

Treatment of osteoporosis in women with early menopause

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Abstract. The study showed that women with premature ovarian insufficiency and early menopause already at a young age develop a marked deterioration in bone quality, mainly by the type of osteopenia, and in some patients (11.9%) — osteoporosis.

In women of reproductive age with estrogen deficiency, basic hormone therapy prevents further bone loss, but osteoanabolic therapy is required to actively restore bone tissue with a more pronounced decrease in mineral density.

Keywords: osteoporosis, early menopause, osteoanabolic therapy

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Introduction. Early menopause is an urgent problem in modern medicine. Early menopause includes characteristic hormonal fluctuations and physiological changes that lead to loss of fertility in women. In addition, early menopause (<45 years) leads to premature and prolonged loss of estrogen, which causes a significant increase in the risk of cardiovascular diseases, osteoporosis (decreased bone mineral density), cognitive impairment (dementia) and premature mortality [1, 2]. Early menopause is a significant risk factor for osteoporosis due to the loss of the protective effect of estrogen on bone density [3]. Menopause has been known for many years as the most important risk factor for bone loss in middle-aged women. Women lose about 50% of their trabecular bone and 30% of their cortical bone during their lifetime, about half of which is lost during the first 10 years after menopause [4]. Although early menopause has been found to be associated with an increased risk of osteoporosis, however, its association with an increased risk of fractures has not been established, as research results are contradictory [5].

Treatment of early menopause is mainly based on hormone replacement therapy (HRT). The choice of HRT should mimic the normal production of steroid hormones by the ovaries as accurately as possible and ensure sufficient levels of estradiol to reduce menopausal symptoms, maintain bone density, minimize the psychological consequences of estrogen deficiency and protect against the early progression of cardiovascular diseases and dementia [6].

Combination therapy using estrofem (estradiol tablets) or divigel (estradiol transdermal gel) supplemented with progesterone is a standard, scientifically proven method of treating symptoms and preventing long-term risks (such as osteoporosis) during early menopause [7, 8].

The goal of any osteoporosis intervention is to prevent fractures. In our opinion, there should be no distinction between prevention and treatment, since the goal remains the same. Treatment of osteoporosis involves preventing fractures, rather than chasing bone mineral density targets. The US Federal Agency for Medicinal Products certifies drugs specific to bone tissue as intended for either prevention, treatment, or both purposes without clearly defining the difference [4].

The aim of the study was to evaluate the effect of various treatment regimens on bone quality indicators according to quantitative ultrasound densitometry in women with early menopause/premature ovarian insufficiency.

Materials and methods. The study included 101 women aged 22-45 years with an established diagnosis of early menopause or premature ovarian insufficiency (POI). All the patients signed an informed consent to participate in the study, which was conducted at the Family Planning Center.

Inclusion criteria: age 22-45 years; laboratory and clinically confirmed early menopause/ POI; lack of hormone therapy at the time of activation; the possibility of ultrasound densitometry.

Exclusion criteria: chronic diseases of the bone system (rheumatoid arthritis, osteosclerosis, etc.); taking drugs that

affect bone metabolism (glucocorticoids, bisphosphonates); severe somatic diseases; recent fractures or operations on the lower extremities; pregnancy and lactation.

The patients were divided into three treatment groups: Group I (n=38)— hormone replacement therapy (HRT) (oral estradiol) + omega-3 polyunsaturated fatty acids (PUFA); Group II (n=33) — HRT (transdermal estradiol) + Omega-3 PUFA; Group III (n=30) — HRT + teriparatide. Group III patients (n=30) receiving hormone replacement therapy in combination with teriparatide were further stratified into subgroups depending on the form of estrogen administration: subgroup IIIa (n=15) — oral estradiol+ teriparatide, subgroup IIIb (n=15) — transdermal estradiol + teriparatide. This division was of a clarifying nature and was aimed at assessing the possible effect of the form of HRT administration on bone tissue parameters. Given the comparability of the results between the subgroups ($p>0.05$), in further analysis they were considered as a single group. The content of vitamin D and parathyroid hormone (PTH) in the blood was determined by immunochemiluminescence analysis. Ionized calcium was measured by potentiometric analysis using ion-selective electrodes.

