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Original Article

Disorders of the mineral exchange and metabolism of bone tissue as a pathogenetic basis of physical rehabilitation patients with coxartarosis

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Abstract:
Purpose. The percent of disabled people due to the coxarthrosis of different genesis is varied between 20% and 30% among incapacitated patients, suffered from joints diseases. *Material:* Aim of the study**:** to identify the peculiarities of a bone remodeling in relation to the mineral metabolism at the patients with coxarthrosis, including the gender and hormonal adjustment. The study is based on the analysis biochemical parameters in the serum of 57 patients, suffering from coxarthrosis I-II stages. Assessment of the metabolic function of a bone tissue included analysis of mineral homeostasis. *Results:* The analysis of macroelement metabolism revealed a decreased level of both total calcium fraction on 9.5% and its ionized form on 6.2%. In the women, deficiency of total calcium was observed in 1.9 times more often than in the men, its level was lower on 5.8%.
At women in the perimenopausal of climacteric period, ionized calcium deficiency was on 6.0% lower than in the postmenopausal period. Increasing of calcium excretion in urine at the women occurred in 1.8 times more often (94.4%) than at the men (52.4%). Calcium deficiency was accompanied by increase of phosphorus on 24.4%. In the women, these changes were observed twice often than in the men, and phosphorus content was higher on 13.5%. In the perimenopausal period at women, level of phosphorus was higher on 8.7% than in the postmenopausal climacteric period. The results show that negative bone balance and disorders in the mineral metabolism as a whole are interrelated process. *Conclusions:* Coxarthrosis in the initial stages of development is accompanied by a negative bone balance more than in half of women and a third part of men. Deepening of a calcium-phosphorus imbalance, magnitude changes in magnesium content and decreasing of a bone formation in women increases in the perimenopausal period of hormonal restructuring.
Key words: coxarthrosis, mineral metabolism, remodeling of a bone tissue, gender differences.

Introduction.

In Ukraine are registered annually up to 350,000 cases primary diseases of joints, among it there is more than 60% concerned to the persons of working age, about 11% of patients with degenerative-dystrophic diseases of joints remain disabled [Kovalenko V.M. (2012), Kovalenko V.N., & Bortkevich O.P., (2005)]. The average primary disability in 2011 due to osteoarthritis (OA) was about 1.5 cases per 10 thousand adults [Kovalenko V.M. (2012)]. Among all forms of OA, more than 40% are coxarthrosis, which in the general structure of joint pathology consistently occupy the second place after gonarthrosis by a frequency of morbidity and the first place – by the terms of temporary and persistent disability [Popova L.A., &. Sazonova N.V, &. Volokitina E.A. (2006), Chabra S.,& Foucher K. (2013)].

Prolonged and slowly progressing course of coxarthrosis, presence of persistent chronic pain syndrome is significantly reduces quality of life of the patients [Kovalenko V.M. (2012), Bossmann T., & Kirchberger I., & Glaessel A, & Stucki G.]. The percent of disabled people due to the coxarthrosis of different genesis is varied from 20 to 30% among incapacitated patients, suffered from joints diseases [Popova L.A., &. Sazonova N.V, &. Volokitina E.A. (2006). , Chabra S.,& Foucher K. (2013)].

At the present stage of development the rehabilitation technologies for the prevention of disability due to a coxarthrosis, methods of physical rehabilitation are not effective enough, which is negatively affects on the quality of life this contingent of patients, leading to the domestic, social and professional disintegration [Kovalenko V.N., & Bortkevich O.P., (2005), Fransen M.,& McConnell S., & Hernandez-Molina G., & Reichenbach S. (2014).]. Lack of persistent effect is most often associated with incomplete examination and

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insufficient consideration of pathogenetic factors of disease progression. An analysis of the current scientific literature on this issue suggests that majority of the research over the last 10 years is focused on the determining an impact of biomechanical factors on the origin and progression of coxarthrosis. In particular, unfortunately a balance of the osteotropic elements is not taken into account. Although it is known that violation of the mineral composition of a bone tissue is one of the leading factors in a progression of coxarthrosis, which leads to the disability of patients.

