EFFECTS OF VITAMIN D ON MUSCLE FUNCTION AND PERFORMANCE: A REVIEW

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Abstract

Vitamin D insufficiency is frequent in the general population. Meta-analyses of randomized controlled trials (RCTs) have shown a decreased risk of falls in elderly treated with vitamin D supplements, which may be due to an improved neuromuscular function in vitamin D-replete subjects. In most observational studies, vitamin D status correlates positively with muscle strength and postural stability. However, as physical activity is associated with vitamin D status as well as muscle strength, effects of vitamin D status on muscular health can only be assessed properly in RCTs. A systematic search was performed and 16 RCTs on the effects of treatment with vitamin D on muscle function were identified. All except one of the studies were performed in subjects above 50 years of age. Baseline 25-hydroxyvitmin D (25OHD) levels were below 50 nmol/l in 11 studies. Plasma 25OHD levels increased significantly in all studies. In seven studies, a beneficial effect of vitamin D treatment was documented on muscle strength of the lower legs, body sway, and/or physical performance. Identified studies were heterogeneous with regard to most aspects including indices measured. No obvious characteristics delineated studies showing beneficial effects from studies showing no effects. Only a few investigators reported the statistical power of measurements performed. In conclusion, evidence from RCTs do support an effect of vitamin D supplements on muscle strength and function in the elderly, but more studies showing a lack of an effect have been published than studies showing beneficial effects. There is a major lack of data on possible effects in younger subjects.

Keywords: elderly, muscle strength, vitamin D

Introduction

For many years, vitamin D has been known to be of importance to musculoskeletal health. It is well known that severe deficiency causes rickets (in children) and osteomalacia ('softening of the bones') in adults. Symptoms include paresthesia in hands and feet as well as aching muscles and bones. Findings include muscle weakness with particularly proximal myopathy causing difficulty getting up from a chair without using arms and by walking on stairs. Gait disturbance occur and gait is often characterized as waddling ('penguin gait'). The clinical feature of the myopathy associated with severe vitamin D deficiency is supported by findings from *in vivo* and *in vitro* experimental studies showing histological and electrophysiological changes in severe vitamin D deficiency. The vitamin D receptor (VDR) is expressed in the cell nuclei of muscle cells and vitamin D has been shown to affect muscle cell contractility. The number of VDRs decreases with age, which supposedly is a contributing factor to reduced muscle strength in the elderly. In addition to a direct effect of vitamin D on muscle cells, vitamin D deficiency causes secondary hyperparathyroidism (SHPT) which may also impair muscle function.

Vitamin D is either ingested from food or synthesized in the skin during sun exposure. In most subjects, sun exposure is the primary determinant of vitamin D status, accounting for 80–90% of the vitamin D body stores. Cholecalciferol (vitamin D3) is synthesized in the skin and found in fatty fish and mammals, whereas ergocalciferol (vitamin D2) comes from yeasts and plants. Vitamin D supplements may contain either vitamin D2 or D3. Previously, the two vitamin D metabolites were considered to have an equal potency, but recent studies have suggested that vitamin D2 may be inferior to vitamin D3 in the treatment of vitamin D insufficiency. Vitamin D2 and D3 are both hydroxylated primarily in the liver to 25-hydroxyvitamin D (25OHD) and subsequently in the kidneys (and different peripheral cells) to become the active vitamin D metabolite, 1,25-dihydroxyvitamin D (calcitriol), which acts on the VDR.

Vitamin D status is usually assessed by measuring plasma 25OHD levels. Plasma 25OHD levels below 50 nmol/l are considered as a state of insufficiency, although an increasing number of studies suggest that levels above 80 nmol/l are needed to ensure an optimal vitamin D status. Vitamin D deficiency is defined as plasma 25OHD levels below 25 nmol/l, and levels below 12 nmol/l are considered as a state of severe deficiency which may cause frank osteomalacia and severe proximal myopathy.

In vitamin D insufficiency, muscle function and physical function may be impaired before clinical or biochemical signs of bone disease are evident. An increased risk of falls in elderly subjects with low vitamin D levels have been documented in several studies and randomized controlled trials (RCTs), and meta-analyses of RCTs have shown a reduced risk of falls in elderly treated with vitamin D supplements. Most likely, this is due to an improved neuromuscular function in response to vitamin D supplementation. Similarly, associations between vitamin D status and muscle strength, body sway and physical performance have been investigated in a large number of cohort and cross-sectional studies with most, but not all, studies showing the beneficial effect of vitamin D status on measured indices. However, interpretation of results from observational studies is difficult, as plasma 25OHD levels, physical activity and muscle strength are closely interrelated. In several studies, physical activity has been shown to correlate positively with vitamin D status which most likely is due to the fact that physically active subjects spend more time outdoors in the sun and accordingly have a higher endogenous vitamin D synthesis than physically inactive subjects. In addition, physical activity improves muscle strength. Although most observational studies have adjusted statistically for potential interactions of physical activity and vitamin D status on muscular strength, residual confounding may exist and accordingly results from RCTs are imperative in order to draw valid conclusions on the effects of vitamin D status on muscle function.

