Restorative Effect of Vitamin D Deficiency on Knee Pain and Quadriceps Muscle Strength in Knee Osteoarthritis

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Abstract- Both vitamin D deficiency and quadriceps muscle weakness are associated with knee osteoarthritis (KOA) and pain. The aim of this study was to determine the restorative effect of vitamin D deficiency on pain and quadriceps muscle strength in knee osteoarthritis. Patients with KOA aged ≥ 30 years, presence of knee pain for at least one month or longer and serum 25-hydroxyvitamin (25-OHD) deficiency were recruited in the study. Participants with KOA compatible with Kellgren-Lawrence grade 4, joint instability, and effusion, history of surgery or inflammatory arthropathies were excluded. Serum 25-OHD was assessed by ELISA method and concentrations <20 ng/ml was considered deficiency. Quadriceps muscle strength was measured by dynamometry method and intensity of knee pain by Western Ontario and McMaster University Osteoarthritis index scored by Likert scale and visual analogue scale. All participants received 50.000 IU oral cholecalciferol weekly for at least two months. The influence of raising serum 25-OHD on quadriceps muscle strength and pain was assessed by calculation of mean changes from baseline at the end of the treatment period using paired t-test. A total of 67 patients with mean age of 50 ± 6.6 years of age were treated for 2 months. Serum 25-OHD reached to sufficient levels in all except one patient. At the end of the study period, serum 25-OHD and quadriceps muscle strength increased significantly as compared with baseline (P=0.007 and P=0.002 respectively), whereas knee pain decreased significantly based on Western Ontario and McMaster University Osteoarthritis index (P=0.001) as well as visual analogue scale scores (P=0.001).These findings indicated that correction vitamin D deficiency in patients with KOA exerts significant favorable effect on quadriceps muscle strength and knee pain.

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Keywords: Knee osteoarthritis; Pain; Quadriceps; Strength; Treatment; Vitamin D

Introduction

Knee osteoarthritis (KOA) results in joint instability and subsequent disability in a substantial proportion of the elderly subjects (1). Stability of knee joint is significantly dependent to lower limbs muscle strength, particularly the quadriceps muscles (2-3). Quadriceps muscle is a primary contributor for stability of knee and a significant determinant in evaluation of physical performance and function of knee joint (3-6). In patients with KOA, the quadriceps, hamstrings and hip muscles strength are significantly impaired as compared with age-matched controls (4-5). Weakness of muscles is attributed to pain or to the relevant structural changes of the knee joint (4,6-8). But, quadriceps muscle weakness may be detectable even prior to KOA development suggesting as an associated factor for initiation of KOA (6,9-10). Muscle strengthening is a component of treatment for relieving pain and prevention of symptoms in KOA (11-13).

Serum vitamin D level inversely correlates with lower limb muscle strength and function and low serum vitamin D is determinant for quadriceps muscle strength (QMS) (14-19). In women with hypovitaminosis D, muscle strength was lower and disability was greater than those without vitamin D deficiency (16). Both vitamin D deficiency and quadriceps muscle weakness play a role in the development or progression of KOA

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(1-3,18-19). There is some evidence that raising serum vitamin D may improve muscle strength and muscle function as well as physical performance in the elderly subjects (20-22). However, the results of studies which addressed the strengthening effect of vitamin D on muscle in KOA are consistent (23-24).

Our previous study indicated an association between vitamin D deficiency and KOA particularly patients less than 55 years of age (25). Regarding the association of quadriceps weakness and vitamin D deficiency with KOA, the present study was designed to investigate the beneficial effect of raising serum vitamin D on quadriceps muscle strength (QMS) and pain in vitamin D deficient KOA.

Materials and Methods

The study patients were selected among subjected with KOA who participated in our previous study to determine the correlation between serum vitamin D and quadriceps muscle strength in KOA in 2013 (unpublished data). All vitamin D deficient KOA were selected for the present study. Diagnosis of KOA was confirmed according to the American College of Rheumatology diagnostic criteria based on clinical and/ radiological findings (26).

Inclusion criteria consisted of all vitamin D deficient KOA aged >/= 30 years who had knee pain for at least one month or longer. Exclusion criteria consisted of severe radiographic KOA compatible with Kellgren -Lawrence grade 4; knee joint instability, joint effusion, history of knee or hip joint surgery, presence or history of inflammatory arthropathies in the knee or other joints. Patients with knee joint instability were excluded because QMS assessment might be affected by joint instability and confound the results.

