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INSTRUMENTAL AND LABORATORY STUDY OF JAW MINERALIZATION LEVEL IN FEMALE PATIENTS WITH ESTROGEN IMBALANCE

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Abstract:

Introduction: Prevention of dental caries and non-carious lesions associated with demineralizing effect of estrogen imbalance in perimenopause women is relevant problem in modern dentistry.
The aim: To improve the effectiveness of prevention of caries and non-carious lesions in female patients with estrogen imbalance.
Materials and methods: 3 groups of patients were selected for the study (20 women in each): the patients of the control group receiving no additional treatment, the patients of experimental group 1 receiving general therapy with complex calcium supplements, the patients of experimental group 2 receiving general therapy of complex calcium medicines combined with aminobisphosphonates.
To quantify bone density of the jaws by computed tomography method, X-ray attenuation scale, called the Hounsfield scale was used. Bone tissues of the jaws were studied using 3D cone beam computed tomography scanner Planmeca ProMax. Planmeca Romexis® software was used for data processing and interpretation. Estrogen level was estimated in all patients to confirm its imbalance. The level of serum acid phosphatase was determined for indirect study of osteoporosis degree.
Results: At the beginning of the research, significant bone demineralization and increased level of acidic phosphatase were observed in all groups of women. In 6 months of treatment the Hounsfield index and the level of acidic phosphatase in the control group were almost unchanged; in experimental group 1 – 1571 ±44 HU and 4.93 ± 0.26 IU/l; in experimental group 2 – 1701±48 HU and 2.43 ± 0.18 IU/l.
Conclusions: Combination therapy consisting of calcium phosphate with vitamin D3 and aminobisphosphonates used for 6 months increased bone mineralization by 13.05% and reduced the activity of acid phosphatase by 64.2%. This therapeutic complex results in decreased destruction of bone tissue and enhances remineralization of bone tissue and dental hard tissues.
Key words: teeth mineralization, osteoporosis, estrogen dysfunction, Hounsfield index.

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INTRODUCTION

An increase in morbidity among women during the perimenopause is caused by the impact of estrogen imbalance due to a sharp decrease in ovarian hormonal activity, which leads to reduction of labor productivity and social deadaptation. The problem of maintaining and promoting health, preserving working capacity, improving the quality and life expectancy of this category of women is a relevant.

Estrogen imbalance in perimenopause women also affects dental health. In spite of definite progress achieved in prevention of dental caries in Ukraine, its high prevalence and intensity is still registered, being an urgent problem in dentistry. According to literature data, the prevalence of permanent teeth caries in 40-50 year-old women ranges from 72.7 to 94.3 % with the intensity of damage 2.5 - 4.7 teeth [1-3].

Decreased resistance of dental hard tissues is influenced by demineralization of bones and teeth. The process of calcium metabolism is influenced by a number of hormones, their concentration changing in various periods of women's life. In women aged 40-50, natural deficiency of blood estrogen level develops due to age-related changes in gonads. The mechanisms of influence of sex hormones on bone tissue are critically important but not studied completely. However, after detection of specific osteoblast receptors to estrogens, androgens, growth hormone and thyroid hormones, it became apparent that spongy substance of bone tissue is a particular kind of target organ for sex hormones. Estrogens exert the most significant effect on bone and mineral metabolism, since they activate osteoblasts, inhibit interleukin production, promote inhibition of bone resorption, decrease bone tissue susceptibility to resorptive effect of parathyroid hormone, increase bone tissue sensitivity to vitamin D3, enhance calcitonin synthesis, regulate the processes of calcium absorption and secretion, activate apoptosis of osteoclasts [4-5]. Decrease of estrogen level leads to accelerated bone metabolism and loss of bone substance. This significantly slows down the processes of bone tissue regeneration and dental hard tissues, leading to decreased resistance of hard tissues of teeth to the effects of aggressive factors [6-7].