The aim of the present paper is to review systematically the current state of knowledge on the effects of vitamin D on muscle strength and performance, based on results from individual RCTs.

Type and duration of interventions

In most studies, vitamin D3 has been administrated orally as either a daily, weekly or monthly dose. In most studies, an average daily dose of between 400 and 1200 IU of vitamin D3 was studied, whereas two studies used substantially higher average doses administrated either weekly (2000 IU/day) or monthly (3700 IU/day). In five studies, vitamin D2 has been administrated as either a single intramuscular or oral dose, as two doses administrated 10 weeks apart, or as a daily oral dose. The doses of vitamin D2 used have varied widely. In nine studies, vitamin D3 has been administrated in combination with a daily calcium supplement and in these studies calcium alone (without vitamin D) has been used as a comparator.

In the WHI study, follow up was performed after an average of 7.1 years, whereas time to follow up has varied from 2 to 24 (average 8) months in the other 15 studies.

Effects of interventions on plasma 25OHD and PTH levels

In all but one study, the effect of treatment on plasma 25OHD levels has been reported, showing a significant increase in 25OHD levels in vitamin D treated subjects compared with controls .

Baseline plasma 25OHD levels were below 50 nmol/l in 11 of the included studies. In 13 studies, the effects of treatment on plasma PTH levels was reported showing either significantly decreased levels or no effects compared with the controls. Vitamin D3 has been co-administrated with calcium in four of the five studies showing decreased PTH levels, as well as in four of the studies showing no effects on PTH levels. No apparent differences exist between studies showing or not showing effects on plasma PTH levels regarding dose of vitamin D administrated or baseline plasma 25OHD levels. However, none of the studies using vitamin D2 showed effects on plasma PTH levels.

Effects on muscle function

Overall, seven studies showed a positive effect of vitamin D treatment on muscle strength, postural sway and/or physical performance, whereas nine studies found no evidence of effects on measured indices.

Effect on muscle strength

Effects of vitamin D on muscle strength was evaluated in 12 studies. In most studies, a dynamometer/strain gauge system was used to measure maximal voluntary isometric muscle strength; Hajj Kenny *et al.*2003;.

Lower legs isometric muscle strength, as assessed by using a strain gauge system, was evaluated in eight studies. Two studies showed an improved isometric muscle strength in response to treatment. Accordingly, in response to 6 months of treatment with 800 IU/day vitamin D3, Pfeifer and colleagues found significantly increased quadriceps strength compared with placebo. Similarly, Moreira-Pfrimer and colleagues found significantly improved maximal isometric strength of hip flexors and knee extensors in vitamin D3-treated subjects compared with placebo.

In addition to using a strain gauge system, effects of vitamin D treatment have been evaluated in a Japanese study in terms of a physical therapist (blinded to treatment allocation) assessing muscle strength using the British Medical Research Council scale. The study included women with poststroke hemiplegia and showed that compared with placebo, 2 years of treatment with 1000 IU/day vitamin D2 caused a significantly improved strength of the gluteus maximus and iliopsoas muscles on the intact side.

Effects of vitamin D treatment on hand grip strength have been evaluated in five studies, none of them showing significant effects.

No obvious differences exist between the studies showing or not showing effects in terms of characteristics of included subjects or effects of treatment on plasma 25OHD or PTH levels.

Conclusions:

In conclusion, several lines of evidence support an effect of vitamin D on muscle function and findings from RCTs have shown beneficial effects of vitamin D supplementation in the elderly. However, an effect is not universally present as more papers showing a lack of an effect have been published than papers showing beneficial effects. Explanations for the discrepant results are not obvious, as no general characteristics seem to separate studies showing beneficial effects from studies showing no effect of an improved vitamin D status. Further studies should try to replicate findings from the studies showing beneficial effects with predefined sample size calculations in order to assure a proper statistical power. Moreover, as low vitamin D levels are common in the general population, more studies are needed in younger subjects in order to assess potential harmful effects of vitamin D insufficiency on neuromuscular health in subjects below the age of 50 years

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