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ORIGINAL RESEARCH ARTICLE

Effects of Alfacalcidol on Back Extensor Strength Gained Through Back Extensor Exercise in Postmenopausal Women with Osteoporosis

ABSTRACT

Hara S, Kishimoto KN, Okuno H, Tanaka M, Saito H, Oizumi A, Itoi E: Effects of alfacalcidol on back extensor strength gained through back extensor exercise in postmenopausal women with osteoporosis. Am J Phys Med Rehabil 2013; 92:101–110.

Objective: The aim of this study was to investigate the additive effect of the active form of vitamin D_3 on the gain in back extensor strength through a back extensor exercise.

Design: A total of 107 postmenopausal women with osteoporosis were randomly divided into two groups: the D_3 group and the control group. Both groups were treated with calcium and alendronate and undertook the back extensor exercise. Alfacalcidol was prescribed only to the D_3 group.

Results: There was no significant difference in the demographic data between the two groups. Ninety-four participants who completed a 4-mo intervention were subjected to per-protocol analysis. There was no significant difference in the improvement in back extensor strength between two the groups ($P = 0.349$). All subjects were further categorized into two subgroups by age. In the older subgroup ($\geq$68 yrs), no significant difference was found in the improvement in back extensor strength ($P = 0.316$). In the younger subgroup ($<$68 yrs), the back extensor strength in the D_3 group was significantly more improved than in the control group ($P = 0.034$).

Conclusions: The results of this study suggest that the administration of the active form of vitamin D_3 enhances the beneficial effects of the back extensor exercise in patients younger than those in their late 60s.

Key Words: Vitamin D, Back Extensor Exercise, Osteoporosis

Vitamin D increases the uptake of calcium from the intestines and has been used in the treatment of osteoporosis. Therapeutic targets of vitamin D mainly exist in the bone and the intestine, where specific receptors of vitamin D are present. However, vitamin D receptors also exist in the skeletal muscle tissue. Vitamin D deficiency is related to muscle weakness[1] or easy fatigability.[2] In particular, vitamin D deficiency contributes to the age-related loss of muscle strength in the elderly.[3]

In postmenopausal women, administration of hydroxylated vitamin D has been clinically proven to prevent fractures.[4] A meta-analysis based on several randomized clinical trials has shown that administration of both vitamin D and the active form of vitamin D reduces the risk of falls.[5,6] Muscle strength is one of the possible factors that affect the risk of falls; hence, the risk of falls could be reduced by strengthening the muscles. Physical exercise improves muscle strength, although muscle protein synthesis after training is slower in the elderly than in the young.[7] Vitamin D supplementation has been shown to improve muscle strength in elderly women taking part in regular physical activities.[8,9] However, whether vitamin D supplementation can improve the effects of exercise on muscle strength has not been elucidated yet.

Postural changes in patients with osteoporosis represent not only the existence of vertebral fractures but also the reduction in back extensor strength. Back extensor strength is known to reduce with age in the elderly[10]; this reduction in strength also affects their quality-of-life (QOL).[11] Back extensor exercise has been proven to improve back extensor strength, posture,[12] and QOL.[13] Stronger back extensor gained through back extensor exercise reduced the incidence of vertebral fracture even 10 yrs after the clinical trial period.[14] The original procedure for back extensor exercise required a trainee to use a backpack containing the weight equivalent to 30% of the maximal back extensor strength.[12] However, according to Hongo et al.,[13] low-intensity back extensor exercise without additional weight is effective and is a safer method of exercise for the elderly with osteoporosis.

The authors hypothesized that the administration of alfacalcidol would have a beneficial impact on the gain in back extensor strength through back extensor exercise. In the current study, a randomized open-label clinical trial was conducted to clarify the effects of active vitamin D_3 on back extensor strength gained through back extensor strengthening exercise in postmenopausal women with osteoporosis.

MATERIALS AND METHODS

Study Design

This was a prospective, randomized, open-label study. The study protocol for this study was approved by the institutional review board. The design of the current clinical trial was registered as UMIN000003925 in the University Hospital Medical Information Network clinical trials registry.

