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VITAMIN D3 IN TREATMENT OF OSTEOPENIC SYNDROME IN CHILDREN WITH GROWTH DISORDERS

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Background. *The efficacy of vitamin D3 agents for impaired growth of children of different cause was studied in the research. A positive effect on bone mineralization and calcium-phosphorus metabolism was evidenced. The treatment and prophylaxis charts using this drug for osteopenic syndrome are developed for children with hypothalamic-pituitary dwarfism, subdwarfism and dwarfism of constitutional genesis.*

Objective. *The aim of the research is to study the effect of calcimine and vitamin D3 in cases of impaired bone mineral density in children aged 6-18 years old with growth retardation of the hypothalamic-pituitary genesis, subdwarfism and dwarfism of constitutional origin.*

Methods. *The study involved 25 children, aged 6-18 years old with growth retardation: hypothalamic-pituitary (10 children), subdwarfism (5 children) and dwarfism of constitutional origin (10 children). The control group consisted of 20 children. The structural and functional state of bone tissue was studied using a two-photon X-ray densitometer "Lunar". In the study of calcium-phosphorus homeostasis, the level of calcium and the level of phosphorus in the blood serum were determined. Serum alkaline phosphatase levels were also studied as a marker for bone formation.*

Results. *In the examined children, there was a significant calcium deficiency at the level of the vertebrae L1–L4. The calcium content in L1 was 72.8%, L2 – 75.7%, L3 – 81.2%, L4 – 80.1%, which significantly differed from bone density in healthy children of a similar age and body weight. It was also revealed that in children diagnosed with growth retardation of the pituitary genesis, bone rarefaction was diagnosed in 100% of cases, while with subdwarfism and dwarfism of constitutional genesis these indicators were 43% and 24%, respectively.*

Conclusions. *A differentiated choice of vitamin D3 treatment, depending on the degree of osteopenia in children, allows adjusting the calcium metabolism and preventing osteoporosis in children with stunted growth. Vitamin D3 in the complex treatment of osteoporosis in children with growth impairment of different genesis normalizes calcium-phosphorus homeostasis, which increases bone mineral density and, therefore, reduces osteoporotic changes by stopping leaching of calcium from bones.*

KEYWORDS: bone mineralization; calcium-phosphorus metabolism; dwarfism; vitamin D3.

Introduction

Violation of the density and structure of bone tissue in childhood is caused by damage to the hypothalamic-pituitary system. Normally, restructuring of bone tissue is characterized by the advantage of bone formation over resorption until reaching the "peak of bone mass". Then insufficient somatotropic function of the pituitary gland causes delayed bone development: ossification nuclei develop with a significant delay and growth zones are open for a long time or close only in adulthood [1, 2]. This causes changes in bone density and impaired mineral metabolism in children with growth retardation. The situation is aggravated by the fact that the average alimentary daily vitamin D3 supply for children is more than 1.5 times less than required. To a large extent, this is due to the insufficient amount of foods containing calcium in the diet of children, socio-economic factors, as well as diverse information about the norms of daily calcium intake. However, endocrinological disorders accompanying growth retardation and a decrease in bone density with impaired mineral metabolism are crucial in this metabolic imbalance. The non-controllable intake of medications also affects, above all the complexes of microelements in the multivitamin compounds or individual preparations, i.e. magnesium, as its increase in the blood causes decreased calcium absorption. Environmental factors are also important, for example, strontium in the ter-

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ritories contaminated with radionuclides, entering the child's body acts as a calcium antagonist. Iodine deficiency territories also have negative impact not only in the formation of calcium-phosphorus homeostasis, but also in the disharmony of physical development, in particular, delayed sexual development, which due to hormonal imbalance affects the level of calcium absorption and osteogenesis. The aim of the study was to study the effect of vitamin D3 on changes in bone mineral density in children with growth retardation of hypothalamic-pituitary genesis, subdwarfism and dwarfism of constitutional genesis.

