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# The Effect of Combined Oral Contraceptives on the Bone Mineral Density in Perimenopausal Women

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## Abstract

Increased life expectancy, lengthening of the reproductive period, early menarche and late menopause, chronic hyperestrogenism in the presence of relative or absolute progesterone deficiency, uncontrolled use of combined oral contraceptives, the formation of the metabolic syndrome are considered high-risk factors for the occurrence and progression of this pathology. Therefore, we aimed to study improvement the principles of preventing the loss and restoration of bone mineral density in women in the perimenopausal period. In women with unfavorable factors of menstrual, reproductive, somatic history in the perimenopausal period, there is a high incidence of the development of pathological decrease in bone mineral density. The use of combined oral contraceptives in the perimenopausal period contributes to the activation of bone remodeling processes.

***Index terms***— combined oral contraceptives; perimenopausal period; bone mineral density; metabolic syndrome; osteoporosis; osteopenia.

Abstract-Increased life expectancy, lengthening of the reproductive period, early menarche and late menopause, chronic hyperestrogenism in the presence of relative or absolute progesterone deficiency, uncontrolled use of combined oral contraceptives, the formation of the metabolic syndrome are considered high-risk factors for the occurrence and progression of this pathology. Therefore, we aimed to study improvement the principles of preventing the loss and restoration of bone mineral density in women in the perimenopausal period. In women with unfavorable factors of menstrual, reproductive, somatic history in the perimenopausal period, there is a high incidence of the development of pathological decrease in bone mineral density. The use of combined oral contraceptives in the perimenopausal period contributes to the activation of bone remodeling processes.

## 1 I.

Introduction pressing problem of modern gynecology is the steady increase in the incidence of osteoporosis in perimenopausal women [1]. Osteoporosis is a systemic metabolic, skeletal disease, characterized by a decrease in bone mineral density in violation of its architectonics, and an increased risk of fractures. Low peak bone mass of women in the late reproductive period, decreased physical activity, poor nutrition, decreased levels and activity of sex hormones lead to the development of osteopenic syndrome and subsequently osteoporosis in women already in the perimenopausal period [2]. Insufficient coverage of this problem in the network of practical obstetric-gynecological care, the inopportuneness, and inadequacy of therapy aimed at normalizing bone mineral density leads to catastrophic bone loss and the occurrence of pathological bone fractures. In women 50 years and older, the risk of a pathological hip fracture is 23% [3]. In Uzbekistan, unfortunately, there is no reliable statistical base for the epidemiology of osteoporosis in perimenopausal women.

Increased life expectancy, lengthening of the reproductive period (early menarche and late menopause), chronic hyperestrogenism in the presence Author ? ?: Department of Obstetrics and Gynecology, Tashkent Medical Academy, Tashkent, Uzbekistan. e-mail: author.uzb@mail.ru of relative or absolute progesterone deficiency, uncontrolled use of combined oral contraceptives, the formation of the metabolic syndrome are considered high-risk factors for the occurrence and progression of this pathology [4].

Combined oral contraceptives (COCs) are a universal group of drugs that simultaneously suppress bone resorption and stimulate bone formation **??**5]. Treatment is usually carried out within 6-12 months; preference

is given to low-and micro-dosage drugs (prevention of thrombophilic complications). COC, which contains ethinyl estradiol 0.03 mg and drospirenone 3 mg (Yasmin), is a highly effective drug with a Perl index of 0.07, providing a stable weight. Drospirenone -progestogen new class -a derivative of spironolactone unique antimineralocorticoid properties prevents hydration of tissues due to estrogen, has antihypertensive effect in women c chronic hypertension, characteristic for the perimenopausal period, no effect on blood pressure in women with normal and hypotension, provides stable weight.

The purpose of the study is to improve the principles of preventing the loss and restoration of bone mineral density in women of perimenopausal period.

