Is Weekly Supplementation of Vitamin D Favorable for Treatment of Osteoporosis in Postmenopausal Women?

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OBJECTIVE: The present study aims to determine whether once weekly supplementation of vitamin D and alendronate is efficient and safe for treatment of postmenopausal osteoporosis.

STUDY DESIGN: Group I (42 women with postmenopausal osteoporosis) received daily supplementation of calcium (1000 mg) and vitamin D (880 IU) while group II (42 women with postmenopausal osteoporosis) had weekly supplementation of vitamin D (2800 IU) along with weekly treatment of alendronate (70 mg).

RESULTS: Group I had significantly lower lumbar spine T-scores before and after treatment. Post-treatment lumbar spine T-scores and femur neck T-scores were significantly higher with respect to pre-treatment scores in both study groups. The alterations in lumbar spine and femur neck T-scores were statistically similar in both group I and group II.

CONCLUSION: Once weekly administration of vitamin D and alendronate is an effective and safe option of treatment for women who cannot take calcium supplements for postmenopausal osteoporosis.

Key Words: Calcium, Osteoporosis, Postmenopausal, Vitamin D

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Introduction

Osteoporosis is a disease affecting many millions of people around the world. It is characterized by low bone mass and micro-architectural deterioration of bone tissue, leading to bone fragility and a consequent increase in risk of fracture.[1]

A number of studies of Vitamin D and calcium supplementation, alone or combination, have shown positive influence on femoral bone mineral density, thus decreasing the risk of osteoporotic fracture later in life. Calcium supplementation, aiming at a total calcium intake of at least 1500 mg/day, has a partial protective effect on postmenopausal bone loss, this effect being documented mainly in women more than 5 years after menopause. It is now widely accepted that prescribing appropriate calcium and vitamin D intake is an important clinical strategy, whether or not other medications are also recommended.[1-5]

It is now possible to measure bone mass with highly precise, safe and noninvasive technology. Dual energy X-ray absorptiometry (DXA) can detect bone loss well before it becomes evident by conventional X-rays or by fracture. Because measurement of bone density is the single most important predictor of fracture risk, it is a critically important to perform it on the population at risk, which includes women who have definable risk factors for osteoporosis, such as menopause, as well as those with a family history of osteoporosis, life-long low calcium intake, smoking, extreme thinness, anorexia, certain diseases and medications.[6-10] The prevention of bone loss associated with menopause and aging and maintenance of bone mineral content by means of calcium and vitamin D supplementation provide important opportunities for the prevention of osteoporosis and fractures.[1-10]

The present study aims to determine whether once weekly supplementation of vitamin D and alendronate is efficient and safe for the prevention of postmenopausal osteoporosis and whether it can be used to replace daily supplementation of calcium and vitamin D along with once weekly administration of alendronate.

Material and Method

The present study was approved by the Institutional

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Review Board and Ethical Committee of Bakirkoy Dr. Sadi Konuk Education and Research Hospital where the study was undertaken.

This study was designed as a randomized study which aims to determine whether once weekly supplementation of vitamin D and alendronate is efficient and safe for the prevention of postmenopausal osteoporosis and whether it can be used to replace daily supplementation of calcium and vitamin D along with once weekly administration of alendronate. Due to ethical considerations, neither a control group nor a placebo group was constituted.

Subjects

A total of 84 Turkish women (age range: 45-75 years) who were diagnosed with postmenopausal osteoporosis were included in the present study. Written informed consent was obtained from each participant.

Women were excluded if their spine bone mineral density was more than two standard deviations or below the normal peak bone mineral density or if they had a history of nontraumatic spine or hip fracture. Women with disorders of bone mineral metabolism were also excluded, as well as those with recent (within one year of study entry) major gastrointestinal disease such as peptic ulcer, esophageal disease, and malasorption. Other exclusion criteria were previous treatment with bisphosphonates or fluoride (>1 mg/day) or treatment within 12 months of enrolment with estrogen, progestin, calcitonin, glucocorticoids, anticonvulsant agents, phosphate-binding antacids, or excessive vitamin A or vitamin B.

The women who regularly used (>four times per week) any treatment that might cause gastrointestinal irritation (such as aspirin), women who smoked more than 20 cigarettes per day, or drank three or more alcoholic beverages per day were also excluded.

