ISSN 2409-9988

Inter Collegas

Experientia docet

2021

N2(8)

INTER COLLEGAS

2021

Vol. 8 No.2

OFFICIAL JOURNAL OF
KHARKIV NATIONAL MEDICAL UNIVERSITY
ISSN 2409-9988

Recommended for publishing
by Scientific Council of Kharkiv National Medical University

24 – Jun.- 2021

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URL:
http://inter.knmu.edu.ua/pub

Periodicity:
4 times a year

CALCIUM-PHOSPHORUS RELATIONSHIPS IN THE COMBINED COURSE OF STABLE CORONARY HEART DISEASE IN PATIENTS WITH OBESITY

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https://doi.org/10.35339/ic.8.2.106–110

Abstract

The purpose of the study was to optimize the diagnosis and prediction of the development of structural and functional disorders of bone tissue in patients with SCHD and obesity. Thus, lipid profile analysis showed a clinically significant increase in total cholesterol and triglycerides in patients with SCHD. Serum bone mineral status did not exceed normal values, but serum total calcium levels were significantly higher in patients with SCHD and obesity compared to other groups. The indicators of calcium-phosphorus metabolism in the daily urine of patients with SCHD were significantly higher. When conducting densitometric studies in patients with SCHD with normal weight, osteopenic conditions were diagnosed more often than in patients with overweight and obesity. That is, the comorbid course of SCHD and obesity is a high risk of osteodeficiency, which is confirmed by early changes in calcium-phosphorus metabolism.

Keywords: *stable coronary heart disease, obesity, mineral metabolism, osteoporosis.*

Introduction

According to the European Association of Cardiologists, coronary heart disease (CHD) accounts for about 7.5 million deaths per year and in almost 75 %, lethal cases of stable coronary heart disease (SCHD) are registered in low- and middle-income countries [1, 2]. Although successful methods of diagnosis and treatment of various forms of SCHD have been developed so far, the lack of confirmation of a single theory of atherosclerosis, immature system of preventive measures and comorbid disease, does not significantly reduce the number of patients with SCHD. Besides, no less significant problem of modern society is obesity, which is rightly called the non-infectious epidemic of the 21st century [2]. According to the WHO statistics, the number of obese people has more than tripled since 1975 [3, 5, 6]. It has been established that among the adult population of Europe, obesity is the cause of SCHD in 35 % of cases [2, 4].

Comorbid pathology, namely, atherosclerosis as an etiological factor in development of coronary heart disease and obesity, leads to negative consequences, characterized by development of complications, among which there is the frequency and medical and social significance of structural and functional disorders of bone architecture [2–4]. But one of the positive aspects of obesity is considered to be its protective effect on development of osteoporosis (OP) [2]. This fact is denied in some scientific papers, but a number of clinical studies have shown a link between the degree of obesity, the manifestations of atherosclerosis and bone mineral density (BMD) [6].

There is an assumption that a certain similarity between the mechanisms of OP development and atherosclerosis is due to the processes that take place with the participation of mononuclear cells [2]. This structural unit in atherosclerosis is differentiated in the vascular wall into macrophage-like "foamy" cells, and in OP – in osteoclasts [5, 8, 9]. Hyperproduction of propulsive growth factors, which, in turn, induce bone resorption, also plays an important role in the development of atherosclerotic vascular lesions [2, 7, 10]. Histological similarity was also found between atherosclerotic plaque and bone tissue [11, 12]. In this case, it can assumed that the protective effect of adipose tissue in osteopenic conditions is a predictor of accelerated formation of athero-

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sclerotic plaques [2, 5]. This assumption became the scientific hypothesis of this study.

2. Purpose, subjects and methods:

2.1.The purpose was to optimize the diagnosis and prediction of development of structural and functional disorders of bone tissue in patients with SCHD and obesity.

2.2. Subjects & Methods

98 persons with SCHD (of them 79 with concomitant obesity -main group, 19 with normal weight -comparison group) were involved in the study. The mean age of patients in the main group was 52.4 ± 1.44 years, in the comparison group – 51.8 ± 1.94 years. The duration of SCHD history was 2.9 ± 1.2 and 2.4 ± 1.6 years, respectively. Gender ratios corresponded to the following: women predominated in both groups – 54.8 % and 52.9 %, respectively. Body mass index was calculated by Quetelet's index. The mean BMI was 31.87 ± 0.26 % in the main group and 23.8 ± 0.24 % in the comparison group. The control group included 20 healthy individuals of the same gender and age. At an earlier stage of the study, the data were published in scientific articles Pasiyeshvili L., Ivanova K. [2, 5].