Participants

The participants were recruited from patients who visited the authors' institution for medical assessment of osteoporosis or related diseases. The patients underwent x-ray examination of the lumbar and thoracic spine and measurement of bone mineral density (BMD) with dual-energy x-ray absorptiometry (DCS-900EX; ALOKA, Japan) at the lumbar spine. All

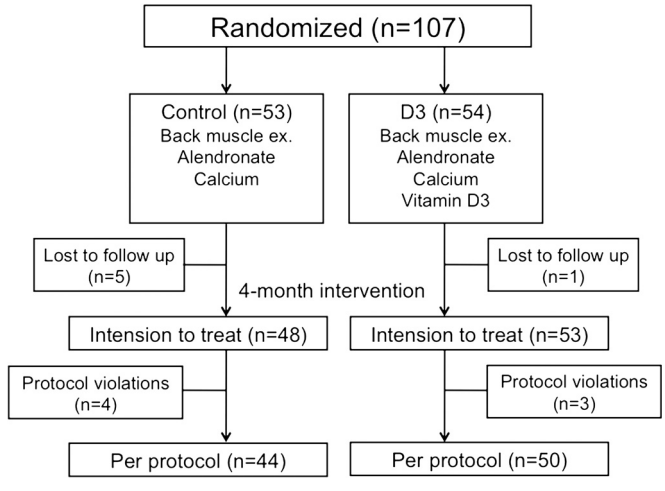

FIGURE 1 *Study design of the current intervention in postmenopausal women. Ex. indicates exercise.*

dual-energy x-ray absorptiometry measurements were taken on the same machine using the same protocol. The quality of measurement was monitored with a phantom every day. Ambulatory postmenopausal women aged between 55 and 75 yrs who had been diagnosed with primary osteoporosis on the basis of Japanese Society of Bone and Mineral Research[15] were invited to participate. Patients were excluded if they had a clinical history of a condition affecting bone metabolism, such as hyperparathyroidism, diabetes mellitus, alcohol abuse, and corticosteroid use. Women with more than three vertebral fractures, who were already treated with vitamin D within 6 mos, or who were unable to perform the back extensor exercise because of back pain or frailness were also excluded.

Participant Allocation and Interventions

A total of 107 women agreed to participate in this study, with written informed consent. The participants were randomly divided into two groups: the D_3 group ($n = 54$) and the control group ($n = 53$). The patients were randomly assigned using sealed opaque envelopes at the outpatient department. Both groups were treated with daily calcium supplementation (200 mg/day) and oral alendronate (35 mg once a week). Daily alfacalcidol (1.0 μg/day: 1 alpha-hydoroxy vitamin D_3) was prescribed only for the D_3 group. The participants in both groups were instructed to perform the back extensor exercise (Fig. 1); the procedure for this back extensor exercise was based on the previous reports.[12,13,16] The participants were instructed to lie in a prone position with a pillow under the abdomen (Fig. 2A). They were then instructed to lift their upper trunk toward the neutral position for 5 secs, ten times per session. They were asked to perform one session of this exercise daily and to keep a logbook.

Laboratory Examinations

Urinary N-terminal telopeptide (NTx) was analyzed as a bone resorption marker at enrollment and