Biochemical markers of a bone remodeling are very important in the diagnosis of bone metabolism. Primary, bone remodeling processes are directly dependent on the mineral metabolism, in particular, a calcium-phosphorus-magnesium homeostasis [Gerk S. A. , & Golovanova O. A., (2015), Gromova O. A., & Kalacheva A. G., &. Torshin I. Yu., &. Grustlivaya N. V. [et al.]. (2014), Baaij J. H., & Hoenderop G. ,& R. J.Bindels (2015)]. However, the data towards the relationship of minerals with remodeling in a case of coxarthrosis are controversial [Karyakina E.V. &. Persova E. A. (2009), . Brodziak-Dopierała B., &. Kwapuli´nski J , & Sobczyk K,& Wiechuła D. (2013)., Okano K.,& Aoyagi K., & Enomoto H., & Osaki M. [et al.], (2014).].

According to the classical notions, the basic macronutrients of bone are calcium, phosphorus, magnesium [Gerk S. A. , & Golovanova O. A., (2015), Gromova O. A., & Kalacheva A. G., &. Torshin I. Yu., &. Grustlivaya N. V. [et al.]. (2014), Baaij J. H., & Hoenderop G. ,& R. J.Bindels (2015).].

Aim of the study: to identify the peculiarities of a bone remodeling in relation to the mineral metabolism at the patients with coxarthrosis, including the gender and hormonal adjustment.

Material and methods.

The study is based on the analysis of biochemical parameters in a blood serum on 57 patients in the I-II stages of coxarthrosis by Kellgren-Lowrence. Patients' age is ranged from 31 to 65 (50.2 ± 1.2) years, women were predominated by gender – 63.2%. The intensity of pain syndrome and degree of functional insufficiency were determined by the algofunctional index WOMAC (Western Ontario and McMaster Universities Arthrose index) with using a visual analog scale (VAS) [Fransen M.,& McConnell S., & Hernandez-Molina G., & Reichenbach S. (2014).]. Assessment of a bone metabolic function included the analysis of mineral homeostasis by a level of phosphorus and magnesium in the peripheral blood, total calcium and its ionized form (Ca ++), an amount of urinary excretion of calcium. The processes of a bone formation were analyzed by the content of bone isoenzyme of alkaline phosphatase (KLF), bone resorption was assessed by the level of tartrate-resistant acid phosphatase (TrKF). The results of biochemical studies were compared with indicators of 25 people at the age (52.6±2.2) years, who did not have a pathology of musculoskeletal system, by the indicators of clinical and laboratory studies. The following people were considered to be healthy. Statistical analysis results of the study were carried out by methods of variational statistics, using the standard package of applications SPSS 13.0 for Windows. Pearson correlation analysis was performed.

Results.

Being interviewed, all patients complained of the morning and "start" pain, as well as pain when walking on a rough terrain, standing and climbing stairs, which was rated as a joint pain syndrome, intensity of which on VAS scale was (59.5±1.2) mm. All patients had also a syndrome of functional insufficiency of the hip joint, severity of which on a scale of VAS was (44.7 ± 1.1) mm. Character of the manifestations of this syndrome is presented in Fig. 1.

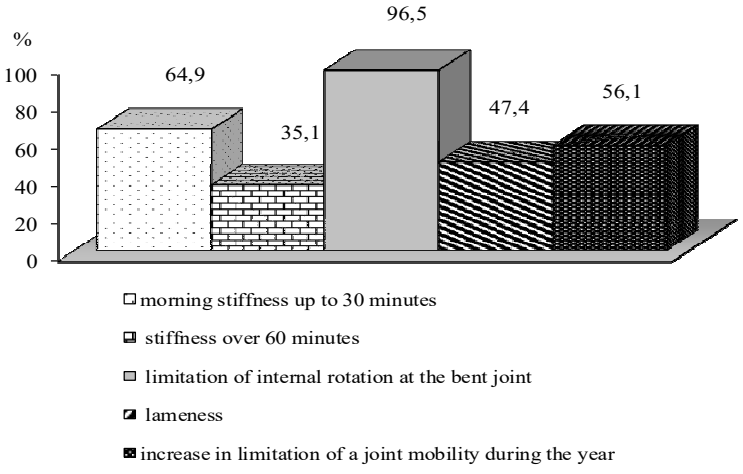

Fig. 1. Frequency and character of manifestations of the hip joint functional insufficiency syndrome..

The analysis of macroelement metabolism revealed a decreased level of both total calcium fractions on 9.5% ($p<0.001$) and its ionized form on 6.2% ($p<0.001$) (table 1). At the same time, the gender differences in changes of these indicators are identified. Thus, in women, deficiency of total calcium was observed in 1.9 times more often (72.2%) than in men (38.1%), and its level was lower on 5.8% ($p<0.05$). The level of physiologically active form of calcium-ionized fraction was also in 1.9 times lower in women (88.9%) than in men (47.6%), without the significant differences in actual rates ($p>0.05$).