Methods

25 children aged 6-18 years old with growth retardation of hypothalamic-pituitary genesis (10 children), subdwarfism (5) and dwarfism of constitutional genesis (10) were exemined. The control group consisted of 20 children. When collecting a history of children with osteoporosis it was established that glucocorticosteroids, anticonvulsants, chemotherapeutic substances, antibiotics (tetracyclines, cyclosporins), antacids were administered. There were also: prematurity, fetal hypoxia, malnutrition, placental pathology, multiple pregnancy, short time between births, chronic diseases of women, drugs and alcohol, smoking during childbirth. The study of the structural and functional state of the bone tissue was carried out using a two-photon X-ray densitometer "Lunar". The following parameters were used for the study: Age Matched, % – the percentage deviation of bone mineral density (BMD) in the patient, the average population indicator of the identical race, sex and age at the level of the lumbar vertebrae L1–L4; Age Matched, Z-criterion – standardized deviation from the same indicator. When analyzing the results obtained, we used reference data on the indicators of the structural and functional state of the skeletal system in children and adolescents according to V.V. Povoroznyuka et al. Statistical analysis was performed using the Microsoft Excel and Statistica 5.0 software packages. In the study of calcium-phosphorus homeostasis, the level of calcium in the blood serum was determined using titrometric and photometric methods; the level of phosphorus in the blood serum was determined using a unified method for the reduction of phosphorus. The level of alkaline phosphatase in blood serum as a marker of bone formation was also studied by a biochemical method.

Results

In the examined children, there was a significant calcium deficiency at the level of the L1–L4 vertebrae. The calcium content in L1 was 72.8%, L2 – 75.7%, L3 – 81.2%, L4 – 80.1%, which significantly differed from bone density in healthy children of a similar age and body weight. It was also revealed that in children diagnosed with growth retardation of pituitary genesis bone loss was diagnosed in 100% of cases, while with subdwarfism and dwarfism of constitutional genesis these indicators were 43% and 24%, respectively, according to the deviation (standardized deviation of the bone tissue strength index of the average population index of the Z-criterion) and the classification of osteopenia and osteoporosis in children and adolescents by A.P. Krys-Pugach [3]. Three degrees of osteopenia were identified at the L1–L4 vertebrae. It was at the first step 1.0-1.5; the second and third, respectively, 1.6-2.0; 2.1-2.5. These children had a tendency to hypocalcemia and to increase in alkaline phosphatase levels. Thus, the content of the trace element calcium in the blood was reduced and fluctuated within 1.76-2.09 mmol/L. The analysis of the level of alkaline phosphatase in the blood as a marker of bone formation showed that its content was 1.54±0.09 μmol/g/L that also indicated bone loss. When comparing the activity of alkaline phosphatase and the concentration of calcium in the blood serum, it was assumed that hypocalcemia under such conditions contribute to further leaching of calcium from the bone tissue. Therefore, creating a vicious circle, in the treatment of such children in addition to etiotropic hormonal treatment, drugs should be used for prevention of leaching of the calcium from the bones before balancing the composition of the diet, which is consistent with age-related requirements for phosphorus and calcium. Vitamin D3 in the form of the drug of Cholecalciferol increases the absorption of calcium in the intestine [4] and improves the reabsorption of phosphorus in the renal tubules, helps to maintain the proper level of calcium and phosphorus in the blood, helps to optimize calcium-phosphorus homeostasis and contributes to the normal formation and growth of bone tissue that is especially important for stunted growth in children. For grade 1 osteopenia, Cholecalciferol was prescribed in courses of 2000 IU per day for 30 days, 2 times a year with an interval of 5 months between courses. In case of degree 2 osteopenia, Cholecalciferol was prescribed in courses of

4000 IU per day for 40 days, 3 times a year with a break of 3 months between courses. In case of degree 3 osteopenia, Cholecalciferol was prescribed in courses of 5000 IU per day for 45 days, 3 times a year with a break of 3 months between courses. The effectiveness of treatment was assessed by repeated densitometric examination of the lumbar spine, 3 months after the first course of treatment, analyzing the Z-criterion. There was a tendency to an increase in the density of mineral tissue according to the Z-score by 4.34-20% in each of the lumbar vertebrae. The effectiveness of the treatment was assessed by the parameters of the content of calcium and phosphorus in the blood serum, the level of alkaline phosphatase during the second examination one month after the first course of treatment. Thus, normalization of the level of calcium and phosphorus, as well as a decrease in the level of alkaline phosphatase to the upper limit of the norm was evidenced (Table 1).