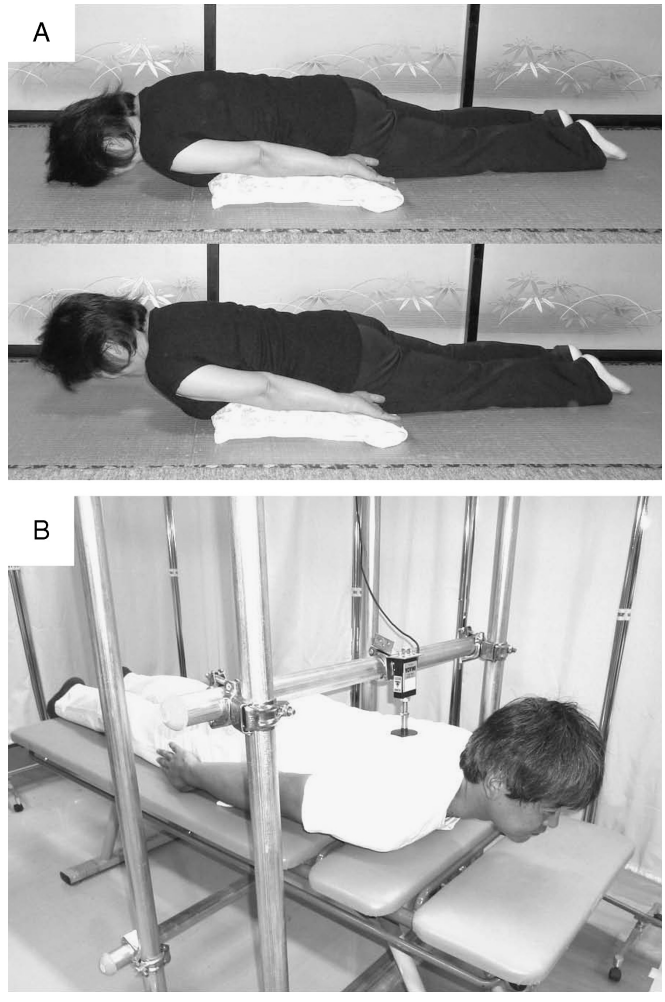

FIGURE 2 *A, Back extensor exercise in the prone position with a pillow under the abdomen; B, measurement of back extensor strength using a strain-gauge dynamometer installed in the specially constructed frame.*

after a 4-mo intervention period. Serum 25(OH)D (reference range, 9.0–33.9 ng/ml) and $1,25(OH)_2D$ (reference range, 20.0–60.0 pg/ml) levels were measured at the baseline examination (BML Inc, Tokyo, Japan).

Back Extensor Strength Measurement

The method for measuring back extensor strength was based on the report by Limburg et al.[17] A strain-gauge dynamometer (ZPS-DPU-1000N; IMADA, Toyohashi, Japan) attached to a specially constructed frame over an examination bed (Fig. 2B) was used for assessment. The participants were instructed to lie on their abdomen with their hips and knees in extension and their arms at the side of the body. Two successive maximal effort trials were measured separately. The maximal strength (newtons: N) of the two trials were recorded and used for data analyses.

Measurement of Spinal Curvature and Range of Motion

Spinal curvature and range of motion were analyzed using a Spinal Mouse (Idiag, Volkerswill, Switzerland). The hand-held device was rolled over the spinal processes from C7 to the top of the intergluteal cleft. The measurements were performed with the trunk in the maximal flexion, upright, and the maximal extension position. Data were telemetered and analyzed using a personal computer.

Evaluation of QOL

QOL was evaluated using the Japanese Osteoporosis Quality of Life Questionnaire (JOQOL).[18] This questionnaire was modified from the Osteoporosis Assessment Questionnaire and the Qualeffo-41 to fit the Japanese lifestyle. The full score is 152 points, and higher scores indicate a higher QOL.

Statistical Analysis

The differences of the two groups at baseline were assessed using Student's t test. The comparisons between the D_3 and control groups in NTx value, BMD, spinal curvature, and JOQOL scores were based on intention-to-treat analyses. The comparison between the D_3 and control groups in the back extensor exercise was based on both intention-to-treat and per-protocol analyses. The effects of the interventions on the back extensor strength, spinal curvature, and QOL scores were analyzed by two-way repeated-measures analysis of variance with a post-hoc test. Differences in these values after the 4-mo intervention within each group were analyzed by paired t test. Differences less than 0.05 were considered statistically significant. Statistical analyses were performed using GraphPad PRISM ver.5 (GraphPad software, La Jolla, CA).