Osteoporosis is a systemic metabolic disease of the skeleton, characterized by lower-than-normal bone mass per unit volume as compared to normal index in individuals of relevant sex, as well as impaired bone tissue microarchitectonics with subsequent progression of bone fragility and increased risk of fractures. Being a common metabolic bone disease, osteoporosis presents a major and growing medical, social and economic burden. Osteoporosis is known to develop gradually and can go unnoticed for years. Manifestations of its characteristic symptoms become most evident after about 10-15 years of osteopenic syndrome onset. There is close relationship between the processes of resorption and bone formation, controlled by hormones and occurring on tissue level. Hormones are among major factors that determine bone mass and bone tissue quality, along with physical activity and good nutrition. Low levels of estrogen in the body during menopause and post-menopause period proved to be associated with increased risk of developing osteoporosis in older women [4, 8-9].

Thus, prevention of dental caries and non-carious lesions associated with demineralizing effect of estrogen imbalance in menopause women is considered to be an urgent problem in modern dentistry. Development of comprehensive measures is required to prevent and slow down osteoporosis progression and dental tissue demineralization, as well as to increase local resistance and reduce the

cariogenic effect of oral microorganisms. Such prophylaxis will improve treatment and prevention of caries in patients with estrogen imbalance.

THE AIM

The aim of this study was to improve the effectiveness of prevention of caries and non-carious lesions in female patients with estrogen imbalance.

MATERIALS AND METHODS

It was a prospective comparative study of female patients aged 45-60 years with clinically and laboratory confirmed estrogen dysfunction. 3 groups of patients were selected for the study: the control group (20 females) – the patients receiving no additional treatment, experimental group 1 (20 females) – the patients receiving general therapy with complex calcium medicines, experimental group 2 (20 females) – those who received general therapy of complex calcium medicines combined with aminobisphosphonates (aminoBPs). Evaluation of patients was performed for three times during the study period: at initial presentation, in three and six months after initiation of treatment.

In the control group no additional treatment was administered, except supervision of the dentist. In experimental group 1, combination of calcium phosphate medicines with vitamin D3 was administered (ATC-code: A12A H., registration No UA/ 3541/01/01 - 04.21.2015 to 04.21.2020). In experimental group 2, combination of calcium phosphate medicines with vitamin D3 was used (ATC-code: A12A H., registration No UA/ 3541/01/01 - 04.21.2015 to 04.21.2020) as well as the medicine of alendronic acid (ATC-code: M05B A04., registration No UA / 7210/01/02 of 20.09.2017. Order No 1116 of 20.09.2017). Three 4-week courses of treatment with four week intervals between them were administered. The patients were prescribed neither non-steroidal anti-inflammatory drugs for long-term use (more than 5 days), nor hormonal drugs, including contraceptives, anticancer chemotherapy drugs. The patients were residents of free of chemical contamination regions, which could affect the results of the study.

Bone tissues of the jaws were studied using 3D cone beam computed tomography scanner Planmeca ProMax. Planmeca Romexis® software was used for processing and interpretation of 2D and 3D images of Planmeca X-ray machines. Integration of the program with other systems, TWAIN protocol support and correspondence to DICOM file suggests the use of Planmeca Romexis with majority of systems.

To quantify bone density of the jaws by computed tomography method, X-ray attenuation scale, called the Hounsfield scale was used (its visual representation on the monitor is black-and-white image spectrum). The Hounsfield scale is known to be a quantitative transformation of the attenuation coefficient. The Hounsfield unit (HU) is a relative quantitative measurement of radio density used by radiologists in the interpretation of computed tomography (CT) images. Hounsfield units (densitometric values), corresponding to the degree of attenuation of X-rays by anatomical structures of the body, range from -1024 to +1024 (in practice, those values may slightly differ depending on the device). The average Hounsfield scale value (0 HU) corresponds to water density, negative values of the scale correspond to density of the air and adipose tissue, positive ones - to density of soft tissues, bone tissue and more dense substances (metal). The studies were performed by determining bone tissue density in definite site of mandibular premolars. To avoid uncertainties in measurements, all studies were performed using one and the same apparatus (3D cone beam

computed tomography scanner) and the same software version (Planmeca Romexis®).