# 2 II.

# 3 Materials and Methods

A comprehensive clinical and laboratory examination of 202 women of the perimenopausal period residing in the city of Tashkent was carried out, of which 103 (50.9%) women were isolated with a decrease in bone mineral density. According to the therapy methods, patients were divided into 2 groups. The main group (n=80) who were prescribed in the complex therapy (Ibadronate 150 mg, single dose per month, duration of treatment 6 months, as well as combination with preparation of calcium and vitamin D (500 mg of elemental calcium and 200 IU of cholecalciferol)) combined oral contraceptive (ethinyl estradiol 0.03 mg, drospirenone 3 mg) and 23 women who received therapy without COCs (comparison group). The control group consisted of 20 perimenopausal women with normal bone mineral density. The average age of women was 47±2.5 years. The survey was conducted for 18 months.

# 4 A

The state of bone mineral density (BMD) of the lumbar vertebrae (L1-L4) and the proximal femur was evaluated based on ultrasound densitometry. The metabolic activity of bone remodeling processes was assessed by biochemical markers of bone remodeling such as formation markers (osteocalcin) and bone resorption (?-Crosslaps).

# 5 a) Statistical analysis

Comparison of groups of observations was made using a number of nonparametric statistics criteria (Pearson correlation, correlation coefficient) and Student's t-test using the statistical package SPSS 15.0, SYSTAT 11.

# 6 III.

# 7 Results and Discussion

Data from numerous researchers was confirmed [6]: a large number of women showed a significant deviation in the nature of the menstrual cycle of the hypomenstrual type: hypomenorrhea in 30.1% of women; oligomenorrhea in 20.4% of women. Hypermenstrual type of menstrual dysfunction was also detected in a large number of women: polymenorrhea in 51 (49.5%) women. In women with a decrease in bone mineral density, menstrual disorders are presented with greater frequency than in women in the control group ($p<0.05$).

In the examined women, there was a high incidence of diseases contributing to the formation of secondary osteoporosis: the gastrointestinal-hepatic complex (in 46.6%); a history of neurological pathology: neurosis and neurosis-like states (100%); neuroendocrine syndrome was detected in 49.5%; thyroid dysfunction in history revealed in 30.1%.

The risk factors for the development of osteoporosis and the preliminary determination of the need for additional research methods have been identified. Minimal risk was detected in less than half of women (31.1%). According to testing, a high risk of osteoporosis was detected in 68.9% of women with a decrease in bone mineral density. The high risk of bone fracture, which is an extremely alarming factor, was hypothetically present in 34.9% of women. Based on the results of the study, prognostically unfavorable result was formed. In perimenopausal women, the minimal risk of osteoporosis was determined only in 31.1%. In 44.7%, a high risk of osteoporosis is hypothetically noted. In 21.4% of women, a high risk of not only low bone mineral density, but also fracture was hypothetically revealed. Thus, the study revealed the need to ascertain the state of bone mineral density in women of the late reproductive period for the prevention of the development of osteoporosis in the perimenopausal period.

An acute shortage of daily intake of calcium and vitamin D with food was also detected: daily calcium intake is performed only in 12 (11.7%), only 6 (5.8%) women receive a daily rate of vitamin D.

The bone mineral density of all women was verified at baseline and after 18 months of observation. In women of the main group (Fig. 1), initial bone mineral density in 31 (38.8%) cases corresponded to osteoporosis, osteopenia was detected in 49 (61.2%) women. After a year of observation (Table 1), only 19 (23.8%) women had osteoporosis, which is 15% less than before treatment. Only in 51 (63.8%) women osteopenia was observed and in 10 (12.5%) cases bone mineral density corresponded to the norm.

On the background of complex therapy with the inclusion of oral combined contraceptives for 6 months, women not only did not decrease bone mineral density but also showed a tendency to its increase and stable state by the 12 th month of observation. A statistically significant increase in bone mineral density in women of the main group ($p<0.01$) was noted. The beneficial effect of COC for 6 months on the state of mineral density, their ability to increase bone mineral density was revealed. In the women of the comparison group (Table 2), osteoporosis was initially detected in 8 (34.8%) cases, and osteopenia in 15 (65.2%) cases. After a year of observation, osteoporosis was observed in 11 (47.8%) women, which is 13% higher than baseline data. Osteopenia was detected in 12 (52.2%) cases. Cases with normal indicators of bone mineral density were not detected. There was a significant decrease in bone mineral density in women of the comparison group for 6 months ($p <0.01$). According to the study, changes in the bone resorption index of ?-CrossLaps were observed in the dynamics of observation, depending on the type and duration of therapy.

