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ANTIRESORPTIVE THERAPY FOR PREGNANCY- AND LACTATION-ASSOCIATED OSTEOPOROSIS


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ҲОМИЛАДОРЛИК ВА ЛАКТАЦИЯ ДАВРИ БИЛАН БОҒЛИҚ ОСТЕОПОРОЗНИНГ АНТИРЕЗОРБТИВ ТЕРАПИЯСИ

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АНТИРЕЗОРБТИВНАЯ ТЕРАПИЯ ОСТЕОПОРОЗА, СВЯЗАННОГО С БЕРЕМЕННОСТЬЮ И ЛАКТАЦИЕЙ

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Резюме. *Ҳомиладорлик ва лактация билан боғлиқ остеопороз (PLO) кам учрайдиган, аммо жиддий касаллик бўлиб, ҳомиладорликнинг учинчи триместрида ёки туғруқдан кейинги эрта даврда юзага келадиган, асосан умуртқа таналарининг кўплаб паст травматик синишлари билан тавсифланади. PLO учун асосий хавф омилларига D витамини етишмовчилиги, тана массаси индекси (BMI) пастлиги, кальцийни етарли даражада истеъмол қилмаслик, жисмоний фаолликнинг камлиги, чекиш ва бошқа ноқулай омиллар киради. Ҳомиладорлик ва лактация даврида нурланиш билан боғлиқ диагностика усулларини қўллаш чекланганлиги сабабли касалликни аниқлаш қийин кечади. Тадқиқотнинг мақсади — ҳомиладорлик ва лактация билан боғлиқ остеопорозни даволаш самарадорлигини баҳолаш. Тадқиқотга 18 ёшдан 40 ёшгача бўлган, PLO ташхиси қўйилган 27 нафар аёл жалб этилди. Барча беморларга лаборатор ва инструментал текширувлар ўтказилди, жумладан қонда кальций, фосфор, ишқорий фосфатаза, паратгормон (PTH), суяк ремоделланиш маркерлари (β-CrossLaps) аниқланди, шунингдек, икки энергияли рентген абсорбциометрияси (DEXA) ёрдамида суяк минерал зичлиги (BMD) баҳоланди. Даволаш фонида ишқорий фосфатаза фаоллиги, β-CrossLaps ва остеокальцин даражаларининг ишончли пасайиши кузатилди. Беморларнинг 45,2% да D витамини концентрацияси адекват даражага (≥30 нг/мл) етди. Умуртқа поғонасида BMD 13,6% га ошгани аниқланди, бунда 54,8% беморларда ўсиш клиник жиҳатдан аҳамиятли бўлди. Сон суяги бўйни соҳасида суяк минерал зичлиги 4,5% га ошди (чап бўйин: даволашдан олдин — 0,795±0,13 г/см²; даволашдан кейин — 0,804±0,13 г/см²; p=0,41), ижобий динамика 29,0% беморларда қайд этилди. Ўнг ва чап сон суякларида BMD мос равишда 4,6% ва 3,5% га ошган бўлиб, бу ўзгаришлар 29,0% ва 41,9% текширилганларда кузатилди. Ўнг сон суяги бўйнида эса 19,4% беморларда BMD 5,3% га ошгани аниқланди. Шундай қилиб, антирезорбтив терапия кальций ва D витамини препаратлари билан биргаликда ҳамда эмизишни тўхтатиш шароитида бел соҳасидаги кучли оғриқни камайтиради, суяк минерал зичлигини ишончли равишда оширади ва умуртқа синишларининг кейинги ривожланиш хавфини пасайтиради.*

Калит сўзлар: *ҳомиладорлик ва лактация билан боғлиқ остеопороз, антирезорбтив терапия, кальций-фосфор алмашинуви, суяк минерал зичлиги.*