The bone tissue condition was assessed by quantitative ultrasound densitometry (QUS) on an Osteosys Sonost 2000 device (OsteoSys Co., Ltd., Korea) with calcaneal bone examination. Unlike dual-energy X-ray absorptiometry (DXA), ultrasound densitometry makes it possible to evaluate not only the mineral

density, but also the elastic and microarchitectural properties of bone tissue sensitive to early estrogen deficiency. The following parameters were determined:

-SOS (Speed of Sound, m/s) — reflects the density and elasticity of bone tissue

- BUA (Broadband Ultrasound Attenuation, dB/MHz) — characterizes the trabecular structure

- SI (Stiffness Index) — an integral bone quality indicator calculated based on the SOS and BUA parameters.

- T- and Z- score are relative indicators of deviation from the reference population.

The study was conducted before treatment and after 12 months of therapy.

Statistical processing was performed using the Statistica 16.0 program. The data is presented as Mean±SD. To assess the effect of treatment, a two-factor analysis of variance with repeated measurements (Repeated measures ANOVA: Group × Time factor) was used. If necessary, Tukey HSD post-hoc analysis was used. The differences were considered statistically significant at $p < 0.05$.

Conclusion of the Ethics Committee of Azerbaijan State Institute of Advanced Medical Education named after A. Aliyev. This study complies with ethical and legal norms, moral principles, and protects the rights and interests of participants. (Extract from Protocol No. 4 dated 17.02.2026 of Advanced Medical Education named after A. Aliyev)

Results and Discussion. The initial characteristics of the patients are presented in Table 1. The groups did not differ in age, vitamin D levels, PTH, and the initial degree of bone loss ($p > 0.05$), which allowed for further comparison of the effectiveness of therapy. The average amylin level was 31.66 ± 13.51 pmol/L, which corresponded to normal reference values in most of the examined patients.

After 12 months of follow-up, improvements in bone quality were noted in all groups, but the severity of the changes varied depending on the treatment regimen (Table 2).

The analysis of the initial values showed that the worst bone tissue parameters were observed in patients of group III: the values of SOS, BUA, SI and T-score were lower compared with groups I and II, which indicated a more pronounced deterioration in bone quality.

After treatment, there was an improvement in ultrasound densitometry parameters in all groups. The SOS, BUA, and SI values increased, and the T-score values became less negative, indicating an increase in bone mineral density.

The most pronounced positive dynamics was registered in group III: SOS increased from 1472.68 ± 18.18 to 1576.03 ± 22.85 m/s, BUA — from 37.47 ± 6.37 to 59.99 ± 0.51 dB/MHz, SI — from 60.08 ± 7.86 to 87.08 ± 0.51 , T-score — from 2.50 ± 0.35 to -1.32 ± 1.03 .

There was also an improvement in indicators in groups I and II, but the severity of the changes was significantly lower.

A two-factor analysis of variance with repeated measurements was performed (the intergroup factor was the treatment group, and the intragroup factor was the follow-up time) (Table 3).

Two-factor analysis of variance with repeated measurements revealed a significant time effect for all indicators ($p < 0.001$), which confirms the overall improvement of bone tissue after treatment. At the same time, a statistically significant group-time interaction ($p < 0.001$) was revealed, indicating different treatment efficacy in the groups.

Post hoc analysis (Tukey HSD) showed that the improvement in indicators in group III was statistically significantly greater than in groups I and II ($p < 0.001$), while there were no differences between groups I and II (Table 4).

For the BUA indicator, there were no intergroup differences in baseline levels ($p = 0.344$), but the differences in the dynamics of the indicator turned out to be highly significant ($p < 0.001$), which confirms the effect of therapy rather than the baseline differences.

An analysis of the magnitude of the changes showed that the greatest improvement in all parameters was noted in group III: the increase in SOS was

+103.34, BUA +22.51, SI +27.01 and T-score +1.177. In groups I and II, the improvements were comparable and significantly less pronounced.

The results obtained demonstrate that the examined women initially showed reduced bone quality according to quantitative ultrasound densitometry, most pronounced in group III, where the SI and T-score values corresponded to the osteopenic range. This confirms the well-known position that estrogen deficiency in premature ovarian insufficiency leads to accelerated bone remodeling with a predominance of resorption over bone formation and deterioration of bone microarchitectonics.

