Effect of Vitamin K and Alendronate Combination Treatment on Bone Mineral Density of Postmenopausal Osteoporosis Patients: A Pilot Study

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Abstract

Introduction: Osteoporosis is a common problem in postmenopausal women. Numerous studies investigated the effects of vitamin K on bone health, which yielded conflicting results. In this study, we aimed to compare the effect of vitamin K and alendronate combination with alendronate alone on Bone Mineral Density (BMD) of women with postmenopausal osteoporosis.

Materials and Methods: This study was performed in Imam Reza Hospital of Mashhad, Iran, during 14 months (January 1, 2014-February 29, 2015). Our patients (n=28) were randomly divided into two groups of receiving calcium, vitamin D, and alendronate (n=13) and receiving the same combination + vitamin K1 supplement (10 mg daily) (n=15). BMD was measured pre- and post-intervention by the same bone scanner.

Results: The baseline characteristics of the two groups did not differ significantly. The mean variation in femoral neck BMD of the alendronate and alendronate + vitamin K groups were -4.20±11.91% and 0.39±11.80%, respectively. There was no significant difference between the two groups in terms of mean change in femoral neck BMD (P=0.32). The mean variations in lumbar spine BMD of the alendronate and alendronate + vitamin K groups were 0.71±0.06% and 0.76±0.11%, respectively. There was no significant difference between the two groups in terms of mean change in lumbar spine BMD (P=0.24).

Conclusion: It was found that combined treatment with vitamin K and alendronate was not more effective than alendronate alone in increasing BMD of postmenopausal osteoporosis patients.

Keywords: Alendronate, Osteoporosis, Vitamin K
on 28 patients with postmenopausal osteoporosis. The patients were referred to the department of Rheumatology of Imam Reza Hospital, Mashhad, Iran. The inclusion criteria were: 1) postmenopausal women, 2) T-score ≤ 2.5 in bone densitometry, and 3) aged 45-65 years.

The exclusion criteria were: 1) having secondary osteoporosis, 2) taking anticoagulants, 3) sustaining digestive and renal problems, 4) having previous history of bisphosphonate therapy side effects, 5) having any contraindication to the use of calcium or vitamin D supplementation, 6) taking other anti-osteoporotic drugs, and 7) requiring vitamin K supplementation (for the alendronate group).

The patients were allocated to alendronate and alendronate + vitamin K groups through permuted-block randomization. The alendronate group received 70 mg alendronate orally (Alenate®, Abidi Company, Iran) once a week. The alendronate + vitamin K group received oral alendronate once a week besides 10 mg of vitamin K (Minoo Company, Iran), which was taken orally on a daily basis. All the patients received calcium and vitamin D (two doses a day, each dose contained 500 mg of calcium carbonate and 200 IU of vitamin D) (calcium-D, Jalinus Company, Iran). The treatment continued for one year, and the patients were examined every two months for adverse side effects of the drugs. At the beginning and end of the study, BMD was measured in all the patients using the same scanner.

We registered our study in the Iranian Registry of Clinical Trials (available at www.irtct.ir; registration No.: IRCT201504141479N3). The Ethics Committee of Imam Reza Hospital, Mashhad, Iran, approved the study protocol, and informed consent was obtained from all the patients.

Intention-to-treat analysis was not performed in this study. The data are presented in frequency tables and indices. Student’s T-test and paired T-test were performed, using SPSS statistical software (Version 21). P-value less than 0.05 was considered statistically significant.

Results

A total of 60 patients referred to our clinic, 47 of whom were eligible for the study. The samples (n=47) were randomly assigned to alendronate and alendronate + vitamin K groups (Figure 1).

The baseline characteristics of the patients are exhibited in Table 1.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Alendronate group (n=13)</th>
<th>Alendronate+ vitamin K group (n=15)</th>
<th>Independent T-test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>59.0±6.3</td>
<td>59.0±6.3</td>
<td>t=0.46 P=0.64</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>1.53±5.6</td>
<td>1.53±5.6</td>
<td>t=0.02 P=0.98</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>59.3±7.0</td>
<td>59.3±7.0</td>
<td>t=0.23 P=0.95</td>
</tr>
<tr>
<td>BMI*</td>
<td>25.1±3.2</td>
<td>25.1±3.2</td>
<td>t=0.11 P=0.92</td>
</tr>
</tbody>
</table>

* Body mass index

Figure1: Flowchart demonstrating the process of assigning patients in the trial arms.

There was no significant difference in the baseline characteristics between the two groups. The mean femoral neck BMDs in the alendronate group before and after the treatment were 0.61±0.09 g/cm² and 0.58±0.09 g/cm², respectively (P=0.20). In the alendronate + vitamin K group, the mean femoral neck BMDs before and after the intervention were 0.56±0.08 g/cm² and 0.56±0.08 g/cm² (P=0.93).

There was no significant difference between the two groups regarding the mean femoral neck BMD change (P=0.32) (Table 2).

