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Review

Effects of vitamin D supplementation on upper and lower body muscle strength levels in healthy individuals. A systematic review with meta-analysis

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ABSTRACT

Objectives: To investigate the effects of vitamin D supplementation on muscle strength in healthy individuals.
Design: A systematic review with meta-analysis.
Methods: In October 2013 a computerised literature search of three databases (PubMed, Web of Knowledge and Scopus) was performed. Included in the review were controlled and randomised controlled trials, published in English, which measured muscle strength and serum vitamin D concentration in participants 18–40 years old. References of identified articles were then cross-checked and citations scanned for additional articles. Quality was assessed using the PEDro scale. Muscle strength and vitamin D levels were extracted for a meta-analysis on upper and lower limb strength with standardised mean differences calculated to analyse effect.
Results: Six randomised controlled trials and one controlled trial were identified and quality assessment showed all seven trials were of 'good quality'. Data was extracted from 310 adults, 67% female, with mean ages ranging from 21.5 to 31.5 years. Trials lasted from 4 weeks to 6 months and dosages differed from 4000 IU per day to 60,000 IU per week. Upper and lower limb muscle strength had a standardised mean difference of 0.32 (95% CI = 0.10, 0.54) and 0.32 (95% CI = 0.01, 0.63) respectively, suggesting vitamin D supplementation significantly increased muscle strength in the experimental group for upper ($P = 0.005$) and lower limbs ($P = 0.04$).
Conclusions: Vitamin D supplementation increases upper and lower limb strength. Further research should focus on its effect on muscle power, endurance and maximal strength.

1. Introduction

Vitamin D is a seco-steroid hormone because one of the rings of its cyclopentanoperhydrophenanthrene structure has a broken carbon–carbon on ring B. As such vitamin D3 is biologically inactive and requires hydroxylation to 25(OH)D3 in the liver and then to 1α,25(OH)2D3, 24*R*,25-dihydroxyvitamin D3 [24*R*,25(OH)2D3] in the kidney to gain biological activity. The classical "vitamin" effects of vitamin D on bone and muscle health is to maintain calcium homeostasis, whereas the hormonal effects are achieved through binding to the vitamin D receptor.[1] Vitamin D is extracted from commonly obtained foods like egg yolks, saltwater fish, and liver,[2] which can be synthesised by humans in the presence of sunlight.[3] However, it has been reported that over a billion people worldwide are vitamin D deficient,[3] with 36–69.9% of the young adult population suffering from deficiency.[4,5]

Vitamin D has many forms; the most common being vitamin D3 which is produced in the epidermis when exposed to UVB radiation.[6] There are three forms of vitamin D3: cholecalciferol, the inactive, unhydroxylated form; calcifedol which is measured in blood samples to give an indication of vitamin D concentrations; and calcitriol, the active form.[6] Vitamin D3 is also the most commonly supplemented form, along with vitamin D2 or ergocalciferol, a provitamin found in mushrooms.[7]

Vitamin D is known to improve immunity to diseases by inhibiting immune reactions.[8] Further, vitamin D promotes bone health by assisting to maintain serum calcium levels.[9] On the other hand, vitamin D deficiency is associated with an increased risk of developing pathologies such as cardiovascular diseases, forms of cancer, and cognitive impairments.[10] Recently, a relationship between vitamin D deficiency and reduced muscle strength has been observed.[11] Vitamin D receptors have been found on skeletal

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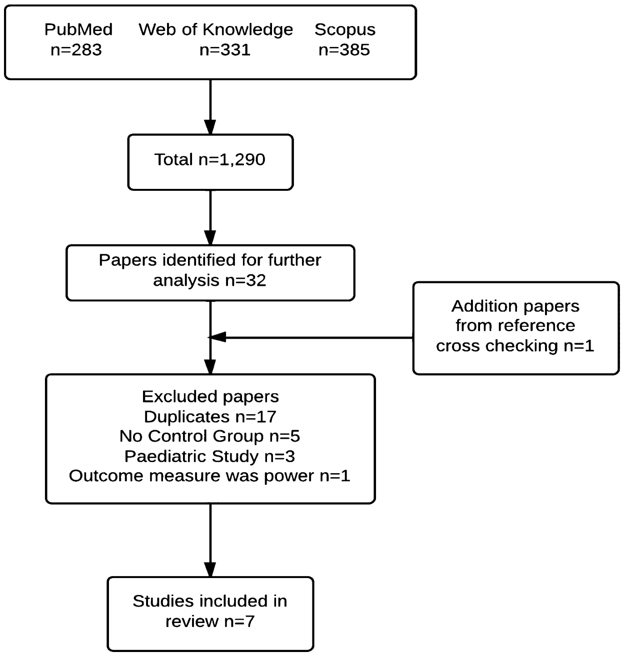

Fig. 1. Flow diagram of the search strategy and results.

muscle fibres,[6,12] and studies have shown that these receptors are involved in protein synthesis within the muscle, promoting muscle growth.