RESULTS

Baseline Demographic Data

There was no significant difference in the baseline demographic data between the D_3 group ($n = 54$)

TABLE 1 Characteristics of the participants at baseline

	D_3 ($n = 54$)	Control ($n = 53$)	P
Age, yrs	68.0 ± 5.3	67.4 ± 4.2	0.485
Height, cm	149.3 ± 5.7	149.4 ± 4.7	0.916
Weight, kg	53.3 ± 6.9	52.8 ± 7.1	0.728
BMI, kg/m^2	24.0 ± 3.3	23.7 ± 3.1	0.655
Serum			
BUN, mg/dl	16.3 ± 4.2	15.9 ± 4.3	0.669
Creatinine, mg/dl	0.6 ± 0.1	0.6 ± 0.2	0.799
Total protein, g/dl	7.4 ± 0.5	7.2 ± 0.4	0.116
Albumin, g/dl	4.3 ± 0.3	4.3 ± 0.3	0.592
Ca, mg/dl	9.4 ± 0.4	9.3 ± 0.6	0.269
P, mg/dl	3.6 ± 0.5	3.6 ± 0.4	0.461
25(OH)D, ng/ml[a]	18.2 ± 6.4	18.4 ± 6.5	0.897
Vitamin D status	Normal, 6% (2/33) Insufficiency, 94% (31/33)	Normal, 12.5% (4/32) Insufficiency, 82.5% (28/32)	
$1,25(OH)_2D$, pg/ml	58.4 ± 18.3	58.8 ± 19.9	0.905
Number of vertebral fracture	One, 42.6% (23/54) Two, 3.7% (2/54)	One, 28.3% (15/53) Two, 5.6% (3/53)	
Back muscle strength, N	152.7 ± 69.0	148.9 ± 60.9	0.767

Values are expressed as mean ± standard deviation. P values are the results of Student's t test.

[a]Analyses were performed in a subset of patients (D_3, $n = 33$; control, $n = 32$).

BMI indicates body mass index; BUN, blood urea nitrogen; Ca, calcium; P, phosporus.

and the control group (n = 53; Table 1). Fifty-three participants in the D_3 group and 48 participants in the control group completed the 4-mo intervention and back extensor strength measurements (intention-to-treat analysis). Three individuals in the D_3 group and four individuals in the control group were excluded from the per-protocol analysis because of protocol violation as a result of taking less than two thirds of the exercise or medication (Fig. 1).

Improvement in Back Extensor Strength

The back extensor strength after the 4-mo intervention was a mean (SD) of 186.0 (69.3) N in the D_3 group and 171.6 (64.7) N in the control group. There was no significant difference in the final back extensor strength between the two groups. The changes in the back extensor strength were analyzed on the basis of the per-protocol analysis. The mean (SD) increase in back extensor strength was 33.6 (43.5) N in the D_3 group (n = 50) and 24.8 (43.3) N in the control group (n = 44), which was not significantly different (P = 0.329).

The subjects were further divided into two subgroups based on the mean age. In the older subgroup (≥68 yrs; n = 54), there was no statistical difference in the baseline characteristics (Table 2). The mean (SD) increase in back extensor strength was 28.9 (35.3) N (n = 31) in the D_3 group and 39.7 (42.7) N (n = 23) in the control group (P = 0.316). In the younger subgroup (<68 yrs; n = 40), there was no significant difference in body composition (Table 2), vitamin D status, BMD, or back extensor strength between the D_3 and control groups. The mean (SD) increase in back extensor strength was 41.2 (54.6) N (n = 19) in the D_3 group and 8.5 (38.6) N (n = 21) in the control group. Thus, the D_3 group showed a significantly greater improvement in back extensor strength than did the control group (P = 0.034; Fig. 3). The intension-to-treat-analysis also showed a significant difference in the improvement in back extensor strength between the two groups (mean [SD], 8.5 [38.6] in the control group [n = 21]; 39.3 [53.8] in the D_3 group [n = 20]; P = 0.042).

Laboratory Examination

After the 4-mo intervention, the urinary NTx examination showed a significant decrease in both groups. The BMD values in the L2–4 spine were significantly increased after the 4-mo intervention in both groups. However, there was no significant difference in the change in NTx and BMD between the two groups (Table 3).

