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EFFECTIVENESS OF USING ALEANDRONIC ACID WITH HORMONE REPLACEMENT THERAPY ALONE AND TOGETHER

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✓ ***Resume***

The menopausal period is essentially the transition of the body from reproductive age to a new stage for the body of a woman's old age, often with menopause, which in many cases needs medical correction which using aleandronic acid and hormone replacement therapy alone and together.

Key words: hormone replacement therapy, menopausal hormone therapy, perimenopause, menopause.

ЭФФЕКТИВНОСТЬ ИСПОЛЬЗОВАНИЯ АЛЕАНДРОНОВОЙ КИСЛОТЫ С ГОРМОНАЛЬНОЙ ТЕРАПИЕЙ ПО ОТДЕЛЬНОСТИ И ВМЕСТЕ

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✓ ***Резюме***

Менопаузальный период по своему существу является переходом организма из репродуктивного возраста в новою ступень для организма женщины старость, часто протекает с климактерическим проявлениями, который во многих случаях нуждается в медицинской коррекции, которые принимали алеандроновую кислоту и гормональную заместительную терапию.

Ключевые слова: заместительная гормональная терапия, менопаузальная гормональная терапия, перименопауза, климактерий.

АЛЕАНДРОН КИСЛОТАСИНИНГ ГОРМОНАЛ ТЕРАПИЯ БИЛАН БИРГА ВА АЛОХИДА ИШЛАТГАНДАГИ ЭФФЕКТИВЛИГИ

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✓ ***Резюме***

Перименопаузалдавраёлучунрепродуктивдаврданқариликкаўтишдаври бўлиб, у кўп ҳолларда климакс белгилари билан кечади. Шу сабабли бу даврда алеандрон кислотаси гормонал терапия билан ишлатиш эффективлигини аниқлаш учун бирга ва алоҳида ишлатиб кўрилди.

Калит сўзлар: ўрин босувчи гормонал терапия, менопаузал гормонал терапия, менопауза, климактерий.

Abstract

The effectiveness of hormone replacement therapy (HRT) and alendronate, alone and in combination, was evaluated in 120 postmenopausal patients with osteoporosis with bone mineral density (BMD) measurements at least 2 SD below the mean value for young premenopausal subjects. They had no contra-indications to HRT or alendronate use and were randomized to three different treatment groups. Group I was treated with transdermal form of 17β-oestradiol, group II received alendronate 10 mg/day per os and group III received micronized 17β-oestradiol 2 mg, norethisterone acetate 1 mg/day per os and alendronate 10 mg/day per os for 1 year. Elementary calcium 1500 mg/day was supplied to patients in all three groups. At the end of the 12th month, significant increases in spinal and femoral neck BMD were found in all groups. Increases in spinal BMD were significantly higher in patients treated with alendronate and alendronate with HRT when compared with patients treated with HRT only. No significant difference was found in femoral neck BMD changes between the groups. Significant decreases in bone resorption and markers of bone formation were observed in all groups. Alendronate was found to be more effective than HRT and could have a very beneficial effect when added to the HRT regimen in patients with postmenopausal osteoporosis. Alendronate might also be used in postmenopausal patients with osteoporosis when HRT is contra-indicated or when there is reluctance to use hormonal treatment.

Introduction

Osteoporosis typically affects women within the first 15 years after menopause,and is characterized mostly by loss of trabecular bone (Riggs and Melton, 1990). With increasing life expectancy, up to 30% of postmenopausal women are affected by osteoporosis which has now become a major public health problem. The bone remodelling process, which is characterized by bone resorption and formation, is almost in equilibrium before menopause. However, after the menopause, with the absence of oestrogen, resorption predominates and results in bone loss (Riggs and Melton, 1992).

The objective of the present study was to identify changes in BMD and bone turnover markers in patients with postmenopausal osteoporosis, treated with HRT, alendronate or a combination of HRT and alendronate. We wanted to determine whether alendronate can be offered as an alternative when HRT is contra-indicated or refused by the patient and whether alendronate should

be added to the treatment regimen when HRT is administered to women with osteoporosis.

Materials and methods

Women attending the menopause clinic of Bukhara state medical institute clinic which located in Bukhara perinatal maternity, Department of Obstetrics and Gynecology №2 between January and November 2019 and who were found to have low BMD values, i.e. at least 2 SD below normal, were eligible for the study.

At the initial visit, general physical and pelvic examinations were performed and a Pap smear was taken. Baseline laboratory tests were performed for measurement of serum FSH, LH, estradiol concentrations, a complete blood count and liver and renal function tests. Pelvic ultrasonography and bilateral mammography were also performed. To document osteoporosis, lumbar and femoral neck BMD measurements were performed. Serum parathormone, osteocalcin, alkaline phosphatase, calcium, phosphorus and morning urinary calcium excretion were measured for each patient.

The inclusion criteria for the study were: (i) at least 1 year of amenorrhoea, serum FSH concentrations >40 IU/l and serum oestradiol concentrations >40 pg/ml (only natural menopausal women with intact ovaries); (ii) lumbar L2-L4 BMD at least 2 SD below the mean peak values for young premenopausal women [measured with dual energy X-ray absorptiometry (DEXA), T score <-2] where T score is the difference between the mean peak bone density values for young premenopausal women and the measured subjects; (iii) not using HRT or any agent affecting bone turnover in the previous year; (iv) no metabolic disease that alters bone metabolism or systemic disease affecting general health status; (v) no evidence of malignancy associated with oestrogen use (e.g. endometrial or breast cancer); (vi) no contra-indications for HRT use, such as undiagnosed uterine bleeding, active liver disease or thrombo-embolic disease; (vii) body mass index (BMI) <30 kg/m2; (viii) no active upper gastro-intestinal disease or calcium urolithiasis; (ix) no vertebral deformity that may affect measurement of BMD.