Treatment

The participants were randomly assigned into two groups. Group I(n=42) received daily supplementation of calcium (1000 mg) and vitamin D (880 IU) along with once weekly treatment of alendronate (70 mg). Group II (n=42) had once weekly supplementation of vitamin D (2800 IU) and alendronate (70 mg).

Follow Up

At baseline physical examination, vital signs were measured and any new worsening symptom was recorded. After standard laboratory evaluation (including evaluation of haematological, renal, and liver function) was accomplished, total body bone mineral density and bone mineral content were assessed. The same assessment was repeated at 12 months later. Dual-energy X-ray absorptiometry (DXA) measurements were performed using a total body scanner (Model QDR 4500, Hologic, Bedford, MA, USA). Total body and segmental (spine, arms, legs, trunk) bone mineral density and bone mineral content was measured by dual energy X-ray absorptiometry (DXA), scans were performed, providing data on fat tissue (kg), lean tissue (kg), and bone mineral content (kg). The fat-free mass from DXA was calculated as the sum of lean tissue and bone mineral content. The body fat percentage from DXA was calculated as fat tissue/body weight.

Statistical Analysis

Collected data were analyzed by Number Cruncher Statistical System and Power Analysis and Sample Size programs in computerized media. Data were expressed as mean±standard deviation or number (percentage), where appropriate. The continuous variables of the two groups were compared by student t test if the variables had normal distribution. However, Mann-Whitney-U test was used when the continuous variables of the two groups had abnormal distribution. Paired sample t-test was used to compare the continuous variables of the same group. Categorical variables were compared by chi-square test. $P<0.05$ was accepted to be statistically significant.

Results

The present study reviews 84 Turkish women who were diagnosed with postmenopausal osteoporosis. The mean age of these women was computed to be 54.95±7.44 (range: 45-75 years). The first group of participants (Group I, n=42) received daily supplementation of calcium (1000 mg) and vitamin D (880 IU) while the second group (Group II, n=42) had weekly supplementation of vitamin D (2800 IU) along with once weekly treatment of alendronate (70 mg).

Table 1 compares the demographic features of women who were randomly assigned into group I and group II. Accordingly, both study groups were statistically similar in aspect of age, duration of menopause, parity and body mass index.

Table 2 demonstrates the lumbar spine T-scores of the women who were recruited into group I and group II. When compared with group II, group I had significantly lower lumbar spine T-scores before and after treatment. Post-treatment lumbar spine T-scores were significantly higher with respect to pre-treatment scores in both study groups. The alteration in lumbar spine T-score was statistically similar in both group I and group II.

Table 3 shows the femur neck T-scores of the women who were randomly allocated into group I and group II. Group I and group II were statistically similar in aspect of pre-treatment and post-treatment femur neck T-scores. Post-treatment

femoral neck T-scores were significantly higher with respect to pre-treatment scores in both study groups. The alteration in femoral neck T-score was statistically similar in both group I and group II.

Neither of the participants gave up the prescribed treatment and no side effects occurred. Hpercalcemia or hypercalciuria was noticed in neither of the recruited women.

Discussion

Alendronates have been commonly used for the prophylaxis and treatment of female or male osteoporosis as well as prevention and treatment of corticosteroid-associated osteoporosis together with supplements of calcium and vitamin D. For instance, Cecilia et al. adopted the triple regimen of alendronate (70 mg, once weekly), calcium (500 mg/day) and vitamin D (400 IU/day) for postmenopausal osteoporosis in 239 women. Thus, femoral neck T-score increased by 2.6%.[11]

It has been previously reported that weekly administration of alendronate for one year caused an increase of 5% in lumbar spine T-score and 2.4% in femur neck T-score.[12-17] A meta-analysis of 9360 women with postmenopausal osteoporosis indicated that administration of 5 mg alendronate for two years increased lumbar spine T-score by %5.8 and femur neck T-score by %3.4. On the other hand, administration of 10-40 mg alendronate for two years increased lumbar spine T-score by 7.5% and femur neck T-score by 4.3% .[18] Alendronate Once-Weekly Study Group observed statistically similar alterations in both lumbar spine and femur neck T-scores of the postmenopausal women who were treated with either 10 mg alendronate once daily or 70 mg alendronate once weekly.[13] Later, the same study group noticed statistically similar alterations in both lumbar spine and femur neck T-scores of the postmenopausal women who received either 70 mg alendronate once weekly or 35 mg alendronate twice weekly.[19]