In all groups, after 12 months of treatment, a statistically significant improvement in ultrasound densitometry parameters (SOS, BUA, SI, and T-score) was revealed, reflecting the positive effect of therapy on the condition of bone tissue. However, the key result of the study was the presence of a reliable interaction of Group×Time factors for all indicators, indicating a different severity of the therapeutic effect depending on the treatment regimen used.

The most pronounced changes were registered in group III: The increase in SOS exceeded similar indicators in groups I and II by more than 3 times, SI — by almost 2 times, and the improvement in T-score reached a clinically significant level. This indicates not only a slowdown in bone resorption, but also a partial restoration of the mechanical properties of bone tissue. The absence of significant differences between groups I and II in the magnitude of changes indicates the comparable effectiveness of these treatment

Table 1

Initial characteristics of the groups before treatment

Indicator	Group I (n=38)	Group II (n=33)	Group III (n=30)
Age, years	37.58 ± 6.83	35.76 ± 6.58	36.1 ± 7.02
The degree of osteopenia/osteoporosis:			
The lower limit of the norm. n (%)	7 (18.4)	9 (27.3)	-
Osteopenia. n (%)	31 (81.6)	23 (69.7)	19 (63.3)
Osteoporosis. n (%)	-	1 (3.0)	11 (36.7)
Vitamin D	28.74 ± 8.13	27.94 ± 7.29	28.18 ± 7.95
PTH, pg/ml	67.07 ± 17.27	67.20 ± 14.20	70.93 ± 12.63
Ionized calcium	1.06 ± 0.11	1.14 ± 0.15	1.23 ± 0.32
SOS, m/s	1518.46 ± 16.56	1525.09 ± 22.02	1472.68 ± 18.18
BUA, dB/MHz	44.13 ± 7.23	46.05 ± 7.28	37.47 ± 6.37
BQI	77.84 ± 7.86	80.95 ± 8.98	60.08 ± 7.86
T-score	-1.44 ± 0.43	-1.28 ± 0.48	-2.5 ± 0.35
Z- score	-0.68 ± 0.44	-0.37 ± 0.57	-1.47 ± 0.52

regimens and suggests that their effect is mainly limited to the stabilization of bone remodeling.

The BUA indicator deserves special attention. Despite the absence of inter-group differences in the initial average values, the dynamics of the parameter significantly differed between the groups. Since BUA reflects mainly the trabecular structure of bone, the data obtained indicate the different effects of therapeutic approaches on the microarchitectonics of bone tissue, and not only on its density characteristics.

It should be emphasized that quantitative ultrasound densitometry evaluates the integral properties of bone — its elasticity, porosity, and structural organization. Therefore, the revealed improvement in indicators should be interpreted as an increase in the quality of bone tissue, and not solely an increase in mineral density. In this context, the pronounced positive dynamics of SI is of particular importance, since this indicator correlates with bone strength characteristics and fracture risk.

The results obtained are consistent with modern ideas about the key role of hormonal deficiency in the formation of early metabolic disorders of bone tissue and confirm the need for early initiation of therapy in women with early menopause / POI [10-13]. The more pronounced effect in group III is probably related to the complex effect of therapy on various parts of bone remodeling: suppression of osteoclastic activity, stimulation of osteoblasts and improvement of calcium metabolism.

It is important to note that the positive dynamics of the indicators was observed already during the first year of treatment, which indicates a high sensitivity of bone tissue to timely correction of hormonal deficiency. This is of clinical importance, since it is the first years after the onset of the hypoestrogenic condition that are characterized by the maximum rate of bone loss.

It should be noted that the available studies, although conducted on small samples, suggest a beneficial effect of combined HT on maintaining bone mineral density in women with early menopause./ POI [14-17].