Estrogen (estradiol) level was estimated to confirm its imbalance. All the patients were in their menopause period having no cyclic fluctuations of hormone levels.

The level of serum acid phosphatase was determined for indirect study of osteoporosis degree. Acid phosphatase is an enzyme that catalyzes the hydrolysis of orthophosphoric monoesters with elimination of a phosphate group which exhibits optimal activity in acidic environment. Acid phosphatase is found in cell lysosomes of various body tissues. Acid phosphatase activity index is of great significance in women: its increased level can be indicative of such diseases as hyperparathyroidism, osteoporosis. To obtain adequate results, the patients were recommended fasting for 12 hours before examination; avoidance of physical and emotional overstrain for 30 minutes before examination; abstinence from smoking for 30 minutes before examination.

The study was carried out in accordance with the main principles of the guidelines for "Ethical Conduct of Research including Human Subjects", approved by the Declaration of Helsinki (1964-2013), ICH GCP (1996), EEC Directive No 609 (of 24.11.1986), Orders of the Ministry of Health of Ukraine № 690 of 23.09.2009, № 944 of 14.12.2009, № 616 of 03.08.2012. An informed consent to participate in the study was received and all patients underwent standard clinical examination in accordance with the medical protocol (Order No. 566 of 11.23.2004).

RESULTS

The degree of bone mineralization was determined using 3D cone beam computed tomography scanner Planmeca ProMax. Planmeca Romexis® software was used for data processing and interpretation. It should be noted that the mandible is represented mostly by cortical bone tissue of type I and type II according to Lekhol and Zarb classification (1985). Study results are presented in Table I and Figure 1.

Table I. Mandibular bone tissue density by Hounsfield scale (HU)

Table I

Mandibular bone tissue density by Hounsfield scale (HU)

	Initiation of treatment	3 months after treatment initiation	6 months after treatment initiation
Control group (n=20)	1495±89	1491±67	1497±63
Experimental group 1 (n=20)	1488±75 $p_1>0,05$	1533±59 $p_2>0,05$	1571±44 $p_3<0,05$
Experimental group 2 (n=20)	1479±84 $p_1>0,05$ $p_4>0,05$	1605±53 $p_2<0,05$ $p_4<0,05$	1701±48 $p_3<0,05$ $p_4>0,05$

Notes:

1. p_1 - significance of differences between the performance of the control group and the experimental groups at the Initiation of treatment.

2. p_2 - significance of the difference between the indices of the control group and the experimental groups at 3 months after treatment initiation.

3. p_3 - significance of the difference between the performance of the control group and the experimental groups at 6 months after treatment initiation

4. p_4 - the probability of a difference between the indices of the experimental groups at the initiation of treatment, 3 months after treatment initiation and 6 months after treatment initiation (i so on in the text for each table).