Table 1. Dynamics of blood biochemical parameters in a group of 25 children (M±m) after the introduction of Cholecalciferol into treatment

Index	Before treatment n=25	After treatment n=25	P
Serum calcium (mmol/L)	1.98±0.11	2.37±0.13	<0.05
Serum phosphorus (mmol/L)	0.93±0.05	1.1±0.06	<0.05

Discussion

The results of the study proved a positive effect of vitamin D3 in the children with decrease of growth of different genesis. According to the literature, growth hormone is one of the most important components of the hormonal system for regulating bone tissue metabolism and phosphorus-calcium metabolism. In norm the restructuring of bone tissue is characterized by the advantage of bone formation over resorption until reaching the "peak of bone mass". With insufficient somatotropic function of the pituitary gland bone development is delayed: ossification nuclei appear with a significant delay, and growth zones remain open for a long time or close only in adulthood. This causes changes in bone density and impaired mineral metabolism in children with growth retardation [1,2]. Cholecalciferol normalized the level of calcium and phosphorus as well as decreased the level of alkaline phosphatase to the upper limit of the norm that prevents osteoporosis and complies the results of studies by other authors [5, 6].

Conclusions

The differentiated approach in prescribing Cholecalciferol depending on the degree of osteopenia in children allows correcting calcium metabolism and thereby ensures prevention of osteoporosis in children with stunted growth. This is caused by the pharmacological action of cholecalciferol, i.e. regulation of calcium-phosphorus metabolism, normal formation of the bone skeleton and teeth in children and preservation of the structure of bones.

Conflicts of Interest

Author declare no conflict of interest

ЗАСТОСУВАННЯ ВІТАМІНУ D В ЛІКУВАННІ ОСТЕОПОРОЗУ У ДІТЕЙ З ЗАТРИМКОЮ РОСТУ РІЗНОГО ГЕНЕЗУ

Н.Ю. Щербатюк

ТЕРНОПІЛЬСЬКИЙ НАЦІОНАЛЬНИЙ МЕДИЧНИЙ УНІВЕРСИТЕТ ІМЕНІ І. Я. ГОРБАЧЕВСЬКОГО МОЗ УКРАЇНИ, ТЕРНОПІЛЬ, УКРАЇНА

Вступ. *У статті наводяться результати застосування препаратів вітаміну D у дітей із затримкою росту різного ґенезу. Продемонстровано їх позитивний вплив на мінеральну щільність кісткової тканини та кальцій-фосфорний гомеостаз. Наводяться схеми лікування та профілактики остеопенічного синдрому у дітей з гіпоталамо-гіпофізарним нанізмом, субнанізмом та нанізмом аліментарно-конституційного ґенезу. Доведено ефективність їх використання.*

Мета – *дослідження впливу використання вітаміну D при змінах мінеральної щільності кісткової тканини у дітей 6-18 років із затримкою росту гіпоталамо-гіпофізарного генезу, субнанізмом та нанізмом конституційного ґенезу.*

Методи. *Обстежено 25 дітей 6-18 років із затримкою росту гіпоталамо-гіпофізарного ґенезу (10 дітей), субнанізмом (5) та нанізмом конституційного ґенезу (10). Контрольну групу становили 20 дітей. Дослідження структурно-функціонального стану кісткової тканини проводили за допомогою рентгенівського двофотонного денситометра "Lunar". При дослідженні кальцій-фосфорного гомеостазу визначали рівень кальцію та рівень фосфору у сироватці крові. Також вивчали рівень лужної фосфатази у сироватці крові як маркера формування кістки.*

Результати. *У обстежених дітей мав місце суттєвий дефіцит кальцію на рівні хребців L1–L4. Вміст кальцію в L1 становив – 72,8%, L2 – 75,7%, L3 – 81,2%, L4 – 80,1%, що суттєво відрізняється від кісткової щільності у здорових дітей аналогічного віку та маси тіла. Також було виявлено, що у дітей, яким було виставлено діагноз затримки зростання гіпофізарного ґенезу у 100% випадків діагностовано розрідження кісткової тканини, тоді як при субнанізмі та нанізмі конституційного ґенезу ці показники становили відповідно 43% та 24%.*

Висновки. *Диференційований підхід у призначенні вітаміну D залежно від ступеня остеопенії у дітей дозволяє скоригувати кальцієвий обмін та забезпечити тим самим профілактику остеопорозу у дітей із затримкою росту. Включення вітаміну D у комплексне лікування остеопорозу у дітей із затримкою росту різного генезу нормалізує кальцій-фосфорний гомеостаз, що сприяє посиленню мінеральної щільності кісткової тканини, а отже, зменшує остеопорозні зміни за рахунок припинення вимивання кальцію з кісток.*

КЛЮЧОВІ СЛОВА: мінеральна щільність кісткової тканини; кальцій-фосфорний гомеостаз; затримка росту; вітамін D3.

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