In women of the main group (Table **??**), there was a decrease in the level of ?-CrossLaps after 1 month of COCs therapy (r=0.52 -medium correlation). By the third month of therapy, the ?-CrossLaps indicator returned to baseline values; by the sixth, there was a tendency to decrease (with r=0.57, the average correlation).

Table **??**: Dynamics of the level of ?-CrossLaps, ng/ml in women of the main group (in patients receiving COCs) Significant changes in the rate of change were observed between the results of the study after 1 and 6 months ($p<0.01$). That is, against the background of COCs, the rate of bone resorption decreases not only during therapy, but also over the next 6 months.Study Time Minimum Maximum M ? m Present ,22**,65 ,4619 ,13151 ,02941 After a month ,20 ,55 ,3200 ,09399 ,02630 After 3 months**

Women in the comparison group without the use of COCs (Table 4) showed an increase in bone resorption rates, starting from the 6th month, continuing to the 12th month of observation, which indicates a continued increased resorptive activity of the bone tissue after the completion of therapy without COCs for more 6 months. All groups of women showed a tendency to a low level of the bone formation marker -osteocalcin at baseline, significantly reacting to the deficiency of female sex hormones.

At baseline in women of the main group (Table 5), the level of osteocalcin corresponded to $9.7375 \pm 0.39149$ ng/ml. The maximum value, 11.89 ng/ml, initially in the group corresponded to the lower limit of normal (11.0 ng/ml). After 1 month of treatment with COCs, a tendency to an increase in osteocalcin levels was noted. A significant increase in the index was observed between the results of the study after 1 and 6 months ($p<0.01$). Consequently, against the background of COCs, an improvement in bone formation was revealed, the maximum by the 6th month of therapy. In women of the comparison group (Table 6), there was a tendency to a significant decrease in osteocalcin levels in comparison with the norm both from baseline and due to the lack of replacement therapy with COCs. Significant changes in the rate of change were noted between the results of the study after 6 months ($p<0.01$). Thus, with a rather low initial level of osteocalcin, a tendency to its decrease was noted, at most by the 6th month. After a year the completion of calcium and vitamin D supplements, the bone-up of osteocalcin was normal, however, in its lower range. Thus, as a result of the study in women of the perimenopausal period, the source of a low index of bone mineral density was revealed: osteoporosis in 37.8%, osteopenia in 62.2%. At the same time, the minimum risk of osteoporosis was observed in 34 (33%), a high risk of osteoporosis in 47 (45.6%), a high risk of bone fracture in 22 (21.3%).

Initially, all women had low osteocalcin levels. Against the background of COCs, an improvement in bone formation was revealed, the maximum by the 6th month of therapy.

IV.

# 8 Conclusion

1. In women with adverse factors of the menstrual, reproductive, somatic history in the perimenopausal period, there is a high incidence of the development of a pathological decrease in bone mineral density. 2. The use of combined oral contraceptives in the perimenopausal period contributes to the activation of bone remodeling processes. [1]

[1]© 2019 Global JournalsThe Effect of Combined Oral Contraceptives on the Bone Mineral Density in Perimenopausal Women