Posture and QOL Evaluation

Measurement of spinal curvature showed a significant increase in lumbar lordosis in the D_3

TABLE 2 Characteristics of the participants in older and younger subgroups at baseline

	D_3	Control	P
Older subgroup (≥68 yrs)	n = 33	n = 27	
Height, cm	147.8 ± 5.3	149.0 ± 5.0	0.397
Weight, kg	53.6 ± 7.3	53.8 ± 7.8	0.907
Serum 25(OH)D, ng/ml[a]	18.4 ± 6.7	17.6 ± 6.6	0.728
Vitamin D status	Normal, 5% (1/20) Insufficiency, 95% (19/20)	Normal, 10% (2/19) Insufficiency, 90% (17/19)	
Serum 1,25(OH)$_2$D, pg/ml	53.3 ± 14.6	57.9 ± 14.6	0.224
NTx, nmol BCE/mmol Cr	61.9 ± 30.0	60.4 ± 27.8	0.845
BMD (spine L2–4), g/cm^2	0.726 ± 0.106	0.740 ± 0.071	0.536
Back extensor strength, N	138.8 ± 61.7	144.8 ± 62.0	0.709
Younger subgroup (<68 yrs)	n = 20	n = 21	
Height, cm	152.0 ± 5.7	150.6 ± 4.3	0.384
Weight, kg	52.3 ± 6.2	52.6 ± 6.6	0.910
Serum 25(OH)D, ng/ml[a]	18.3 ± 6.0	19.1 ± 7.2	0.956
Vitamin D status	Normal, 8% (1/13) Insufficiency, 92% (12/13)	Normal, 15% (2/13) Insufficiency, 85% (11/13)	
Serum 1,25(OH)$_2$D, pg/ml	72.8 ± 21.9	59.7 ± 13.8	0.226
NTx, nmol BCE/mmol Cr	64.1 ± 26.0	61.2 ± 18.0	0.716
BMD (spine L2–4), g/cm^2	0.761 ± 0.080	0.733 ± 0.021	0.315
Back extensor strength, N	181.3 ± 70.9	160.5 ± 61.4	0.323

Values are expressed as mean ± standard deviation. P values are results of Student's t test. The subjects were divided into two subgroups based on the mean age: older (≥68 yrs) and younger (<68 yrs) subgroups.

[a]Analyses were performed in a subset of patients (older group: D_3, n = 20; control, n = 19; younger group: D_3, n = 13; control, n = 13).

NTx indicates N-terminal telopeptide; BCE, bone collagen equivalent; Cr, creatinine; BMD, bone mineral density.