The absence of statistically significant differences between oral and transdermal forms of estrogen administration both in groups I and II, and with additional analysis within group III, indicates the comparable effectiveness of these routes of administration in terms of effects on bone tissue. This has important clinical significance, allowing individualization of therapy taking into account the safety

Table 2

Dynamics of ultrasound densitometry (QUS) indicators in the study groups (M±SD)

Groups	Duration of treatment	SOS, m/s	BUA, dB/MHz	SI	T-score	Z- score
Group I (n=38)	Before	1518.46±16.56	44.13±7.23	77.84±7.86	-1.44±0.43	-0.68±0.44
	After	1552.54±21.45	53.30±3.94	94.40±4.92	-1.12±0.31	-0.61±0.40
Group II (n=33)	Before	1525.09±22.02	46.05±7.28	80.95±8.98	-1.28±0.48	-0.37±0.57
	After	1550.46±18.23	54.34±3.96	93.41±6.51	-0.97±0.30	-0.27±0.44
Group III (n=30)	Before	1472.68±18.18	37.47±6.37	60.08±7.86	-2.5±0.35	-1.47±0.52
	After	1576.03±22.85	59.99±0.51	87.08±0.51	-1.32±1.03	-1.13±0.33

Note: In group III, patients were divided into subgroups depending on the form of HRT administration (oral and transdermal); there were no statistically significant differences between the subgroups ($p>0.05$), and therefore the data are presented collectively.

Table 3

Results of two-factor analysis of variance with repeated measurements (Group × Time)

Indicator	Effect	F (df)	p	partial η^2
SOS	Group	F(2.93)=6.170	0.003	0.117
	Time	F(1.93)=468.828	<0.001	0.834
	Group×Time	F(2.93)=94.566	<0.001	0.670
BUA	Group	F(2.98)=1.080	0.344	0.022
	Time	F(1.98)=496.167	<0.001	0.835
	Group×Time	F(2.98)=59.558	<0.001	0.549
SI	Group	F(2.98)=39.788	<0.001	0.448
	Time	F(1.98)=549.128	<0.001	0.849
	Group×Time	F(2.98)=28.485	<0.001	0.368
T-score	Group	F(2.98)=25.109	<0.001	0.339
	Time	F(1.98)=108.379	<0.001	0.525
	Group×Time	F(2.98)=25.711	<0.001	0.344

Table 4

Changes in ultrasound densitometry parameters (Δ post-pre, 95% CI)

Indicator	Group I	Group II	Group III
SOS	+36.15 [28.54; 43.75]	+25.36 [15.94; 34.78]	+103.34 [94.28; 112.41]
BUA	+9.17 [7.78; 10.56]	+8.29 [6.02; 10.56]	+22.51 [20.00; 25.03]
SI	+16.56 [14.34; 18.78]	+12.45 [10.39; 14.52]	+2.01 [23.04; 30.98]
T-score	+0.316 [0.249; 0.383]	+0.315 [0.215; 0.415]	+1.177 [0.825; 1.528]

Примечание. По Tukey HSD группа III > I и II ($p<0.001$), различий I-II нет.

profile and concomitant risk factors without loss of effectiveness.

Conclusion. The study showed that women with premature ovarian insufficiency and early menopause develop a marked deterioration in bone quality at a young age, mainly by the type of osteopenia, and in some patients (11.9%) — osteoporosis. The greatest effectiveness was noted when using a combination of hormone replacement therapy with teriparatide, in which the

maximum increase in SOS, BUA and SI indicators was recorded, as well as the most pronounced improvement in the T-test. In the groups of patients treated with HRT + omega-3 PUFA, bone tissue stabilization and moderate improvement were observed, however, the addition of the osteoanabolic drug teriparatide led to a significantly more pronounced restoration of bone microarchitectonics. Ultrasound densitometry is an effective method of monitoring therapy and can

be used to personalize the prevention of osteoporotic fractures.

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Variability of mortality risk among women aged 15–29 in the regions of Azerbaijan

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Abstract. An analysis of medical death certificates for women aged 15-29 years was conducted, collected by covering all cases for 2020, 2021, 2022 and 2023 (242, 303, 298 and 293 cases, respectively). The material was grouped by administrative districts and cities (places of permanent residence), united in the form of economic districts (12 economic districts in total). The mortality rate was calculated per 100,000 women aged 15-29 years. In the cities of republican subordination, the indicator ranged from 14.5 ± 5.5 to 43.0 ± 21.500000 . The mortality rate of women aged 15-29 in Azerbaijan is 26.6 ± 1.500000 . In its regions, it ranges from 9.9 ± 4.4 to 36.0 ± 18.000000 , the differences in indicators in administrative districts, cities and economic regions are significant.

Keywords: variability, mortality risk, woman, age, region

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