Serum vitamin D was assessed by measurement of serum 25-hydroxyvitamin D level (25-OHD) by ELIZA method using vitamin D Kit (DRG, instruments, GmbH, Germany). Serum 25-OHD concentrations less than 20 ng/ml was considered as deficient, levels at 20- 29 ng/ml as insufficient and 30 ng/ ml or more as sufficient level (27).

The QMS was measured in both limbs by dynamometry method. In this method a full knee joint extension was performed in a seated position against a fixed dynamometer which was positioned 5 cm above the lateral malleolus on the tibia. The average value of three measurements was considered for analysis. The reliability of QMS measurements was confirmed by test-retest reliability method in 20 consecutive patients in whom QMS measurement was repeated after 30 minutes rest. The correlation coefficient value between the two sets of QMS scores was 0.97(P=0.001). The validity of dynamometer was tested by known specified metal weights of 5-kg, 10 -kg, and 20-kg at the beginning of the study and thereafter during the study periods.

The intensity of knee pain was assessed by both visual analogue scales (VAS), where 0 represented no pain and 100 mm indicated maximal knee pain, as well as by Western Ontario and McMaster University Osteoarthritis (WOMAC) pain scale consisted of 4 items. Each component of WOMAC index was scored by Likert scale from 0-4 (28). All patients received oral cholecalciferol 50.000 IU weekly for at least two months to achieve sufficient serum 25-OHD level. All participants were tested for QMS measurement, knee pain one week before the treatment and at the end of the study period.

The objective of this study was to determine the influence of raising serum 25-OHD level on QMS and knee pain. The effect of raising serum 25-OHD on QMS and knee pain was assessed by determination of mean changes from baseline with 95% confidence interval. In statistical analysis baseline data were compared with endpoint values using paired t-test. Levels of p-value less than 0.05 was considered significant. SPSS software version 18 was used for analysis. This study was approved by the Ethic Committee of the Babol University of Medical Sciences, Babol, Iran.

Results

A total of 65 patients (female: 86.5%) with KOA and serum 25-OHD deficiency (< 20 ng/ml) entered the study. Mean age of the patients was 50 ± 6.6 years. All patients received cholecalciferol for a mean period of 68.6 ± 4.7 days (60-78 days).

Serum 25-OHD reached to sufficient levels in all except one patient in whom serum raised to 24 ng/ml. At the end of the study period mean serum 25-OH concentration and QMS value increased significantly as compared with baseline values (P=0.007 and P=0.002, respectively) whereas, knee joint pain based on both WOMAC and VAS scores decreased significantly (P=0.001 for both) (Table1). At end point, the median QMS value increased by 47% (11-120%), as compared with baseline value whereas knee pain decreased by 78% (33-96%) based on WOMC score and 71% (48-94%) by VAS score.

Table 1. Mean changes from baseline in quadriceps muscle strength and knee pain in patients with knee osteoarthritis after two months treatment with cholecalciferol 50.000 IU weekly

Variables	Base line	endpoint	Mean diff. (95%CI)	*P.* value
Serum25-OHD, ng/ml	13.02±4.05	37.9±5.8	24.89± 5.9 (23.4 to 26.3)	0.007
Quadriceps muscle strength, kg	14.6±1.89	21.3±2.1	6.7 ± 2.2 (6.1 to 7.2)	0.001
Knee pain, WOMAC (0-16)	9.16±1.84	2.04±.97	-7.1 ± 1.7 (-7.5 to - 6.6)	0.005
Knee pain, VAS (0-100) mm	39.3 ± 6.1	13.2 ± 4.	-26.1 ± 5.4 (-27.4 to -24.8)	0.001

Discussion

The results of this study indicated that in patients with KOA, restoration of vitamin D deficiency to sufficient level resulted in significant improvement of QMS and reduction of knee pain. These findings are consistent with the results of many published studies which have shown improvement of muscle strength or limb muscle function after vitamin D supplementation in vitamin D deficient elderly subjects (15,21-22).