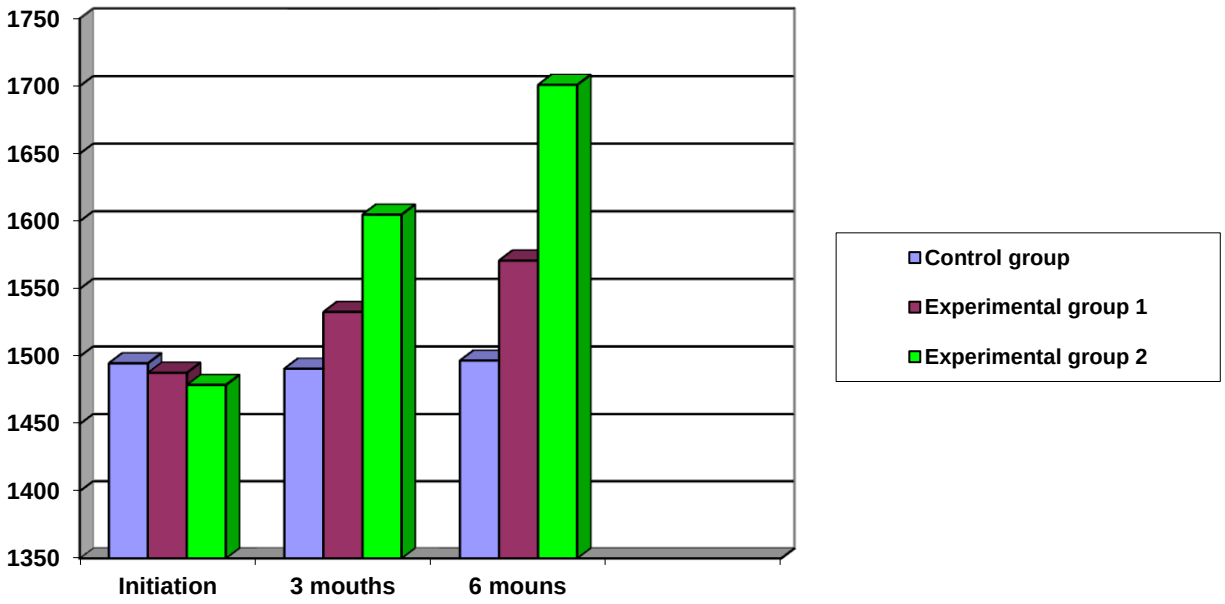

Fig. 1. Mandibular bone tissue density by Hounsfield scale (HU)

The patients of all study groups appeared to have significant demineralization of bone tissue at the baseline. Mandibular mineralization index was rather low – 1495±89 HU, 1488±75 HU ($p_1>0,05$), 1479±84 HU ($p_1>0,05$, $p_4>0,05$) in the control group, experimental group 1, and experimental group 2, respectively (normal value - 1600-1700 HU).

After 3 months of treatment, the following results were obtained. In the control group, the Hounsfield index was 1491±67 HU, i.e. similar to the baseline values. In experimental group 1, the Hounsfield index was 1533±59 HU ($p_2>0,05$). In experimental group 2, the Hounsfield index was 1605±53 HU ($p_2<0,05$, $p_4<0,05$).

After 6 months of treatment the Hounsfield index remained practically unchanged in the control group – 1497±63 HU, indicating no dynamics in that group. In experimental group 1, the Hounsfield index was 1571±44 HU ($p_3<0,05$). In experimental group 2, the Hounsfield index was 1701±48 HU ($p_3<0,05$, $p_4<0,05$).

All study female patients were examined for blood levels of estrogen to confirm estrogen imbalance. Indices of blood plasma estrogen (estradiol) levels in study patients are presented in Table II.

Table II. Indices of blood plasma estrogen (estrodiol) levels, pg/ml

Table II

Indices of blood plasma estrogen (estrodiol) levels

Blood plasma estradiol level,**pg/ml**

	Initiation of treatment	3 months after treatment initiation	6 months after treatment initiation
Control group (n=20)	53.4±2.29	53.8±1.19	55.2±1.24
Experimental group 1 (n=20)	52.9±2.56 $p_1>0,05$	53.1±1.41 $p_2>0,05$	55.6±1.26 $p_3<0,05$
Experimental group 2 (n=20)	53.1±2.73 $p_1>0,05$ $p_4>0,05$	53.6±1.36 $p_2>0,05$ $p_4>0,05$	56.4±1.18 $p_3<0,05$ $p_4>0,05$

In the control group, indix of blood plasma estrogen (estradiol) levels was from 53.4±2.29 pg/ml to 55.2±1.24 pg/ml within 6 months (normal value – 150-750 pg/ml).