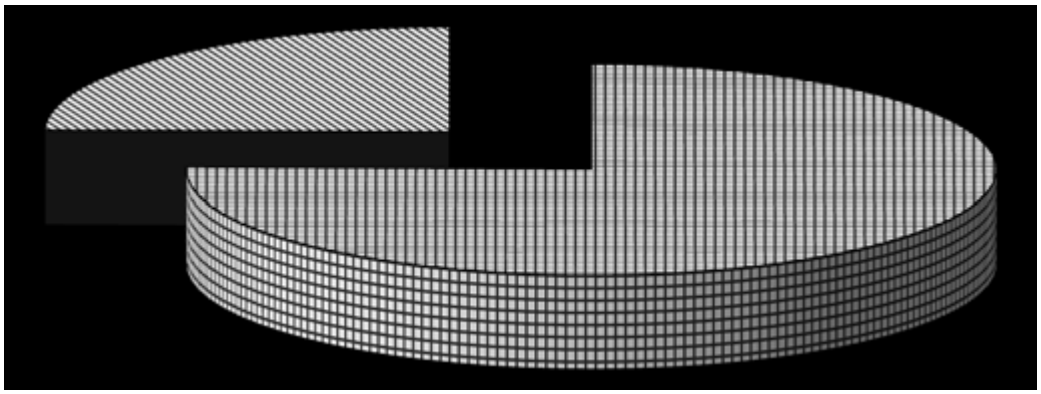

Figure 1: The

**1**

| Study Time | Minimum | Maximum | M | ? | M |
|---|---|---|---|---|---|
| Original | -2,30 | 1,50 | -,7050 | 1,26052 | ,28186 |
| After a year | -1,80 | 1,60 | -,5500 | 1,22066 | ,27295 |

Figure 2: Table 1 :

**2**

| Study Time | Minimum | Maximum | M | ? | M |
|---|---|---|---|---|---|
| Present | -2,80 | 1,80 | -1,1850 | 1,30193 | ,29112 |
| After a year | -3,50 | 1,50 | -1,6000 | 1,26574 | ,28303 |

Figure 3: Table 2 :

**4**

| Study Time | Minimum | Maximum | M | ? | M |
|---|---|---|---|---|---|
| Present | ,14 | ,56 | ,2838 | ,10869 | ,02430 |
| After a month | ,45 | 2,01 | ,9786 | ,41711 | ,02815 |
| After a trimester | ,34 | 1,61 | ,8450 | ,34317 | ,02963 |
| After 2 trimesters | ,33 | 1,56 | ,6917 | ,39760 | ,03533 |
| After a year | ,12 | ,70 | ,2842 | ,13786 | ,03083 |

Figure 4: Table 4 :

**5**

| | Minimum | Maximum | M | ? | M |
|---|---|---|---|---|---|
| Present | 5,35 | 11,89 | 9,7375 | 1,75079 | ,39149 |
| After a month | 6,04 | 30,50 | 13,7275 | 5,23536 | ,7825 |
| After a trimester | 7,85 | 32,40 | 18,4520 | 7,73216 | , 9327 |
| After 6 months | 14,22 | 43,79 | 27,5640 | 7,87755 | 0,9418 |
| After a year | 16,58 | 45,34 | 32,2495 | 8,66377 | 1,93728 |

Figure 5: Table 5 :

**6**

| | Minimum | Maximum | M | ? | M |
|---|---|---|---|---|---|
| Present | 11,91 | 13,67 | 12,9110 | ,58862 | ,13162 |
| After a month | 7,20 | 35,00 | 15,7550 | 7,73791 | ,13284 |
| After 3 months | 6,50 | 30,20 | 12,9990 | 6,45318 | ,45710 |
| After 6 months | 3,75 | 11,76 | 7,1400 | 1,98844 | ,27012 |
| After a year | 5,35 | 17,25 | 12,7240 | 2,47147 | ,55264 |

Figure 6: Table 6 :

[Fedorovich et al. ()] *Detection of osteopenic syndrome in women with hypothyroidism // Successes of modern natural science. Appendix ? 2*, O K Fedorovich , V A Novikova , Karakhalisl , Yu , N N Vaskonian . 2014. p. .

[Fedorovich and Novikova ()] *Evaluation of the effectiveness of Calcium D3 -Nicomed-Forte in women with drug-induced hypoestrogenism*, O K Fedorovich , V A Novikova . 2013. p. .

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