Abstract. *Pregnancy- and lactation-associated osteoporosis (PLO) is a rare but serious condition characterized by multiple low-trauma fractures, primarily of the vertebral bodies, occurring in the third trimester of pregnancy or early*

postpartum. The main risk factors for PLO include vitamin D deficiency, low body mass index (BMI), inadequate calcium intake, low physical activity, smoking, and other adverse factors. Diagnosis is challenging due to restrictions on the use of imaging techniques during pregnancy and lactation. The aim of this study was to evaluate the effectiveness of treatment for pregnancy- and lactation-associated osteoporosis. The study included 27 women aged 18 to 40 years with a diagnosis of PLO. All patients underwent laboratory and instrumental studies, including determination of calcium, phosphorus, alkaline phosphatase, parathyroid hormone (PTH), bone remodeling markers (β-CrossLaps), and bone mineral density (BMD) assessment using dual-energy X-ray absorptiometry (DEXA). During therapy, a significant decrease in alkaline phosphatase activity, β-CrossLaps, and osteocalcin levels was noted. Vitamin D concentrations reached adequate levels (≥30 ng/ml) in 45.2% of patients. A 13.6% increase in spinal BMD was observed, with the increase being clinically significant in 54.8% of patients. Bone mineral density in the femoral neck increased slightly by 4.5% (left neck: before treatment 0.795±0.13 g/cm²; after treatment 0.804±0.13 g/cm²; p=0.41), with positive dynamics noted in 29.0% of patients. BMD of the right and left femurs increased by 4.6% and 3.5%, respectively, with an increase in indicators recorded in 29.0% and 41.9% of the examined patients. In the right femoral neck, an increase in BMD by 5.3% was detected in 19.4% of patients. Thus, antiresorptive therapy in combination with calcium and vitamin D preparations, as well as cessation of breastfeeding, help to reduce the severity of back pain, significantly increase bone mineral density and reduce the risk of further vertebral fractures.

***Keywords**: pregnancy- and lactation-associated osteoporosis, antiresorptive therapy, calcium-phosphorus metabolism, bone mineral density.*

Pregnancy- and lactation-associated osteoporosis (PLO) is a rare but serious condition characterized by multiple low-trauma fractures, primarily affecting the spine. Fractures typically occur in the third trimester of pregnancy or the early postpartum period [7; 11].

Women with PLO usually experience severe back pain. Risk factors for PLO include a history of fractures or osteoporosis, vitamin D deficiency, low body mass index (BMI), insufficient calcium intake, low physical activity, anticoagulant, and proton pump inhibitor therapy, elevated levels of parathyroid hormone-related protein, high bone turnover, and, finally, smoking [5; 8].

During pregnancy and lactation, women are generally not screened, as standard diagnostic methods involve radiation exposure, which is avoided due to potential fetal harm and postnatally due to the demands of newborn care [4].

Currently, there is no consensus on the optimal methods and medications for treating PLO. Existing treatment protocols are primarily based on postmenopausal osteoporosis management. Upon diagnosis of PLO, breastfeeding is generally recommended to be discontinued. Individualized pharmacological treatment should be administered based on pain severity, bone mineral density, bone remodeling markers, and pre-pregnancy health planning.

The aim of the study was to evaluate the outcomes of treatment for pregnancy- and lactation-associated osteoporosis (PLO).

Materials and Methods. The study included 27 women aged 18–40 years who were diagnosed with pregnancy- and lactation-associated osteoporosis.

For each patient, a standardized questionnaire was completed, documenting personal data, osteoporosis risk factors, laboratory findings, and instrumental examination results.

Laboratory biochemical tests included the measurement of total calcium, phosphorus, alkaline phosphatase, and parathyroid hormone (PTH) levels in blood as well as biochemical markers of bone remodeling—β-CrossLaps (analyzed using an ELECSYS automatic analyzer with electrochemiluminescent analysis and ELECSYS β-CrossLaps assay kits).

Bone mineral density (BMD) was assessed using dual-energy X-ray absorptiometry (DEXA) on a Prodigy bone densitometer (GE Lunar Corporation, USA). This method was also used to evaluate the effectiveness of the administered treatment.