In experimental group 1, indix of blood plasma estrogen (estradiol) levels was from 52.9±2.56 pg/ml ($p_1>0,05$) to 55.6±1.26 pg/ml ($p_3>0,05$) within 6 months

In experimental group 2, indix of blood plasma estrogen (estradiol) levels was from 53.1±2.73 pg/ml ($p_1>0,05$) to 56.4±1.18 pg/ml ($p_3>0,05$, $p_4>0,05$) within 6 months

Serum acid phosphatase level was determined for indirect study of osteoporosis degree (destruction of bone tissue). Indices of serum acid phosphatase level in study patients are presented in Table III and Figure 2.

Table III. Serum levels of acid phosphatase

Table III

Serum levels of acid phosphatase, IU/l

	Initiation of treatment	3 months after treatment initiation	6 months after treatment initiation
Control group (n=20)	6.75±0.29	6.84±0.19	6.79±0.24
Experimental group 1 (n=20)	6.81±0.56 $p_1>0,05$	5.11±0.41 $p_2>0,05$	4.93±0.26 $p_3<0,05$
Experimental group 2 (n=20)	6.79±0.73 $p_1>0,05$ $p_4>0,05$	4.28±0.36 $p_2<0,05$ $p_4<0,05$	2.43±0.18 $p_3<0,05$ $p_4>0,05$

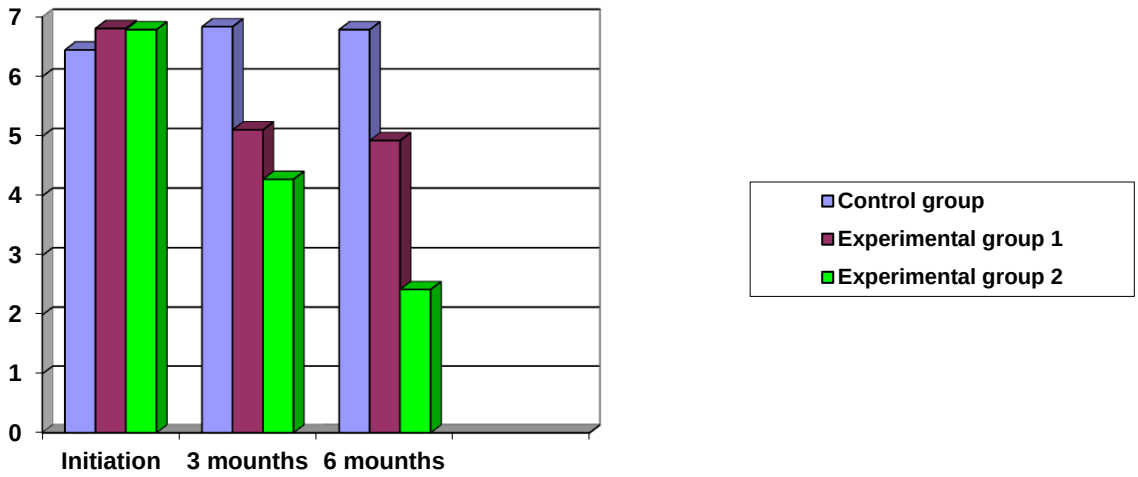

Fig. 2. Serum levels of acid phosphatase, IU/l.

At study initiation, all patients were found to have significantly increased level of acid phosphatase: 6.75±0.29 IU/l, 6.81±0.56 IU/l ($p_1>0,05$), 6.79±0.73 IU/l ($p_1>0,05$, $p_4>0,05$) in the control group, experimental group 1, and experimental group 2, respectively (normal value – 0-5.5 IU/l).

After 3 months of treatment, the following results were obtained. In the control group, acid phosphatase level was 6.84±0.19 IU/l. In experimental group 1, acid phosphatase level was 5.11±0.41 IU/l ($p_2>0,05$) and in experimental group 2 – 4.28±0.36 IU/l ($p_2<0,05$, $p_4<0,05$).