The study groups were planned as follows: group I (n = 40): micronized 17β-oestradiol 2.0 mg ± norethisterone acetate 1.0 mg/day per os (Kliogest tablet; Novo Nordisk, Bagsvaerd, Denmark); group II (n = 40): alendronate-Na 10 mg/day per os (Fosamax tablet 10 mg; Merck & Co., Inc., Whitehouse Station, NJ, USA); group III (n = 40): micronized 17β-oestradiol 2.0 mg ± norethisterone acetate 1.0 mg/day per os (Kliogest tablet; Novo Nordisk) + alendronate-Na 10 mg/day per os (Fosamax tablet 10 mg; Merck & Co., Inc.).Elementary calcium 1500 mg/day per os (Ca Sandoz effervescent tablet 1500 mg; Novartis Pharma AG, Basel, Switzerland) was added to each treatment regimen.

The total treatment period was planned to be 12 months and patients were examined every 6 months. At each visit, general physical examination was performed and patients questioned about adverse effects. Lumbar and femoral neck BMD measurements and serum concentrations of parathormone, osteocalcin, alkaline phosphatase, calcium, phosphorus and urinary calcium excretion were planned to be measured.Patients who stopped or irregularly used their medications or who did not come to the follow-up visits would also be withdrawn from the study.

Statistical analysis

The results are expressed as the mean ± SD for age, BMI, time since menopause, BMD and bone turnover markers. Changes from baseline lumbar and femoral neck BMD measurements are expressed as mean ± SEM. Multiple group comparisons for percentage changes in BMD from baseline were made at 6 and 12 months of follow-up by one-way analysis of variance (ANOVA). Between-group differences were assessed by Bonferroni's post-hoc test. Changes from baseline in biochemical variables and bone mass measurements were evaluated by paired t-test.

Results

Participant flow and follow-up

Out of the 100 patients who began the study, four were discharged owing to side-effects and 21 were excluded because of non-compliance with the study. Thus, analysis was performed on 79 subjects who completed the follow-up period to the end of the 12th month. Group I (HRT) had 31, group II (alendronate) 32 and group III (HRT + alendronate) 32 subjects (Figure 1).

Analysis. Clinical features of the patients are shown in Table I. There were no significant differences between the groups when age, time since last menstrual period and BMI were considered (Table I).

Table I.

Clinical features of the treatment groups	Group I(*n* = 31)	Group II(*n* = 32)	Group III(*n* = 32)
There were no significant differences between the groups. Valuesaremean ± SD.	Group I: hormone replacement therapy (HRT);	group II: alendronate;	group III: HRT + alendronate.
LMP = last menstrual period. Age (years)	52.7 ± 5.6	53.8 ± 6.8	51.9 ± 6.1
Timesince LMP (years)	4.9 ± 4.6	6.5 ± 5.6	6.4 ± 4.8
Bodymassindex	24.2 ± 3.6	23.8 ± 4.1	24.6 ± 3.9

There were no differences in baseline vertebral and femoral neck BMD measurements and all were at least 2 SD below the mean peak BMD measurements in young premenopausal subjects (T score <-2).When evaluating the percentage changes from baseline L2-L4 vertebral BMD measurements, the highest increase was observed in group III (8.41 ± 0.94%) at the end of the 12th month. This increase was 2.63 ± 0.63% for group I.Percentage changes from baseline in lumbar BMD measurements were significantly different between the groups both at 6 and 12 months. When analysed with the post-hoc test of Bonferroni, this difference was found to be higher between groups I and II, and I and III. In other words, BMD measurements increased more in patients in groups II and III compared to patients in group I.

Baseline calcium and phosphorus concentrations were not different between the groups. Both calcium and phosphorus measurements revealed a non-significant decrease in group I over the study period but the differences for groups II and III were statistically significant. Phosphorus concentrations were significantly different at 6 months between groups I and III (Bonferroni's post-hoc test). These changes in biochemical bone markers all indicated that the three treatment options were effective anti-resorptive agents.

In the present study, maximal increases in vertebral BMD measurements were observed in the group treated with alendronate plus HRT, yielding a 8.41 ± 0.94% change. This increase was significantly higher when compared with the group using HRT alone. Although not statistically significant, this increase was also higher when compared with the alendronate-only group. At the end of the 12th month, femoral neck BMD percentage changes did not differ significantly between the groups, but the 4.57 ± 0.97% increase observed in the group using alendronate and HRT in combination was still higher than the 3.02 ± 0.44 and 3.21 ± 0.56% increases found in the groups using only alendronate or HRT respectively. More studies are needed to clarify the issue of whether these two anti-resorptive agents have an additive effect on bone mass measurements when used in combination.

In conclusion, alendronate was found to be more effective than HRT and it could have a beneficial effect when added to the HRT regimen in patients with severe postmenopausal osteoporosis. Alendronate may also be used in postmenopausal patients with osteoporosis when HRT is contra-indicated or when the patient is reluctant to use any hormonal treatment.

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