In order to evaluate the safety and tolerability of an additional 2800 IU vitamin D3 single tablet supplement, Binkey et al. conducted a randomized, 15-week-long, double-blind

Table 1: Demographic Features of Women with Postmenopausal Osteoporosis

	Group I (n=42) Mean±SD (Median)	**Grup II (n=42) Mean±SD (Median)**	***p***
+Age (years)	55.28±7.93	54.50±6.84	***0.656***
++Menopause (years)	9.21±7.31 (6)	8.00±5.03 (7)	***0.771***
++Parity	3.26±1.70 (3)	3.22±1.62 (3)	***0.896***
+Body mass index (kg/m^2)	27.04±4.53	27.29±3.63	***0.795***

+Student t test ++ Mann Whitney U test

Table 2: Lumbar Spine T Scores of Women with Postmenopausal Osteoporosis

Lumbar Spine T Scores	**Group I (n=42) Mean±SD (Median)**	**Group II (n=42) Mean±SD (Median)**	***p***
Pre-treatment+	0.72±0.05	0.75±0.06	***0.018****
Post-treatment+	0.75±0.06	0.80±0.08	***0.012****
Alteration ++***p***	***0.001****	***0.001****	
Alteration (%)+++	4.95±6.28 (4.39)	6.00±6.99 (4.84)	***0.520***

+Student t test ++ Paired sample t test +++Mann Whitney U test
** p<0.05 ** p<0.01*

Table 3: Femur Neck T Scores of Women with Postmenopausal Osteoporosis

Femur Neck T Score	**Group I (n=42) Mean±SD (Median)**	**Group II (n=42) Mean±SD (Median)**	***+p***
Pre-treatment	0.66±0.11	0.69±0.09	***0.208***
Post-treatment	0.68±0.11	0.71±0.08	***0.180***
Alteration ++***p***	***0.003****	***0.024****	
Alteration (%)+++	3.23±6.08 (2.39)	3.36±10.56 (3.92)	***0.570***

+Student t test ++ Paired sample t test +++Mann Whitney U test
*** p< 0.01*

study on a cohort of men and postmenopausal women. They reported that supplementation of vitamin D3 (2800 IU) alongside with once weekly administration of alendronate (70 mg) and cholecalciferol (2800 IU) for 24 weeks was favorable and caused no serious side effects related with hypercalcemia and hypercalcuria. Therefore, the authors concluded that this triple combination was sufficient to meet the minimal requirement of vitamin D and, thus, could be used to treat postmenopausal osteoporosis effectively and safely.[16]

Similarly, Recker et al. designed a 15-week-long, randomized, double-blind, multi-center, active-controlled study over 35 men and 682 postmenopausal women who avoided sunlight and vitamin D supplementation. Consequently, it was demonstrated that once weekly tablet containing alendronate and cholecalciferol provided equivalent antiresorptive efficacy, reduced the risk of low serum 25OHD, improved vitamin D status over 15 weeks, and was not associated with hypercalcemia, hypercalciuria or other adverse findings, versus alendronate alone in osteoporosis patients who avoided sunlight and vitamin D supplements.[17]

Osteoporosis Research Advisory Group conducted an extensive meta-analysis which included 15 clinical studies that reviewed 1806 women with postmenopausal osteoporosis. This meta-analysis found out that solitary supplementation of calcium only mildly improved the bone mineral density in postmenopausal women.[3,20] On the other hand, calcium supplementation is contraindicated in case of hypersensitivity, hypercalcemia, hypophosphatemia, nephrolithiasis, hypercalciuria, renal impairment and hyperparathyroidism as well as gastrointestinal bleeding and obstruction.[3]

The present study aims to determine whether once weekly supplementation of vitamin D along with alendronate is efficient and safe for the prevention of postmenopausal osteoporosis and whether it can be used to replace daily supplementation of calcium and vitamin D along with once weekly administration of alendronate. Therefore, 84 women with postmenopausal women were randomly assigned into two groups that were statistically similar in aspect of age, body mass index, parity and duration of menopause. The first group received daily supplementation of calcium (1000 mg) and vitamin D (880 IU) while the second group (Group II, n=42) had weekly supplementation of vitamin D (2800 IU) along with weekly treatment of alendronate (70 mg).

