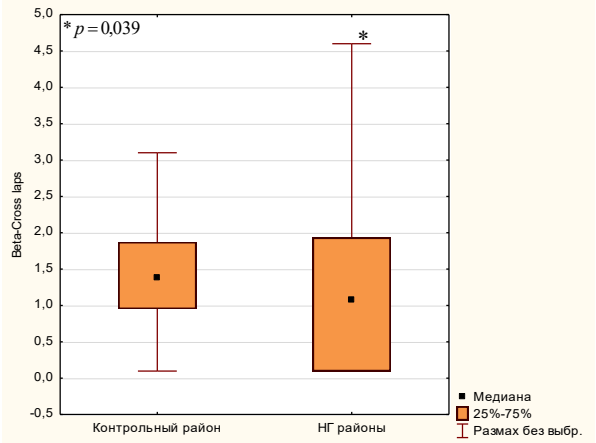

Figure 3 – Level of P1NP among children of main and control groups

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ОСОБЕННОСТИ БИОЭЛЕМЕНТНОГО СТАТУСА ДЕТЕЙ И ПОДРОСТКОВ, ПРОЖИВАЮЩИХ В НЕФТЕГАЗОНОСНЫХ РЕГИОНАХ

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В условиях интенсивной разработки газовых месторождений вопросы экологической безопасности приобретают все большее значение. Высокие темпы добычи газа и рост его химической переработки превратили предприятия газовой отрасли в мощный источник загрязнения окружающей среды, что представляет реальную угрозу для здоровья населения, способствует росту заболеваемости и экологически обусловленных патологических состояний. Цель исследования - изучение минерализации костной ткани у детей с разным уровнем физического развития, определение вариантов физического развития, которые могли бы являться критериями отнесения детей к группам повышенного риска развития остеопении и показаниями к проведению углубленного лабораторного и инструментального обследования. Обследовано 519 подростков в возрасте 14-17 лет, из них 349 проживали в нефтегазоносном регионе и 170- контрольная группа. Проводились антропометрия и биохимическое обследование крови для определения показателей костного обмена (остеокальцин, кальций, фосфор, ПТГ, P1NP,b-Crosslaps). В результате было выявлено: что физическое развитие и показатели костного метаболизма у детей нефтегазоносного региона ниже по сравнению с контрольной группой. Показатель, характеризующий соотношение процессов P1NP/b-Crosslaps, костного ремоделирования оказался практически в 2 раза ниже у детей основной группы (p = 0,039), что может свидетельствовать об относительном превалировании резорбтивных процессов над синтетическими в костной ткани у детей нефтегазоносного региона.

Ключевые слова: костный метаболизм, подростки, минеральная плотность костной ткани, остеопения

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МҰНАЙ-ГАЗДЫ АЙМАҚТАРДА ТҰРҒАН БАЛАЛАР МЕН ЖАСӨСПІРІМДЕРДІҢ БИОЭЛЕМЕНТТІК МӘРТЕБЕСІНІҢ ЕРЕКШЕЛІКТЕРІ

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Газ кен орындарын қарқынды игеру жағдайында экологиялық қауіпсіздік мәселелері күн өткен сайын маңызды бола түсуде. Газ өндірудің жоғары қарқыны және оны химиялық өңдеудің өсуі газ саласы кәсіпорындарын қоршаған ортаның ластануының қуатты көзіне айналдырды, бұл халықтың денсаулығына нақты

қауіп төндіреді, аурушаңдықтың жоғарылауына және экологиялық себеп болған патологиялық жағдайлардың өсуіне ықпал етеді. Зерттеудің мақсаты әр түрлі дене даму деңгейіндегі балалардағы сүйек тіндерінің минералдануын зерттеу, остеопенияның даму қаупі жоғары топтарға балаларды жіктеу критерийлері бола алатын физикалық даму нұсқаларын анықтау және оларды әрі қарай терең зертханалық-аспаптық зерттеу жүргізуге көрсеткішті анықтау. 14-17 жас аралығындағы 519 жасөспірім тексерілді, оның 349-ы мұнай-газ аймағында тұрады, 170-і бақылау тобы. Сүйек метаболизмінің параметрлерін анықтау үшін антропометрия және биохимиялық қан анализі жүргізілді (остеокальцин, кальций, фосфор, PTH, P1NP, b-Crosslaps). Нәтижесінде мұнай-газ аймағындағы балалардағы физикалық даму және сүйек метаболизмі көрсеткіштері бақылау тобына қарағанда төмен екендігі анықталды. P1NP/b-Crosslaps, сүйектерді қайта құру процестерінің арақатынасын сипаттайтын индикатор негізгі топ балаларында шамамен 2 есе төмен болды (p=0,039), бұл мұнай-газ аймағында тұратын балалардың сүйек тініндегі резорбтивті процестердің, синтетикалыққа қарағанда салыстырмалы басым екендігін көрсете алады.

Кілт сөздер: сүйектің метаболизмі, жасөспірімдер, сүйектің минералды тығыздығы, остеопения