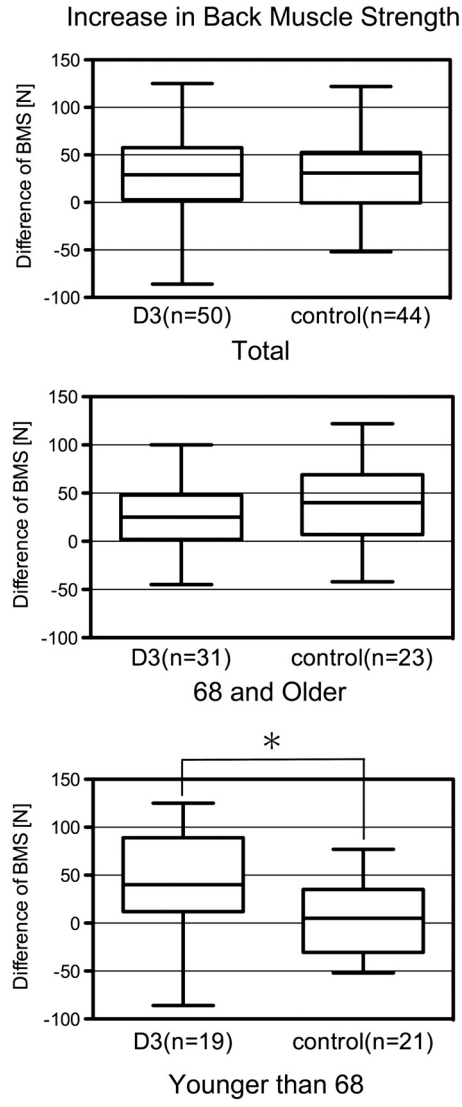

FIGURE 3 *Difference in back extensor strength after the 4-mo intervention based on a per-protocol analysis. Back extensor strength increased by a mean (SD) of 33.6 (43.5) N in the D_3 group and by 24.8 (43.3) N in the control group. There was no significant difference between the two groups (P = 0.329). In the older subgroup (≥68 yrs), the back extensor strength increased by a mean (SD) of 28.9 (35.3) N (n = 31) in the D_3 group and by 39.7 (42.7) N (n = 23) in the control group (P = 0.316). In the younger subgroup (<68 yrs), back extensor strength increased significantly (P = 0.034) in the D_3 group (mean [SD], 8.5 [38.6] N) than in the control group (41.2 [54.6] N). BMS indicates back muscle strength.*

group, whereas the control group did not show any significant change. Moreover, a significant difference was noted in lumbar lordosis between the two groups. No significant difference was found in thoracic kyphosis, sacral inclination, or spinal range of motion (Table 4).

The JOQOL scores exhibited a significant increase after the 4-mo intervention in both groups. Each domain of the JOQOL scores was also analyzed separately. The pain and general health scores in the JOQOL were significantly increased after the 4-mo intervention in both groups. The activities of daily living and recreational and social activities scores were also increased in the D_3 group. However, there was no significant difference in individual domain between the two groups (Table 5).

DISCUSSION

In the current study, the back extensor exercise improved the back extensor strength in postmenopausal women with osteoporosis in 4 mos. The increase in back extensor strength in the 4-mo period was not significantly different between the two groups. However, in the younger subset of participants (<68 yrs), administration of an active form of vitamin D_3 further improved the increase in the back extensor strength in 4 mos compared with the control group. The results of this study suggest that administration of the active form of vitamin D_3 may enhance the beneficial effects on the muscle strength gained through back extensor exercise in postmenopausal women younger than those in their late 60s.

Bunout et al.[19] conducted a prospective randomized clinical study on the effects of vitamin D supplementation and exercise training. Vitamin D–deficient subjects 70 yrs or older performed strength training with or without supplementation of vitamin D. The combination of exercise and vitamin D resulted in a gain of higher gait speed and lower Romberg ratio than did the exercise alone. Although the exercise improved quadriceps muscle strength, vitamin D did not show any beneficial effect on the improvement in muscle strength. Their findings on muscle strength in the subjects 70 yrs or older were consistent with the results of this study in the elder subset of participants. In the previous report, an immunohistochemical investigation of biopsied muscle revealed that vitamin D receptor expression in the skeletal muscle decreases with age and did not correlate with the serum 25(OH)D or $1,25(OH)_2D$ levels.[20] Thus, hyporesponsiveness of the muscle to vitamin D supplementation in the elderly may be attributed to the low expression level of its receptor. Nevertheless, in the older subset of participants in this study, back extensor strength significantly improved after the 4-mo intervention in both

TABLE 3 Bone turnover marker and BMD examinations at baseline and after the 4-mo intervention

	Groups: Intention to Treat		
	D_3 (n = 53)	Control (n = 48)	P
NTx, nmol BCE/mmol Cr			0.461
Baseline	62.7 ± 27.7	60.9 ± 23.8	
4 mos	29.0 ± 18.9[a]	31.2 ± 17.8[a]	
BMD (spine L2–4), g/cm^2			0.158
Baseline	0.739 ± 0.098	0.734 ± 0.077	
4 mos	0.780 ± 0.102[a]	0.769 ± 0.084[a]	

Values are expressed as mean ± standard deviation. Analyses were based on intention to treat. P values are the results of two-way repeated-measures ANOVA. Significant changes within the group were also indicated.

[a] $P < 0.001$.

NTx indicates N-terminal telopeptide; BCE, bone collagen equivalent; Cr, creatinine; BMD, bone mineral density; ANOVA, analysis of variance.

groups. This result indicates that back extensor exercise is an effective method for increasing back extensor strength even in the elderly, regardless of administration of the active form of vitamin D.