Additionally, all women reporting back pain underwent magnetic resonance imaging (MRI) to determine the localization, number, and type of vertebral fractures. Women with confirmed vertebral fractures on MRI underwent bone histomorphometry.

Statistical analysis of the collected data was performed using IBM SPSS Statistics 23.0 software. The Kolmogorov-Smirnov test was used to check the normality of data distribution in each variable group. To identify differences between variables in different groups, nonparametric tests, including the Student's t-test and Mann-Whitney U test, were applied for two independent groups.

Results. Currently, commonly used medications include calcium and vitamin D, calcitonin, bisphosphonates, teriparatide, denosumab, etc. Calcium and vitamin D remain the mainstay of treatment.

Comparative laboratory test results of the studied women over time are presented in Figure 1.

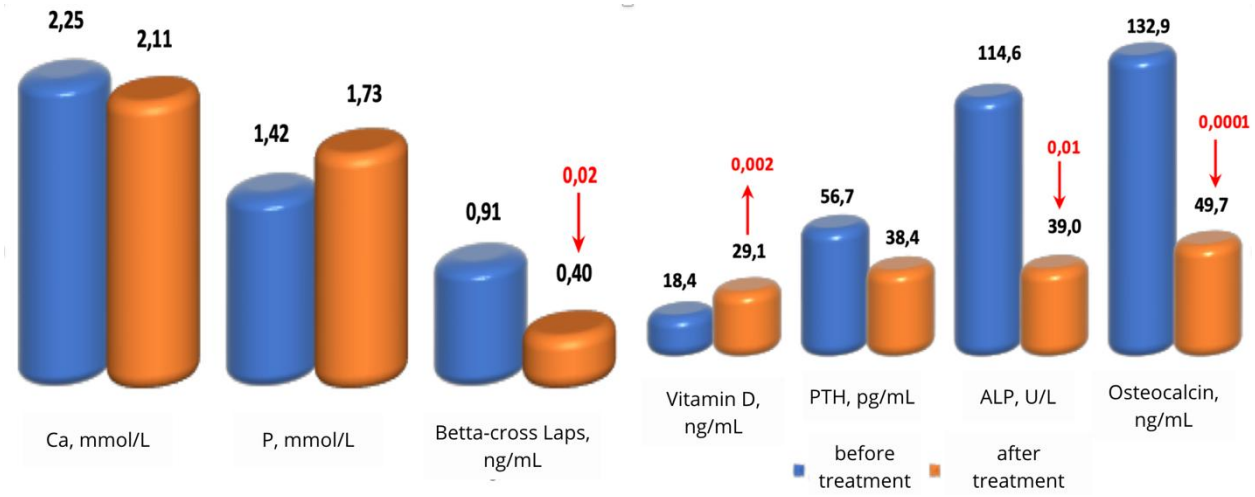

Fig. 1. Biochemical markers over time

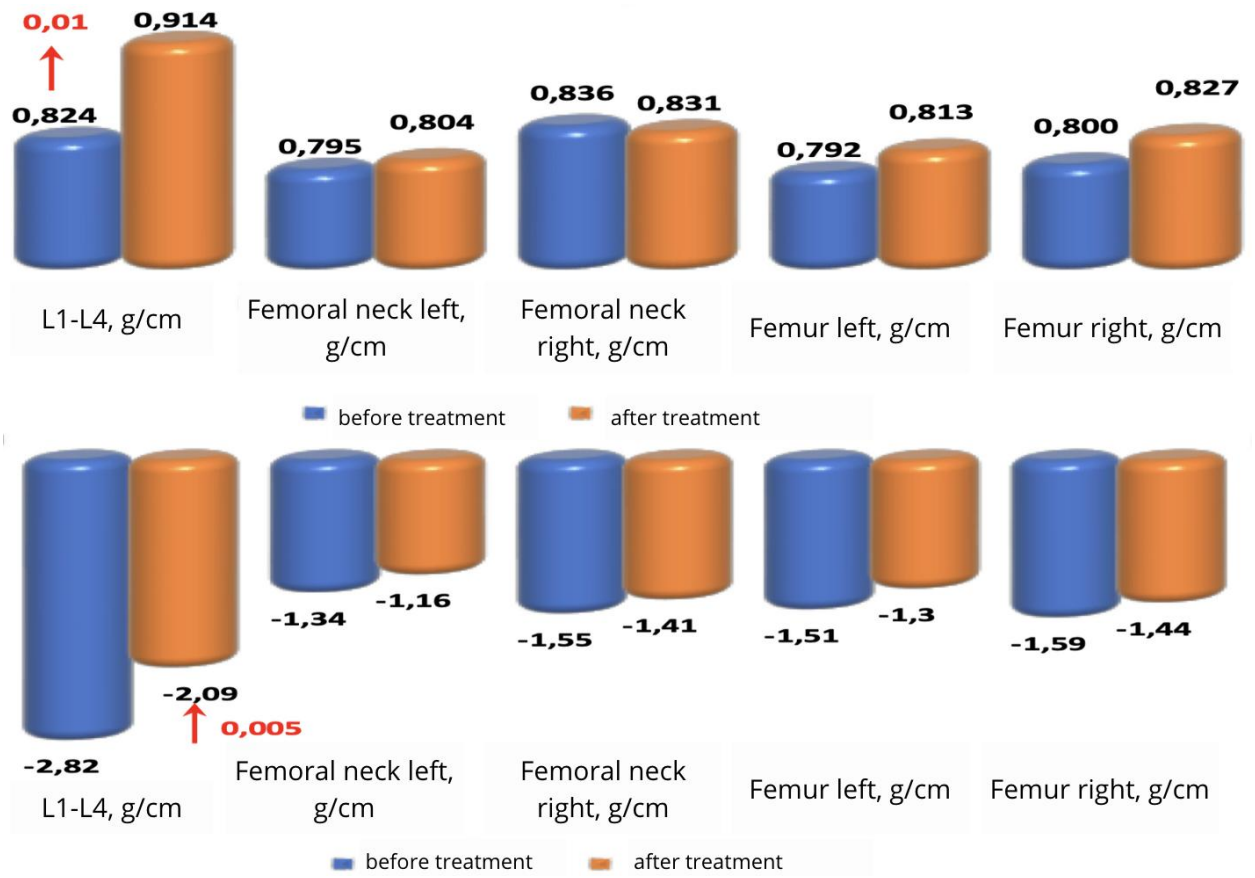

Fig. 2. DEXA parameters over time