Recent meta-analyses have reported vitamin D supplementation to improve muscle strength in frail, deficient, and elderly women.[13,14] However, to our knowledge, there has been no published evidence which systematically summarises the effects of vitamin D supplementation on muscle strength levels in young, healthy individuals. While some narrative reviews[12,15] are available, these were exposed to selection bias and they did not include any meta-analysis, therefore making data quantification difficult. Therefore, the aim of this systematic review is to evaluate the effects of randomised supplementation of vitamin D on upper and lower limb muscle strength in young, healthy individuals.

2. Methods and materials

Search strategy. Three databases, PubMed, Web of Knowledge and Scopus were searched from inception up until October 2013, and full-text articles retrieved. Two independent researchers (PT & CJ) performed the search, and each title and abstract was revised for final inclusion into the study. Any discrepancies in study inclusion between the researchers were discussed, and a third researcher was used to reach consensus if necessary. The MESH terms used in the search strategy were vitamin D OR vitamin D2 OR vitamin D3 OR 1-alpha hydroxyvitamin D3 OR 1-alpha hydroxycalciferol OR 1,25-dihydroxyvitamin D3 OR 1,25 dihydroxycholecalciferol OR 25 hydroxycholecalciferol OR 25 hydroxyvitamin D OR calcitriol OR ergocalciferol OR Cholecalciferol OR calcifediol OR alfacalcidol OR calcidiol OR calciferol AND supplementation OR supplement AND muscle OR muscle function OR muscle strength NOT aged. A detailed flow diagram of the search strategy is shown in Fig. 1.

Inclusion/exclusion criteria. Studies were included if they were published in English, employed a control group, and measured muscle strength as one of their primary outcome measures. Studies were required to supplement participants with vitamin D only in at least one arm of their study. Studies involving participants under the age of 18, animals, and non-healthy subjects were excluded from this review. Conference abstracts, PhD theses, reviews of the literature and letters to editors were also excluded.

Review process. References of included studies were scanned for any articles that had not been recovered in the initial search. All searches were imported into Endnote Online (Thomson Reuters 2013, www.myendnoteweb.com) and duplicates then removed. For meta-analysis, the following information was extracted: author, year of publication, sample size, anthropometric assessments, length of intervention, baseline measurements of serum vitamin D levels, post-intervention serum vitamin D levels, and muscular strength. Where studies did not report their serum concentrations in nmol/L, results were converted using an online converter (ChronicIllnessRecovery, 2013 https://chronicillnessrecovery.org/calc/index.php). To determine the overall effect of each outcome measure employed, effect size (standardised mean difference, SMD), and confidence intervals were calculated.

Quality assessment. To assess the quality of the methodology of the RCT included studies, the PEDro checklist[16] and CONSORT guidelines[17] were used. PEDro scores were out of a total of 11 and any result between nine and 11 was regarded as excellent, six to eight good, four to five fair and less than four is considered a bad quality study. Any non-RCTs were assessed using the Downs and Black assessment scale[18] which provided an overall score for study quality and a numeric score out of a possible 30 points. All studies included were assessed for quality by two, independent researchers (PT & CJ).

Meta analysis. In addition to extracting and presenting the data from the individual studies, a meta-analysis was performed using the Review Manager Software (version 5.2). A fixed effects model was used and standardised mean differences with 95% confidence intervals were calculated to compare reported outcome measures. Boundaries of 0.8 (large effect size), 0.5 (moderate effect size) and 0.2 (small effect size) were used to categorise the effect size.[19] Data was divided into lower limb and upper limb outcome measures. Heterogeneity was determined to measure the variability between the studies identified for the analysis. I^2 statistic was employed to calculate how comparable the studies are amongst each other, and therefore, understand what proportion of variability is due to inter-trial heterogeneity compared to sampling error.

3. Results

Study characteristics. The initial search returned 1290 studies. After consulting the relevance of the title and abstracts, thirty two of these studies were retrieved for further analysis and reference cross-checking found one additional study. Of these 32 studies, 17 were duplicates, three studies involved children, five did not involve control groups, and one study measured muscle power.

A total of seven papers,[20–26] met the inclusion criteria and therefore were included into the review. A total of 310 subjects were involved, of which 67.4% were female. Five studies reported the age-range of the participants and these were used to calculate the average age of 270 subjects as 24.1 years. Subjects from three studies were of an athletic population,[21–23] two studies used medical students and medical professionals,[24,25] one study recruited healthy adults,[20] and one study enrolled adults wishing to undergo a resistance training programme.[26] Table 1 depicts in details the characteristics of studies included.

Quality assessment. The PEDro mean score was 8.7 ± 1.4 out of a possible 10 with studies mainly losing points due to participant dropouts. Four of the studies were classified as 'excellent'[20,23,24,26] and two were classified as 'good'.[22,25] The CONSORT scores ranged from 13 to 22 with two studies[22,26] not accurately describing the flow of participants through the study and ambiguous statements regarding blinding. One non-randomised trial had a high Downs and Black score.[21]

Intervention. All seven studies used vitamin D as a supplement; six administered Cholecalciferol (vitamin D3)[20,22–26] and one study

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