The bone resorption marker, NTx, was significantly suppressed after the 4-mo intervention in both groups in this study (Table 2). Forty-five of 48 participants and 51 of 53 participants in the control and D_3 groups, respectively, commenced bisphosphonates therapy at their enrollment in this study. Physical exercise, which is also known to suppress bone resorption,[21] may work cooperatively with this therapy. Furthermore, the active form of vitamin D can suppress bone turnover.[22] However, there was no significant difference in the suppression of NTx between the two groups. The combined effects of alendronate and exercise may have been strong enough to mask the effects of the active form of vitamin D. BMD in the L2–4 spine was significantly improved after the 4-mo period (Table 2). A previous controlled trial showed that the back extensor exercise did not increase spinal BMD in postmenopausal women.[23] Thus, in this study, alendronate seems to have mainly contributed to an increase in the spinal BMD. The mean increases of BMD in the D_3 and control groups were 5.5% and 4.8% during the 4-mo intervention, respectively. These improvements of BMD seemed to be slightly better than the results in the clinical trial of alendronate carried out in Japanese patients with osteoporosis.[24] As a

TABLE 4 Measurements of spinal posture at baseline and after the 4-mo intervention

	Groups: Intention to Treat		
	D_3 (n = 52)[a]	Control (n = 48)	P
Spinal curvature, degree angle			
Thoracic kyphosis			0.957
Baseline	39.7 ± 14.0	39.1 ± 12.3	
4 mos	41.5 ± 14.5	40.0 ± 14.6	
Lumbar lordosis			0.024[b]
Baseline	17.2 ± 13.8	18.2 ± 11.8	
4 mos	20.8 ± 11.2[b]	16.6 ± 15.3	
Sacral inclination			0.129
Baseline	4.6 ± 8.1	5.4 ± 8.3	
4 mos	7.1 ± 7.9	5.0 ± 9.1	
Spinal ROM			0.810
Baseline	80.2 ± 22.7	76.6 ± 26.4	
4 mos	86.5 ± 20.9	83.9 ± 22.2	

Values are expressed as mean ± standard deviation. Analyses were based on intention to treat. P values are the results of two-way repeated-measures ANOVA. Significant changes within the group were also indicated.

[a] One case in the D_3 group could not be measured by Spinal Mouse because of acute back pain at the time of measurement after the 4-mo intervention.

[b] $P < 0.05$.

ROM indicates range of motion; ANOVA, analysis of variance.

TABLE 5 Measurements at baseline and after 4-mo intervention

	Groups: Intention to Treat		
	D_3 (n = 35)	Control (n = 33)	P
JOQOL			
Total score (152 points)			0.944
Baseline	114.4 ± 19.4	111.3 ± 18.3	
4 mos	119.4 ± 16.9[b]	116.5 ± 15.6[a]	
Pain (20 points)			0.203
Baseline	15.5 ± 4.0	14.6 ± 4.6	
4 mos	17.4 ± 3.3[c]	15.7 ± 4.2[a]	
Activities of daily living (64 points)			0.887
Baseline	58.6 ± 8.4	57.4 ± 8.4	
4 mos	59.7 ± 7.3[a]	58.7 ± 6.7	
Recreational and social activities (20 points)			0.107
Baseline	11.3 ± 4.4	11.4 ± 4.1	
4 mos	12.8 ± 3.5[b]	11.7 ± 3.1	
General health (12 points)			0.563
Baseline	5.7 ± 2.3	5.3 ± 1.6	
4 mos	6.6 ± 2.6[a]	6.5 ± 2.2[b]	
Posture and figure (16 points)			0.095
Baseline	11.1 ± 3.3	10.9 ± 3.4	
4 mos	10.7 ± 3.8	11.6 ± 3.3	
Falls and psychologic effect (20 points)			0.433
Baseline	12.2 ± 3.2	11.7 ± 3.2	
4 mos	12.4 ± 3.3	12.6 ± 3.0	

Values are expressed as mean ± standard deviation. Data with incomplete entry of questionnaire sheets were excluded from the analyses. P values are the results of two-way repeated-measures ANOVA. Significant changes within the group were also indicated.