Blood calcium levels (before treatment: 2.25±0.21 mmol/L; after treatment: 2.11±0.40 mmol/L; p=0.06) and phosphorus levels (before treatment: 1.42±0.50 mmol/L; after treatment: 1.73±3.67 mmol/L; p=0.36) did not change significantly after the course of treatment. However, calcium levels increased in 22.6% of patients, and phosphorus levels in 25.8%.

During therapy, a significant decrease in alkaline phosphatase activity was observed (before treatment: 114.6±27.4 U/L; after treatment: 38.99±31.7 U/L; p=0.01). The β-CrossLaps level (0.91±0.99 ng/ml) significantly decreased after treatment (0.40±0.41 ng/ml; p=0.02), along with a reduction in osteocalcin levels (before treatment: 132.9±66.1 ng/ml; after treatment: 49.7±37.4 ng/ml; p=0.0001).

The PTH level also decreased but not significantly (before treatment: 56.7±40.9 pg/ml; after treatment: 38.4±19.9 pg/ml; p=0.05).

In contrast, vitamin D levels increased significantly (before treatment: 18.4±7.93 ng/ml; after treatment: 29.1±17.1 ng/ml; p=0.002), although they did not reach the target range of 30–60 ng/ml. Almost half (45.2%) of the patients had adequate vitamin D levels (≥30 ng/ml) after treatment.