Table2: The mean femoral neck bone mineral density (g/cm²) before and after the intervention in the two groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Before the intervention</th>
<th>After the intervention</th>
<th>Difference</th>
<th>Change (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alendronate group (n=13)</td>
<td>0.61±0.09</td>
<td>0.58±0.08</td>
<td>-0.03±0.07</td>
<td>-4.20±11.91</td>
</tr>
<tr>
<td>Alendronate + vitamin K group (n=15)</td>
<td>0.56±0.09</td>
<td>0.56±0.08</td>
<td>-0.001±0.06</td>
<td>0.39±11.80</td>
</tr>
</tbody>
</table>

Paired T-test: t=1.32 P=0.20

In the alendronate group, the mean lumbar spine BMDs before and after the intervention were 0.71±0.06 g/cm² and 0.76±0.04 g/cm², respectively (P=0.009). In the alendronate + vitamin K group, the mean lumbar spine BMDs before and after the
intervention were 0.76±0.11 g/cm² and 0.79±0.12 g/cm², respectively. Likewise, there was no significant difference between the two groups in terms of the mean change in lumbar spine BMD (P=0.24) (Table 3). In these two groups, no osteoporotic fracture was reported.

| Table3: The mean bone mineral density (g/cm²) of the lumbar spine before and after the intervention in the two groups |
|---------------------------------|---------------------------------|---------------------------------|
|                                | Alendronate group (n=13)        | Alendronate+ vitamin K group (n=15) | Independent T-test |
| Before the intervention         | 0.71±0.06                      | 0.76±0.11                      | t=1.39 P=0.17      |
| After the intervention          | 0.76±0.04                      | 0.79±0.12                      | t=0.80 P=0.43      |
| Difference                      | 0.04±0.05                      | 0.02±0.06                      | t=0.97 P=0.34      |
| Change (%)                      | 0.71±0.06                      | 0.76±0.11                      | t=1.18 P=0.24      |
| Paired T-test                   | t=3.11                         | t=1.57                         | P=0.009            |

Discussion

Given the scarcity of studies on the effect of combined treatment with vitamin K and alendronate on osteoporosis, this study aimed to investigate the effect of vitamin K supplement on the treatment of postmenopausal osteoporosis.

In a study by Booth and colleagues (2003), the effect of dietary vitamin K intake on BMD of 553 female and 335 male samples was investigated. In their study, although no association between vitamin K intake and bone density was found, an indirect correlation between the number of bone fractures and amount of vitamin K intake was demonstrated (6). A 10-year prospective study, performed on 72,327 healthy female nurses, showed that dietary vitamin K intake of less than 109 μg (per day) had a direct correlation with hip fracture (7). In a review of the literature (2006), Cockayne and colleagues found that vitamin K supplement diminished bone loss (8).

In a controlled clinical trial (2008), vitamin K was administered to 440 postmenopausal osteopenic patients for 2-4 years. In the mentioned study, although no change in BMD was observed, bone fractures were fewer in vitamin K group (9). In another study (2008), vitamin K supplementation (500 μg per day) was given to male and female samples, aged 60-80 years, for three years. This study showed that bone density did not differ between vitamin K and control groups (10).

Ishida and colleagues (2004) conducted a study in Japan to investigate the effects of hormone replacement therapy (HRT), calcitonin, etidronate, alfalcacidol, and vitamin K on BMD of 396 postmenopausal osteoporosis patients (11). HRT, etidronate, calcitonin, alfalcacidol, and vitamin K caused 2.0%, -0.5%, 1.6%, -3.6%, and -1.9% variations in BMD after two years of treatment, while a mean change of -3.3% was reported in control group. Moreover, 26% of the patients in the control group developed new vertebral fractures. In comparison with the control group, the relative risks of spinal fracture were 0.35 for HRT, 0.40 for etidronate, 0.41 for calcitonin, 0.56 for alfalcacidol, and 0.44 for vitamin K.

A study by Miki and colleagues (2003), performed in Japan, evaluated the impact of vitamin K₂ on reducing serum level of undercarboxylated osteocalcin (a biomarker of vitamin K deficiency). For this purpose, 20 elderly osteoporosis women with vertebral fracture were divided into two groups of calcium and calcium + vitamin K₂. The results showed that vitamin K₂ significantly reduced the serum level of undercarboxylated osteocalcin (12).

In a study by Hidaka and colleagues (2002) (13), which aimed to evaluate the effectiveness of HRT and vitamin K in 94 postmenopausal osteoporosis patients who were treated with HRT, a decrease in BMD was observed. The results indicated that co-administration of vitamin K₂ and HRT significantly increased BMD (P=0.03). A review (2009) on the effect of vitamin K on postmenopausal women concluded that despite the lack of change in BMD, high-doses of vitamin K could promote bone strength and lower the risk of femoral neck fracture (14).

Only few studies have investigated the effects of combination therapy with bisphosphonates and vitamin K on postmenopausal osteoporosis patients (5). Sasaki and colleagues (15) studied the effects alendronate and vitamin K₂ combination therapy on BMD and bone strength of ovariectomized mice. They concluded that both treatment regimens (alendronate alone and combined treatment with alendronate and vitamin K₂) could significantly increase BMD, but the combination therapy was more effective than alendronate alone in improving bone density.

A recent randomized, open-label study, conducted on 98 postmenopausal osteoporosis patients, demonstrated significantly decreased fracture rates in 23 patients (2 out of 23) taking vitamin K₂ (45mg/ day) and 25 patients (2 out of 25) taking etidronate (200 mg/day for two weeks every three months), compared to 24 patients (6 out of 24) taking calcium lactate (2 g/day). The fracture rate in 26 samples (1 out of 26) taking vitamin K₂ and etidronate decreased more than the others (5). The above-mentioned studies have shown conflicting results on the efficacy of vitamin K for the treatment of osteoporosis. Although it is possible that vitamin K alone cannot increase BMD, it seems that vitamin K improves bone quality and attenuates bone fracture risk. The results of the present study showed that combined treatment with vitamin K and alendronate was not more effective than alendronate alone in increasing BMD of postmenopausal osteoporosis patients. Our study was the first attempt to investigate the effects of this regimen on osteoporosis. The limitations of our study include: 1) the small sample size, 2) short study duration, and 3) high rate of dropout.

Conclusion

In our study, combined treatment with vitamin K and alendronate was not more effective than alendronate alone in increasing BMD of postmenopausal osteoporosis patients. It is recommended to conduct prospective long-term studies with larger sample sizes to investigate this issue.

Acknowledgement

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References