[a] $P < 0.05$.

[b] $P < 0.01$.

[c] $P < 0.001$.

JOQOL indicates Japanese Osteoporosis Quality of Life Questionnaire; ANOVA, analysis of variance.

limitation of this study, however, precision of dual-energy x-ray absorptiometry scanning was not assessed between radiologic technologists. Therefore, the dual-energy x-ray absorptiometry results in this study potentially included precision error.

The analyses of spinal curvature using the Spinal Mouse revealed that lumbar lordosis increased after the 4-mo intervention in the D_3 group (Table 3), which reflected improvement in posture. However, thoracic kyphosis and sacral inclination did not change. Moreover, the posture and figure score in the JOQOL did not indicate an improvement (Table 4). Thus, it is unclear whether the lumbar lordosis findings of this study are related to the postural improvement.

Kawate et al.[24] compared the impact of alendronate and alfacalcidol on the JOQOL sores in postmenopausal women. They reported that alendronate, but not alfacalcidol, improved the pain-related QOL score. On the other hand, alfacalcidol improved fall and psychologic effect scores.[25] It is also known that the back extensor exercise improves the QOL score. Hongo et al.[13] reported that the back extensor exercise especially improved the activities of daily living and the posture-related QOL than in the control group without the exercise. Thus, alendronate, alfacalcidol, and back extensor exercise can improve the QOL of patients with osteoporosis. Differences in characteristics of the participants and experimental design among the different studies may explain the differences in the findings on the QOL data.

Serum concentration of 25(OH)D is known to be the best marker for vitamin D insufficiency and deficiency. On the other hand, serum concentration of $1,25(OH)_2D$ depends mainly on renal function, an intact parathyroid hormone level, and calcium and phosphate supplementation. Unfortunately, the analysis of serum 25(OH)D was not covered by health insurance, even for those with vitamin D deficiency in the region in which this study was executed. Thus, the authors could not analyze the 25(OH)D for all participants. Recently, Okazaki et al.[25] proposed a serum 25(OH)D level of 28 ng/ml as a threshold for vitamin D insufficiency in Japanese subjects. Based on this criterion, most of the participants in whom the authors measured 25(OH)D would be diagnosed with vitamin D insufficiency. The participants in the current study were ambulatory women, mostly engaged in agriculture. Their

diet may not be adequately fortified with vitamin D to achieve a sufficient 25(OH)D level. Moreover, the participants in the D_3 group were treated with the active form of vitamin D; given the metabolic pathways involved, the administration of alfacalcidol would not be expected to elevate the level of 25(OH)D.

The administration of the active form of vitamin D increases the uptake of calcium from the intestine. Accordingly, administration of alfacalcidol and calcium may increase the risk of hypercalciuria, hypercalcemia, and urolithiasis. In this study, the participants were supplemented with 200 mg of calcium. Higher levels of calcium supplementation could increase the effects of alfacalcidol; however, urolithiasis, a side effect of alfacalcidol, could be a major concern. Nevertheless, this clinical trial was successfully conducted without any report of urolithiasis throughout the study period. Recently, it is reported that calcium supplementation increases the risks of myocardial infarction and stroke.[26] However, the dose of calcium supplementation was quite low as compared with the reported critical level.

There were several limitations in the present study. The number of participants in the subgroups of younger than 68 yrs *vs.* 68 yrs or older were 40 and 54, respectively. This sample size may not be sufficiently large to detect the differences between the groups. Moreover, the authors did not select the participants on the basis of their 25(OH)D levels. Clinical trials that targeted subjects with vitamin D deficiency may show a clearer difference between a control group and a group receiving the active vitamin D. In addition, the period of intervention was 4 mos, similar to a previous clinical trial.[13] The period of intervention may have various effects on the outcome; a new study using a longer period of intervention is currently underway.

In conclusion, the subjects younger than 68 yrs treated with the active form of vitamin D gained significantly greater back extensor strength by means of back extensor exercise compared with the control subjects. These data may suggest that the active form of vitamin D is beneficial for back extensor strengthening in postmenopausal women younger than those in their late 60s.

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