To assess bone mineral density (BMD), patients underwent a follow-up dual-energy X-ray ab-

sorptiometry (DEXA) scan, and the results are presented in Figure 2.

On therapy, a significant increase in spinal BMD was observed (before treatment: 0.824±0.12 g/cm²; after treatment: 0.914±0.10 g/cm²; p=0.01), with a substantial increase (by an average of 13.6%) in 54.8% of patients.

A slight increase (by 4.5%) in femoral neck BMD was noted (left femur: before treatment: 0.795±0.13 g/cm²; after treatment: 0.804±0.13 g/cm²; p=0.41), with BMD improvement in 29.0% of patients.

BMD of the right femur increased by 3.5% (before treatment: 0.800±0.10 g/cm²; after treatment: 0.827±0.10 g/cm²; p=0.22), with BMD improvement in 29.0% of patients.

BMD of the left femur increased by 4.6% (before treatment: 0.792±0.12 g/cm²; after treatment: 0.813±0.11 g/cm²; p=0.47), with BMD improvement in 41.9% of patients.

The mean BMD of the right femoral neck slightly decreased after therapy (before treatment: 0.836±0.20 g/cm²; after treatment: 0.831±0.12 g/cm²; p=0.28), but 19.4% of patients showed a 5.3% increase in BMD.

DEXA analysis revealed that the mean T-score of the sp ine significantly improved (before treatment: -2.82±0.95; after treatment: -2.09±0.83; p=0.005).

No significant differences were found in the T-score of the left femoral neck (before treatment: -1.55±0.92; after treatment: -1.41±0.97; p=0.31) or the right femur (before treatment: -1.34±0.79; after treatment: -1.16±0.91; p=0.27).

Similarly, the T-score of the left femur (before treatment: -1.59±0.96; after treatment: -1.44±0.93; p=0.30) and the right femur (before treatment: -1.51±0.75; after treatment: -1.30±0.81; p=0.23) did not show significant changes.

Discussion. Pregnancy- and lactation-associated osteoporosis (PLO) is a rare form of early osteoporosis in which young women develop fractures, typically multiple vertebral fractures, during late pregnancy or lactation [6].

It is generally observed that women with PLO have lower BMD and T-scores in the lumbar spine than in the femur [9].

Our study found that treatment resulted in a significant increase in spinal BMD by an average of 13.6%, with 54.8% of patients showing improvement.

Notably, patients treated with teriparatide (daily subcutaneous injections) in combination with calcium (1250 mg) and vitamin D3 (60,000 IU/day) showed significant improvements in bone mineral density (BMD). The BMD increase relative to baseline was 16.1% in the L1–L4 region, 12.7% in the left femoral neck, 7.2% in the right femur, and 9.3% in the left femur.

Raffaetà G. et al. [10] reported two cases of PLO. In one case, after treatment with risedronate (35 mg), calcium (1500 mg), and vitamin D3 (400 IU/day), BMD increased by 34% over two years and by 42% over four years.

According to Anagnostis P. et al. [1], teriparatide is the most commonly used anti-osteoporotic drug. Teriparatide therapy demonstrates an increase in lumbar spine BMD of 8.0–24.4% after 12 months, 7.4–36.0% after 18 months, 24.1–32.9% after 24 months, and 23.4–30.3% after 36 months. An increase in BMD of 3.9% to 12.6% (12 months), 3.7% to 13.8% (18 months), 8.4% to 18.6% (24 months), and 10.0% to 16.3% (36 months) has also been noted.

During pregnancy and lactation, especially in the third trimester, calcium demand increases, placing a strain on maternal calcium homeostasis. This increase is physiologically compensated by enhanced intestinal absorption, reduced urinary calcium excretion, and increased bone resorption [12].

It has been suggested that bone resorption in PLO may result from elevated secretion of parathyroid hormone-related protein (PTHrP) from the mammary gland during lactation [2]. Some researchers raise concerns about pre-existing osteopenia before pregnancy, which is difficult to verify due to the lack of data on PLO.