Table 1

Indicators of mineral exchange in the examined patients

Indicator, units	Control (n=20)	General population (n=57)	Men (n=21)	Women (n=36)	P between men and women
total calcium of the blood, mmol / l	2.42± 0.03	2.19±0.03[3]	2.27±0.04[2]	2.14±0.04[3]	<0.05
Ca ++ of the blood, mmol / l	1.08± 0.02	0.99±0.01[3]	1.01±0.02[1]	0.98±0.01[3]	>0.05
phosphorus of the blood, mmol / l	0.96± 0.05	1.27±0.03[3]	1.15±0.06[1]	1.33±0.04[3]	<0.05
magnesium of the blood, mmol / l	0.91± 0.03	0.84±0.02	0.86±0.03	0.83±0.03	>0.05
calcium in the urine, mmol / day	2.92± 0.37	3.93±0.10[2]	3.76±0.17[1]	4.04±1.12	>0.05

Notes: [1]– $p<0.05$; [2] – $p<0.01$; [3]–$p<0.001$ – level of reliability the changes between indicators of the sick and healthy persons.

One of the factors, which shown an insufficiency of both total and ionized calcium was increased excretion of this microelement with urine and , respectively, content of which was increased on 25.7% ($p<0.01$).

In women, urinary calcium excretion was increased in 1.8 times more frequently (94.4%) than in men (52.4%) .

Calcium deficiency was accompanied by increase of phosphorus on 24.4% ($p<0.001$) (see table 1).

In women, these changes were observed twice as often (80.6%) than in men , and the phosphorus content was on 13.5% higher ($p<0.05$). Besides, in women which were in the perimenopause the level of phosphorus (1.49±0.02) mmol/l was on 8.7% higher, than in the postmenopausal climacteric period (1.36 ± 0.04) mmol/l ($p< 0.01$).

The mixed data have been obtained on the concentration of magnesium in the serum. Thus, if the average levels of this macronutrient did not significantly change, compared to the control values, then in a detailed analysis it was found that in 84.4% of women this indicator was reduced on 17.6%, consisting (0.75±0.01) mmol/l, ($p<0.001$), and in 15.6% of cases was observed its increasing on 23.5%, reaching (1.19±0.03) mmol/l ($p<0.001$). However, significant differences were found between women in the perimenopausal and postmenopausal periods. Thus, in the perimenopausal period, the level of magnesium was reduced in all women on 20.9% ($p<0.001$), consisting (0.72±0.01) mmol/l. In the postmenopausal period, changes in magnesium concentration were observed in 52.8% of patients. Among these patients, in 73.7% it was reduced on 14.3% ($p<0.001$) to (0.78±0.01) mmol/l, in 26.3% of cases this indicator increased on 23.5% ($p <0.001$) to (1.19±0.03) mmol /l.

Changes of magnesium in the serum were observed in men less frequently in twice (42.9%) than in women, but hypomagnesemia was predominant by the character of changes (88.9%), the same way as in women, with decreased concentration of magnesium on 18.7%, to (0.74±0.03) mmol/l. Hypermagnesemia occurred only in the isolated cases.

Magnesium level was negatively correlated with the intensity of pain syndrome by VAS scale and directly with the total calcium concentration and its ionized fraction.

Therefore, despite the ambiguity of changes in the magnesium content, they nevertheless indicate an imbalance in the process of bone remodeling, as it is well-known that the deficiency of this macronutrient indirectly indicates the loss of trabecular component of a bone mass, due to the reduced bioavailability of bone loss. Excess of magnesium content carried out to the osteoclast stimulation and dysfunction of a bone [Gerk S. A. , & Golovanova O. A., (2015), Gromova O. A., & Kalacheva A. G., &. Torshin I. Yu., &. Grustlivaya N. V. [et al.]. (2014)].

The revealed changes are indirectly indicated about the possibility of violations in the processes of a bone remodeling, so it became necessary to analyze the indices of a bone formation and resorption, characteristics of which are shown in the table 2.

According to the given data, activity of KLF was reduced on 7.6% by average indicators ($p<0.05$), in women – on 8.5%, compared with the control values ($p<0.05$). The activity of osteoblasts was associated with the total calcium content and its ionized fraction, as well as with magnesium concentration.