This research was conducted in compliance with all relevant diagnostic and treatment standards of the requirements for the ethical component of clinical trials (GCP, 1997). Before the study, the patients were informed about the essence of the study, its purpose and possible results. All study participants provided written informed consent. This study was approved by the local ethics committee according to the recommendations of the ethical committees for biomedical research, Ukrainian legislation on health protection, the 2000 Helsinki Declaration and the directives of the European Partnership 86/609 on the participation of people in biomedical research [6].

The diagnoses of obesity and SCHD were verified the basis of unified clinical protocols of medical care "Obesity" and "Stable coronary heart disease" (WHO, 1997; Order of the Ministry of Health of Ukraine No. 152 dated 02.03.2016).

The state of bone mineral metabolism was assessed by the content of total and ionized calcium and serum phosphorus.

The indicators of lipid metabolism were determined by the content of total cholesterol (TC), low lipoprotein cholesterol (LLC), very low lipoprotein cholesterol (VLLC) and high density lipoprotein (HDL), triglycerides (TG) using standard test systems. The atherogenic index (AI) was calculated using the formula: AI = (TC – HDL) / HDL.

Bone mineral density was determined by X-ray dual-energy bone densitometry of the lumbar spine (DEXA-Dual-energy X-ray Absorbtiometry). Deviation of BMD from the normal values was determined by the value of the T-criterion (T-score), an indicator adopted by the WHO to verify osteopenic syndrome. T-test is the number of standard deviations from the mean peak of bone mass of a healthy population [2, 5].

T-test was calculated automatically using DEXA software and a database of BMD values of healthy age- and sex-matched individuals, downloaded into the memory of the device. The values of the T-test + 2.5 ... -1 standard deviation (SD) from the peak bone mass were considered normal indicators of BMD. Osteopenia included T-criteria -1 -2.5 standard deviations, osteoporosis – T-criteria -2.5 standard deviations and below [8, 13].

Prior to the examination, the patients did not receive therapy for osteoporotic conditions correction.

Exclusion criteria were acute coronary syndrome, chronic heart failure of functional class IV (NYHA) and other diseases accompanied by osteodeficiency (intestinal disease, diabetes, thyroid disease, etc.).

Statistical analysis was performed using the software package "Statistica 10.0".For quantitative characteristics, the results were presented as the median (Me) with an interquartile range [Q25 %; Q75 %] taking into account the lack of normal distribution [2, 5]. Quantitative and ordinal variables were compared using the Mann-Whitney criteria. In all procedures of statistical analysis, the significance level p was assumed to be equal to or less than 0.05.

3. Results & Discussion

The study of patients with SCHD allowed positioning of this category as a group of high cardiovascular risk. In addition to the traditional characteristics of this risk (age, high functional class of angina, the presence of chronic heart failure, various comorbid conditions), most patients in the main group were characterized by the absence of clinical manifestations of osteopenic syndrome.

Comparative analysis of lipid metabolism revealed a significant difference between the groups (*Table 1*).

Thus, the level of TC in patients with SCHD with obesity was 1.04 times higher than in patients with isolated SCHD ($p < 0.005$) and 1.27 times higher than in healthy people ($p < 0.001$). Analysis of LLC also revealed a significant difference between the groups: it was 1.6 times higher in the main group compared to the control and 1.7 times higher in

Table 1

The level of lipid metabolism in patients with SCHD and its combination with obesity

Indexes	Main group n=79	Comparison group n=19	Control group n=20
TC, mmol/l	5.89 (5.65;6.24)*	5.64(4.97;6.0)*	4.63 (4.25;4.79)
LLC, mmol/l	4.33 (4.09;4.62)*	4.24 (3.69;4.61)*	4.24 (3.69;4.61)
VLLC, mmol/l	0.73 (0.64;0.86)*	0.6 (0.55;0.64)*	0.38 (0.36;0.41)
HDL, mmol/l	0.82 (0.76;0.88)*	0.81(0.77;0.92)*	1.4 (1.23;1.55)
RG, mmol/l	1.61 (1.41;1.9)*	1.32 (1.22;1.41)*	0.82 (0.78;0.9)
AI	6.27 (5.70;6.8)*	5.63 (5.13;6.6)*	1.91 (2.96;2.65)

Notes: p <0.05 *, – in relation to the control group.

the comparison group compared to the control ($p < 0.001$). LLC values in patients with SCHD did not differ statistically. The level of VLLC was 1.2 times higher in the main group than in the comparison group and 1.9 times higher than in the control group ($p < 0.001$). The difference in VLLC values of the comparison and control groups also had a significant difference ($p < 0.001$). The results of HDL were significantly lower in the main and comparison groups mmol/l relative to the control group, ($p < 0.001$), and did not differ statistically in patients with SCHD, ($p = 0.36$). TG values were 1.2 times higher in the main group compared with the comparison group and 2 times higher than in the control group ($p < 0.001$). The TG level of the comparison group was also significantly higher than in the control group ($p < 0.001$). The AI of the main group was 1.1 times higher than in the comparison group 3.3 times higher than the control group. These data coincide with previously obtained results, which show that the characteristic potentially atherogenic indicators of the blood lipid profile are not so much an increase in TC levels, but an elevated TG level and a decreased level of LLC [12]. Some indicators of lipid metabolism in SCHD significantly differed from the control group, but were within the normative values, which may be the result of receiving lipid-lowering therapy.