The present study points out that lumbar spine T-score has increased by 5% in group I and by 6% in group II after 12-month-long treatment of once weekly alendronate (70 mg). Much alike, femoral neck T-score has increased by 3.3% in group I and 3.4% in group II after 12-month-long treatment of once weekly alendronate (70 mg). Thus, the gain in bone mineral density of lumbar spine and femoral neck complies with literature. The more obvious increase in bone mineral density of lumbar spine can be attributed to the fact bone turnover is relatively more rapid in trabecular bone tissue with regard to cortical bone tissue.[9]

The findings of the present study indicate that the improvement in bone mineral density of lumbar spine and femoral neck was statistically similar in women who received daily supplementation of calcium and vitamin D and once weekly supplementation of vitamin D along with once weekly alendronate treatment. Moreover, no side effects related with hypercalcemia or hypercalciuria occurred. Therefore, it can be suggested that once weekly administration of vitamin D and alendronate is an effective and safe option of treatment for women who are diagnosed with postmenopausal osteoporosis and who cannot take calcium supplements.

To the best of our knowledge, the present study is the first to specify the efficiency of weekly vitamin D treatment in the prevention of postmenopausal osteoporosis. This study reviews a homogeneous study cohort that included only women with postmenopausal osteoporosis. The recruited subjects were randomly assigned into two study groups that were matched for age, body mass index and duration of menopause. However, the present study has some limitations. First of all, the study cohort is relatively small when compared with the previously published studies. Secondly, the basal lumbar spine T-scores of women in group I were significantly lower than those of women in group II. That's why; the alteration in bone mineral density of lumbar vertebras after one-year-long treatment could be biased. Further research is warranted for better understanding of once weekly replacement of vitamin D.

Haftada Bir Uygulanan Vitamin D Desteği Postmenopozal Osteoporoz Tedavisinde Yeterli mi?

AMAÇ: Sunulan çalışma, haftada bir uygulanan vitamin D ve alendronat tedavisinin postmenopozal osteoporoz tedavisinde etkin ve güvenilir olup olmadığını belirlemeyi amaçlamaktadır.

GEREÇ VE YÖNTEM: Bu çalışmada, postmenopozal osteoporozu olan 42 kadına haftada bir alendronat (70 mg) ile birlikte günlük kalsiyum (1000 mg) ve vitamin D (880 IU) uygulanırken postmenopozal osteoporozu olan 42 kadına haftada bir alendronat (70 mg) ve vitamin D (2800 IU) verilmektedir.

BULGULAR: Grup II olgularla karşılaştırıldığında, grup I olgularda tedavi öncesi ve sonrası lumbar T skorları anlamlı olarak düşüktü. Her iki çalışma grubunda da, tedavi öncesi skorlarla kıyaslandığında, tedavi sonrası lumbar ve femur boynu T skorları anlamlı olarak yüksek bulundu. Grup I ve grup II, lumbar ve femur boynu T skorlarında meydana gelen değişiklikler bakımından istatistiksel olarak benzerdi.

SONUÇ: Haftada bir uygulanan alendronat ve vitamin D desteği, postmenopozal osteoporoz tanısı konulan ve kalsiyum desteği alamayan kadınlarda etkin ve güvenilir bir tedavi seçeneğidir.