Table 2

Characteristics of the indicators a bone remodeling in the examined patients (M ± m)

Indicator, units	Control (n=20)	General population (n=57)	Men (n=21)	Women (n=36)	P between men and women
KLF, units / l	68.3± 2.2	63.1± 0.6[1]	64.0± 1.1	62.5± 0.8[1]	>0.05
TrKF, units	53.2± 2.4	58.1± 0.70[1]	56.6± 1.1	63.4± 0.3[2]	<0.001

Notes: [1]– $p < 0.05$; [2]– $p < 0.001$ – level of reliability the changes between indicators of the sick and healthy persons.

There were no significant differences in the incidence of osteoblast deficiency in men (33.3%) and women (58.3%). The level of decrease in KLF activity was not significantly dependent on the gender of the patients, but was more significant in women in the perimenopausal hormonal adjustment period .

With osteoblastic insufficiency, resorptive processes in a bone tissue increased), as evidenced by increased activity of TrKF on 8.7% ($p<0.05$). This was typically for women, among which TrKF hyperactivity with increased level on 16.1% was observed in 55.6% of cases ($p<0.001$). Moreover, in the perimenopausal period, level of this excess was on 4.5% higher than in the postmenopausal period, adding up accordingly (64.2±0.3) units and (61.4±0.5) units ($p<0.001$). Increase in absorption processes was observed in men almost twice less (28.6%) than in women, but this difference was not statistically significant, i.e. the level of increase TrKF activity was lower, than in women on 10.7% ($p<0.001$). The intensification of absorption processes occurred as well as the magnesium level in the serum was reduced. In general, it should be noted the unidirectional changes in a bone remodeling, characterized by insufficient bone formation with the increased resorption. The given results shown, that negative bone balance and disorders in the mineral metabolism as a whole are an interrelated process. The revealed differences should be taken into account in the pathogenetic substantiation and development an individual program of physical rehabilitation of patients with coxarthrosis.

Discussion.

In the recent scientific literature over the last decade, the issue of bone mineralization in a case of coxarthrosis has been actively discussed. In this case, various researchers express polar thoughts. According to some authors, demineralization is one of the pathogenetic factors for the rapid progression of this disease [2, 4], while others authors deny this fact [Okano K.,& Aoyagi K., & Enomoto H., & Osaki M. [et al.], (2014), Schneider D. L.,& Barrett-Connor E., & Morton D. J., & Weisman M. (2002)]. This polarity of thought may be related to the fact that the results obtained were related to the general population of patients without taking into account their age and gender characteristics, whereas these factors are very important for the construction of individual physical rehabilitation programs.

Gender and age characteristics of metabolic ability of a bone tissue in the pathology of musculoskeletal system devoted numerous studies. However, it is noted that the majority of these studies were performed in the patients with severe coxarthrosis who are vitally needed surgery [Karyakina E.V. &. Persova E. A. (2009), Kovalenko V.N., & Bortkevich O.P., (2005), . Rodionova L.V., & Dmitrieva L.A., & Taranenko E.N.. & Koshkareva Z. V. (2005). Brodziak-Dopierała B., &. Kwapuli´nski J , & Sobczyk K,& Wiechuła D. (2013)], whereas in the initial stages of the disease, which are the most promising for the effective use of rehabilitation programs, such studies were rarely conducted.

The interest in the mineral composition and processes of a bone remodeling in the degenerative-dystrophic diseases of the joints in connection with hormonal restructuring of women is quite clear, since the female population is most vulnerable to their development, as evidenced by numerous studies. However, most of them relate to the postmenopausal stage of the menopausal period, while its early stages remain virtually out of a limelight of researchers, requiring a careful study this aspect of the problem. Thus, our study confirmed that coxarthrosis is accompanied by a negative bone balance at the initial stages of development. But we have found that more than half of women and a third of men suffer from disorders of the calcium-phosphorus-magnesium metabolism, the main manifestations of which are deficiency of magnesium and calcium due to its increased excretion, with an excess content of phosphorus. Deepening of a calcium-phosphorus imbalance, magnitude changes in magnesium content and decreasing of a bone formation in women increases in the perimenopausal period of hormonal restructuring (Afanasiev S. (2017).).

Conclusions.

In the development of technologies for physical rehabilitation, insufficient attention is paid to the mineral metabolism and metabolic function of a bone tissue, taking into account gender characteristics of the patients with coxarthrosis and periods of hormonal restructuring of women. The answers to these questions are needed as a pathogenetic basis for the development of individualized physical rehabilitation programs.

Conflict of interest.

The authors declare no conflict of interest.

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