Analysis of mineral metabolism revealed some patterns (*Table 2*). Although the level of phosphorus-calcium metabolism did not exceed the reference values, there was a tendency to increase total calcium in patients with SCHD and obesity compared with isolated SCHD and the control group ($p < 0.001$). The difference in blood phosphorus parameters was not significant, but there was a tendency to increase phosphorus levels in patients with SCHD and obesity mmol/l compared with the control group ($p = 0.36$).

Experimental studies show that elevated calcium levels may play an important role in the pathogenesis of cardiovascular disease. Thus, there are studies in which a positive relationship has been established between normal serum calcium levels and atherosclerosis of the carotid arteries [2, 14, 15], as well as between blood calcium levels and obesity [16, 17].

Comparative analysis of indicators of phosphorus-calcium metabolism in urine (*Table 3*) revealed a significant difference between the level of urinary calcium in patients of the main group, comparison group and control one with a tendency to increase urinary calcium excretion in patients with SCHD and obesity. Thus, the level of calcium in the daily urine of the main group was 2 times higher than in the comparison group ($p < 0.001$). Urinary phosphorus levels were statistically lower in patients with SCHD with normal weight compared to other groups, but was within the reference values ($p < 0.001$).

That is, in the presence of atherosclerosis there is an increased excretion of calcium in the urine and concomitant obesity exaggerate this process [2]. These data deny the assumption that adipose tissue plays a protective role in the development of osteoporosis. At the same time, the results of the densitometric study showed the opposite result. Thus, when conducting a densitometric study in the comparison group,

Table 2

The content of phosphorus-calcium metabolism in the serum of patients with SCHD and comorbidity with obesity (mmol/l)

Indexes	Main group n=79	Comparison group n=19	Control group n=20
Phosphorus	1.5 (1.4;1.7)	1.5 (1.35; 1.6)	1.44 (1.22; 1.58)
Total calcium	2.5(2.4;2.56)*	2.4(2.35; 2.46)*	2.21 (2.13; 2.27)

Notes: p <0,05 *, – in relation to the main group.

Table 3

The content of indicators of phosphorus-calcium metabolism in the urine of patients with SCHD and its combination with obesity

Indexes	Main group n=79	Comparison group n=19	Control group n=20
Phosphorus, g/day	1.34 (0.99;1.72)	0.98(0.77;1.12)**	1.07 (0.86.1.45)
Calcium, mg/day	377(230;450)*	320(220;400)*	195 (158.5;289)

Notes: p <0.05 * – in relation to the comparison group; p<0.05 ** – in relation to the control group.

osteopenic conditions were diagnosed in 54 % of patients (35.6 % – osteopenia, 18.4% – osteoporosis) against 28.5% of osteopenia in patients of the main group (p < 0.05). There were no signs of osteoporosis in patients with SCHD and obesity.

Thus, the changes in calcium-phosphorus metabolism in patients with SCHD and obesity can be considered as a predictor of osteopenic conditions. Whereas, according to the results of densitometric research, the percentage of patients with osteopenic conditions is lower in the presence of excess weight or obesity. Probably, the level of protective mechanisms is influenced by the degree of obesity and the peculiarities of adipose tissue distribution, so the data obtained require further study.

Conclusions

The course of stable coronary heart disease occurs against the background of changes in blood lipid spectrum and calcium-phosphorus metabolism. In patients with SCHD in combination with obesity there is an increase in total calcium and serum phosphorus, which can be considered as a factor that enhances the development of atherosclerotic vascular lesions.

The comorbid course of SCHD and obesity is an unfavorable factor of high risk of developing osteodeficiency states, which is confirmed by early changes in calcium-phosphorus metabolism.

For the purpose of early diagnosis of osteoporotic conditions in patients with SCHD and obesity, it is advisable to determine the bone mineral density according to the indicators of phosphorus-calcium metabolism and/or conduct a densitometric study.

Declarations:

Statement of Ethics

The authors have no ethical conflicts to disclosure.

Consent for publication

All authors give their consent to publication.

Disclosure Statement

The authors have no potential conflicts of interest to disclosure.

Funding Sources

This study was not supported by any grants from public, commercial or other sectors

Data Transparency

The data can be requested from the authors.

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Received: 07-Feb-2021
Accepted: 21-Jun-2021