A prospective, double-blind, placebo-controlled, randomized trial by Moreira-Pfrimer et al. revealed significant improvement of hip flexor and knee extensor muscles strength by oral cholecalciferol in institutionalized people aged 60 years and older (15). In the present study, the efficacy of vitamin D supplementation on knee pain should be attributed to improvement of QMS. The strengthening effect of quadriceps muscle on knee pain and joint function has been shown in several studies (6,11-13,29-30).

In one study of women and men aged 49-80 years, the association of muscle strength and muscle performance with serum vitamin D, was most pronounced when serum 25-OHD was lower than 24 ng/ml) but not at levels higher than 24 ng/ml (31). This study confirms that vitamin D supplementation is more effective at lower levels of serum vitamin D. Likewise, in another study, the effect of vitamin D supplements in patients with osteoarthritis and knee pain or hip pain was more evident in patient with baseline serum 25-OHD level <10 ng/ml rather than >10 ng/ml (32).

These observations in agreement with findings of the present study justify correction of vitamin D deficiency and indicate that restoration of serum 25-OHD deficiency in KOA is expected to be effective on both muscle strength and pain.

Similar findings were observed in a prospective placebo controlled study which included KOA patients with baseline serum 25-OHD levels <20 ng /ml. In this study raising serum 25-OHD level in the treatment group was associated with significant improvement of knee pain and muscle strength whereas in the placebo group knee pain aggravated (33). In another study of elderly subjects aged 70 years or more with baseline serum 25-OHD concentration of 16 ng/ml or lower, vitamin D supplementation has raised serum 25 OHD level to 25.8 ± 6.5 ng/ml and increased QMS value and physical performance significantly (22).

In contrast, in one placebo-controlled study, treatment of KOA with vitamin D for 2 years did not reduce knee pain and cartilage loss despite raising serum 25-OHD to 36 ng/ml (34). The difference may be attributed to patient's characteristics, particularly mean baseline serum vitamin D levels which were greater than 20 ng/ml in both groups at the first and the second year of treatment period. Overall, evidence from RCTs do support efficiency of vitamin D supplemental on muscle strength and function in the elderly, nonetheless,this issue requires further studies with emphasis on baseline serum vitamin D level (35).

Both vitamin D deficiency and KOA are prevalent in elderly subjects (2) and so the clinical significance of restoration of vitamin D deficiency in patients with KOA is not limited to reduction of knee pain and improvement of lower limb muscles strength but extends to extra-skeletal systems including prevention of falls, bone loss and physical activities (21-22,27,36). It was shown that elderly men and women, for optimal physical performance, should be encouraged to maintain their serum 25-OHD levels as high as 40 ng/ml (37).

In a study of community-dwelling elderly women with mean age of 77 years who had serum 25-OHD less than 31.2 ng/ml , raising serum 25-OHD to higher levels significantly decreased falls and body sway, and increased quadriceps strength (21). In hemodialysis and chronic obstructive lung disease patients, treatment with vitamin D increases QMS and muscle size, strength, and lung function (36,37-39). The benefit of vitamin D supplementation on muscle functions in the elderly subjects with serum 25-OHD less than 20 ng/ml has

been shown in a meta- analysis of randomized controlled trials (40).

Vitamin D is assumed to have a role in nociception and impaired neuromuscular function in patients with chronic pain. In one study, opioid users who had inadequate levels of vitamin D have reported worse physical functioning and health perception as compared with opioid users with adequate serum vitamin D (41). Depending upon seasonality, latitude, and body covering, a substantial proportion of general population may have inadequate serum 25-OHD levels and therefore may not achieve the maximal protective musculoskeletal benefits. Concerning the design of the present study which lacks a control group, the association between vitamin D supplementation and muscle strength does not indicate causality. Probably, improvement of QMS can be attributed to decreasing of pain. The relationship between muscle strength and knee pain has been shown in several studies (11-13).The findings of this study indicated that vitamin D supplementation reduces KOA pain by its strengthening effect on quadriceps muscles. (14-19). The beneficial effects of vitamin D in this study should not be attributed to seasonal variation of serum vitamin D, in this geographic region (40).

In conclusion, this study indicated that normalization of serum 25-OHD in vitamin D deficient patients with KOA significantly improves QMS and decreases knee pain. Further prospective placebo-controlled studies consisted of patients with different stages of radiographic KOA can provide additional data in detecting patients who are more responsive to vitamin D supplement.

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