A positive family history of postmenopausal osteoporosis is observed more frequently in pregnancy-associated osteoporosis than in the control group. This may indicate the presence of a genetic component [3].

Conclusions. A significant decrease in alkaline phosphatase activity, β-CrossLaps, and osteocalcin levels was observed during therapy. In 45.2% of patients, vitamin D levels reached an adequate level (≥30 ng/ml).

An increase in spinal BMD by 13.6% was recorded, with 54.8% of patients showing a significant improvement. A slight increase (by 4.5%) in femoral neck BMD was observed (left femur: before treatment - 0.795±0.13 g/cm²; after treatment - 0.804±0.13 g/cm²; p=0.41). BMD improvement was noted in 29.0% of patients. BMD of the right and left femur increased by 4.6% and 3.5%, respectively, with increases observed in 29.0% and 41.9% of patients, respectively. In the right femoral neck, 19.4% of patients showed a BMD increase of 5.3%.

Anti-resorptive therapy, combined with calcium and vitamin D supplementation and simultaneous cessation of breastfeeding, appears to reduce severe back pain, significantly increase bone mineral density (BMD), and help prevent further vertebral fractures.

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АНТИРЕЗОРБТИВНАЯ ТЕРАПИЯ ОСТЕОПОРОЗА, СВЯЗАННОГО С БЕРЕМЕННОСТЬЮ И ЛАКТАЦИЕЙ

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Резюме. *Остеопороз, связанный с беременностью и лактацией (PLO), является редким, но серьёзным заболеванием, характеризующимся множественными низкотравматическими переломами, преимущественно тел позвонков, возникающими в третьем триместре беременности или в раннем послеродовом периоде. К основным факторам риска PLO относятся дефицит витамина D, низкий индекс массы тела (BMI), недостаточное потребление кальция, низкая физическая активность, курение и другие неблагоприятные факторы. Диагностика заболевания затруднена в связи с ограничениями на использование методов лучевой диагностики в период беременности и лактации. Цель исследования — оценить эффективность лечения остеопороза, связанного с беременностью и лактацией. В исследование были включены 27 женщин в возрасте от 18 до 40 лет с установленным диагнозом PLO. Всем пациенткам проведены лабораторные и инструментальные исследования, включавшие определение уровня кальция, фосфора, щелочной фосфатазы, паратгормона (PTH), маркеров костного ремоделирования (β-CrossLaps), а также оценку минеральной плотности костной ткани (BMD) методом двухэнергетической рентгеновской абсорбциометрии (DEXA). На фоне проводимой терапии отмечено достоверное снижение активности щелочной фосфатазы, уровня β-CrossLaps и остеокальцина. У 45,2% пациенток концентрация витамина D достигла адекватного уровня (≥30 нг/мл). Установлено увеличение BMD позвоночника на 13,6%, при этом у 54,8% пациенток прирост был клинически значимым. Минеральная плотность костной ткани в области шейки бедренной кости увеличилась незначительно — на 4,5% (левая шейка: до лечения 0,795±0,13 г/см²; после лечения 0,804±0,13 г/см²; p=0,41), при этом положительная динамика отмечена у 29,0% пациенток. BMD правой и левой бедренной кости увеличилась соответственно на 4,6% и 3,5%, повышение показателей зарегистрировано у 29,0% и 41,9% обследованных. В правой шейке бедренной кости у 19,4% пациенток выявлено увеличение BMD на 5,3%. Таким образом, антирезорбтивная терапия в сочетании с препаратами кальция и витамина D, а также прекращение грудного вскармливания способствуют уменьшению выраженности болевого синдрома в спине, достоверному повышению минеральной плотности костной ткани и снижению риска дальнейших переломов позвонков.*

Ключевые слова: *остеопороз, связанный с беременностью и лактацией, антирезобтивная терапия, кальций-фосфорный обмен, минеральная плотность костной ткани.*