Anahtar Kelimeler: Kalsiyum, Osteoporoz, Postmenopoz, Vitamin D

References

1. Malabanan AO, Holick MF. Vitamin D and bone health in postmenopausal women. J Womens Health 2003;12:151-6.
2. Feskanich D, Willet WC, Colditz GA. Calcium, Vitamin D. Am J Clin Nutr 2003;77:504-11.
3. Campbell BG, Ketchell D, Gunning K. Do calcium supplements prevent posmenopausal osteoporotic fractures? J Farm Pract 2003;52: 234-7.
4. Dawson-Hughes BB, Harris SS, Krall EA, Dallal GE. Effect of withdrawal of calcium and vitamin D supplements on bone mass in elderly men and women. Am J Clin Nutr 2002;72:745-50.
5. Peacock M, Liu G, Carey M, McClintock R, Ambrosius W, Hui S, et al. Effect of calcium or 25OH Vitamin D3 dietary supplementation on bone loss at the hip in men and women over the age of 60. J Clin Endocrinol Metab 2000; 85:3011-9.
6. Wallace LS, Ballard JE. Lifetime physical activity and calcium intake related to bone density in young women. J Womens Health Gend Med 2002;11:389-98.
7. Huuskonen J, Vaisanen SB, Kroger H, Jurvelin JS, Alhava E, Rauramaa R. Regular physical exercise and bone mineral density: a four-year controlled randomized trial in middle-aged men, The DNASCO study. Osteoporos Int 2001;12:349-55.
8. Jensen LB, Kollerup G, Quaade F, Sorensen OH. Bone minerals changes in obese women during a moderate weight loss with and without calcium supplementation. J Bone Miner Res 2001;16:141-7.
9. Shapses SA, Von Thun NL, Heymsfield SB, Ricci TA, Ospina M, Pierson RN, et al. Bone turnover and density in obese premenopausal women during moderate weight loss and calcium supplementation. J Bone Miner Res 2001;16: 1329-36.
10. Shapses SA, Heshka S, Heymsfield SB. Effect of calcium supplementation on weight and fat loss in women. J Clin Endocrinol Metab 2004;89:632-7.
11. Cecilia D, Jódar E, Fernández C, Resines C, Hawkins F. Effect of alendronate in elderly patients after low trauma hip fracture repair. Osteoporos Int 2009;20:903-10.
12. Yan Y, Wang W, Zhu H, Li M, Liu J, Luo B, Xie H, Zhang G, Li F; The efficacy and tolerability of once-weekly alendronate 70 mg on bone mineral density and bone turnover markers in postmenopausal Chinese women with osteoporosis. J Bone Miner Metab 2009;27:471-8.
13. Schnitzer T, Bone HG, Crepaldi G, Adami S, McClung M, Kiel D, Felsenberg D, Recker RR, Tonino RP, Roux C, Pinchera A, Foldes AJ, Greenspan SL, Levine MA, Emkey R, Santora AC 2nd, Kaur A, Thompson DE, Yates J, Orloff JJ. Therapeutic equivalence of alendronate 70 mg once-weekly and alendronate 10 mg daily in the treatment of osteoporosis. Alendronate Once-Weekly Study Group. Aging (Milano) 2000;12:1-12.
14. Luckey M, Kagan R, Greenspan S, Bone H, Kiel RD, Simon J, Sackarowitz J, Palmisano J, Chen E, Petruschke RA, de Papp AE. Once-weekly alendronate 70 mg and raloxifene 60 mg daily in the treatment of postmenopausal osteoporosis. Menopause 2004;11:405-15.
15. Rosen CJ, Hochberg MC, Bonnick SL, McClung M, Miller P, Broy S, Kagan R, Chen E, Petruschke RA, Thompson DE, de Papp AE; Fosamax Actonel Comparison Trial Investigators. Treatment with once-weekly alendronate 70 mg compared with once-weekly risedronate 35 mg in women with postmenopausal osteoporosis: a randomized double-blind study. J Bone Miner Res 2005;20:1261-4.
16. Binkey N, Ringe JD, Reed JI, Ljunggren Ö, Holick MF, Mine HW, Liu M, Lamotta A, West JA, Santora AC. Alendronate/Vitamin D3 70 mg/2800 IU with and without additional 2800 IU vitamin D3 for osteoporosis: Results from the 24-week extension of a 15-week randomized, controlled trial. Bone 2009;44:639-47.
17. Recker R,Lips P,Felsenberg D,Lippuner K, Benhamou L, Hawkins F, Delmas PD, Rosen C, Emkey R, Salzmann G, He W, Santora AC. Alendronate with and without cholecalciferol for osteoporosis: Results of a 15-week randomized controlled trial. Current Med Research and Opinion 2006;22:1745-55.
18. Ann Cranney, George Wells, Andrew Willan. The Osteoporosis Methodology Group and The Osteoporosis Research Advisory Group. II Meta-Analysis of Alendronate for the Treatment of Postmenopousal Osteoporosis. Endocr Rev 2002;23:508-16.
19. Rizzoli R, Greenspan SL, Bone G 3rd,Schnitzer TJ, Watts NB,Adami S, Foldes AJ, Rouz C, Levine MA, Uebelhart B, Santora AC 2nd, Kaur A, Peverly CA, Orloff JJ; Alendronate Once-Weekly Study Group. Two–year results of once-weekly administration of alendronate 70 mg for the treatment of postmenopausal osteoporosis. J Bone Minner Res 2002;17:1988-96.
20. Shea B, Wells G, Cranney A, Zytaruk N, Robinson V, Griffith L, et al. Meta-analyses of therapies for postmenopausal osteoporosis. VII. Meta-analysis of calcium supplementation for the prevention of postmenopausal osteoporosis. Endocr Rev 2002;23:552-5.