After 6 months of treatment, the level of acidic phosphatase was practically unchanged in the control group (6.79±0.24 IU/l). In experimental group 1, acid phosphatase level was 4.93±0.26 IU/l ($p_3<0,05$). In experimental group 2, acid phosphatase level was 2.43±0.18 IU/l ($p_3<0,05$, $p_4<0,05$)

DISCUSSION

The patients of all study groups appeared to have significant demineralization of bone tissue at the baseline. Mandibular mineralization index was rather low – 1495±89 HU, 1488±75 HU, 1479±84 HU in the control group, experimental group 1, and experimental group 2, respectively (normal value - 1600-1700 HU).

After 3 months of treatment, the following results were obtained. In the control group, the Hounsfield index was 1491±67 HU, i.e. similar to the baseline values. In experimental group 1, the Hounsfield index was 1533±59 HU, which is 3% higher as compared to the baseline. In experimental group 2, the Hounsfield index was 1605±53 HU, i.e. the level of mineralization had increased by 7.85%.

After 6 months of treatment the Hounsfield index remained practically unchanged in the control group – 1497±63 HU, indicating no dynamics in that group. In experimental group 1, the Hounsfield index was 1571±44 HU, which is 5.28% higher as compared to the baseline. In experimental group 2, the Hounsfield index was 1701±48 HU, being 13.05% higher than the baseline value.

Having analyzed the results, the conclusion was made that complex medicine of calcium phosphate and vitamin D3 used for 6 months improved bone tissue mineralization of the jaws

by 5.28%. At the same time, complex therapy consisting of calcium phosphate medicines with vitamin D3 and aminobisphosphonates used for 6 months increased bone mineralization by 13.05%. Increase of mineralization of undamaged bone tissue by more than 10% over the period of 6 months is considered to be an excellent result.

According to the data obtained, all patients had moderately decreased level of estrogen, being indicative of age-related changes in the endocrine system of women (normal value – 150-750 pg/ml).

At study initiation, all patients were found to have significantly increased level of acid phosphatase: 6.75±0.29 IU/l, 6.81±0.56 IU/l, 6.79±0.73 IU/l in the control group, experimental group 1, and experimental group 2, respectively (normal value – 0-5.5 IU/l). Such elevated level of acid phosphatase implies the predominance of demineralization and osteolysis processes.

After 3 months of treatment, the following results were obtained. In the control group, acid phosphatase level was 6.84±0.19 IU/l, which was slightly higher as compared to the baseline value. In experimental group 1, acid phosphatase level was 5.11±0.41 IU/l (24.9% less versus baseline) and in experimental group 2 – 4.28±0.36 IU/l (36.9% less versus baseline).

After 6 months of treatment, the level of acidic phosphatase was practically unchanged in the control group (6.79±0.24 IU/l), implying no dynamics in that group. In experimental group 1, acid phosphatase level was 4.93±0.26 IU/l, being 27.6% less than the baseline value. In experimental group 2, acid phosphatase level was 2.43±0.18 IU/l, being 64.2% less compared with the baseline value.

Having analyzed the results of acid phosphatase level measurements, it was found that complex medicine of calcium phosphate and vitamin D3 used for 6 months reduced the activity of acid phosphatase by 27.6%. At the same time, complex therapy consisting of calcium phosphate medicines with vitamin D3 and aminobisphosphonates used for 6 months reduced the activity of acid phosphatase by 64.2%.

Thus, on the basis of all data obtained, the use of this therapeutic complex proved to decrease the destruction of bone tissue and hard tooth tissue, as well as to enhance their remineralization. Therefore, it can be recommended for prevention of caries and non-carious lesions in women with estrogen imbalance.

CONCLUSIONS

Complex therapy consisting of calcium phosphate with vitamin D3 and aminobisphosphonates used for 6 months increases bone mineralization by 13.05% and reduces the activity of acid phosphatase by 64.2%.

This therapeutic complex suggested for prevention of caries and non-carious lesions in female patients with estrogen imbalance results in decreased destruction of bone tissue and enhances remineralization of bone tissue and dental hard tissues.

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