Muscle strength and mobility in vitamin D-insufficient female geriatric patients: a randomized controlled trial on vitamin D and calcium supplementation

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ABSTRACT. Background and aims: Insufficient vitamin D status, commonly found in older people, has been associated with muscle weakness which, in old age, impairs mobility and is a risk factor for falling. In a randomized, double-blind placebo-controlled trial, we tested the hypothesis that vitamin D + calcium supplementation improves muscle strength and mobility, compared with calcium mono-therapy in vitamin D-insufficient female geriatric patients. Methods: Seventy female geriatric patients >65 years of age with serum 25-hydroxyvitamin D₃ (25OHD) concentrations between 20 and 50 nmol/L, visiting an outpatient geriatric department, were included. Participants received either cholecalciferol 400 IU/day + calcium 500 mg/day (D-Cal group) or a placebo + calcium 500 mg/day (Plac/Cal group) for 6 months. At baseline and 6 months, muscle strength, power and functional mobility were tested. Results: At baseline, 25OHD was significantly (p<0.03) associated with knee extension strength (r=0.42), handgrip strength (r=0.28), leg extension power (r=0.34), Timed Get Up and Go (r=-0.31) and Modified Cooper test (r=0.44). At 6 months, a significant difference in 25OHD (77.2 vs 41.6 nmol/L, p<0.001) and 1,25OHD was found between the two groups. Significantly improving vitamin D status in the D-Cal group compared with the Plac/Cal group did not result in a significant difference in strength or functional mobility between the two groups. Conclusions: Daily 400 IU vitamin D + 500 mg calcium supplementation is not enough to significantly improve strength or mobility in vitamin D-insufficient female geriatric patients.

INTRODUCTION

Older people are prone to develop vitamin D deficiency, predominantly because of low exposure to sunlight, decreased capacity of the skin to synthesize provitamin D, and inadequate dietary vitamin D intake to compensate (1).

As the serum 25OHD concentration gradually declines from a state of hypovitaminosis D to vitamin D insufficiency (<50 nmol/L), secondary hyperparathyroidism (sHPT) develops and bone metabolism and muscle function are compromised (2). Further decline, leading to vitamin D deficiency, is associated with osteomalacia and symptoms of malaise, musculoskeletal pain (3) and muscle weakness, particularly of proximal muscle groups (4). Histologically, type II muscle fiber atrophy is found in vitamin D deficiency (5).

It is thought that muscle weakness associated with advancing age (sarcopenia) is partly caused by vitamin D deficiency (6). Indeed, muscle weakness and reduced physical performance have been associated with low vitamin D status in older people (7-9). However, evidence from randomized controlled trials is conflicting (10, 11). In a meta-analysis by Latham et al., 13 trials were evaluated according to intervention applied. Of the six trials that studied mono-therapy with vitamin D or an analog, none yielded a positive effect on muscle strength, physical functioning or fall reduction. Combined treatment with calcium and vitamin D showed a reduction in falls in three out of seven trials (11). This matches the results of a meta-analysis by Boonen et al., which showed that only combined calcium and vitamin D supplementation reduced hip fracture risk by 18% (12).

In this paper, we present the results of a randomized, double-blind, placebo-controlled trial on the effect of vitamin D and calcium supplementation, compared with calcium mono-therapy on muscle strength, power and functional mobility in vitamin D-insufficient female geriatric patients.

Key words: Female geriatric patients, mobility, muscle strength, vitamin D insufficiency.

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SUBJECTS AND METHODS

Subjects

Women attending the outpatient clinic of the Department of Geriatric Medicine at the University Medical Centre, Utrecht, The Netherlands, were included if they were >65 years of age, able to walk and follow simple instructions, and had a serum 25OHD concentration between 20 and 50 nmol/L. Exclusion criteria were: treatment with vitamin D or steroids in the previous 6 months, a history of hypercalcemia or renal stones, liver cirrhosis, serum creatinine >200 micromol/L, malabsorptive bowel syndrome, primary hyperparathyroidism, uncontrolled thyroid disease, anticonvulsant drug therapy, and/or presence of any other condition that would probably interfere with the patient’s compliance (i.e., surgery planned). Most women lived in residential homes for the elderly. All subjects gave their written informed consent. The study was approved by the Ethics Committee of the University Medical Centre Utrecht, The Netherlands.

Intervention and measurement protocol

Subjects were randomly assigned to either vitamin D (cholecalciferol) 400 IU/day + calcium 500 mg/day, or identically appearing placebo tablets + calcium 500 mg/day. Trial medication was provided by an independent hospital pharmacist who also performed the randomization. Randomization was done in blocks of six, to minimize any seasonal influence between the treatment groups. No person involved, i.e., subjects, investigators, or physicians who treated the subjects, had access to the randomization procedure.

Treatment period was six months (24 weeks ± 2 weeks). Measurements were carried out at baseline and 6 months. To stimulate and monitor compliance, subjects were contacted at 3 months, to answer questions and repeat information given at baseline. All measurements were made by the principal investigator (first author).

Demographics and anthropometry

Age, medical history, use of medication, body weight while wearing light indoor clothing (to the nearest 0.1 kg) and height (to the nearest 0.1 cm) were recorded, and the Body Mass Index (kg/m²) was calculated.

Knee extension strength

Isometric knee extension strength (IKES) was measured with fixed dynamometry. The subject was seated in an adjustable, straight-backed chair, with the lower leg unsupported and the hip and knee flexed at a 90° angle, with an adjustable belt around the hips. In both legs, isometric knee extension strength in Newton (N) was measured with a strain gauge applied with a strap around the ankle just proximal to the maleoli (13). After one ‘try-out’, the best of three measurements was recorded on both sides.

Handgrip strength

Handgrip strength (HGS) was measured with a dynamometer (Takei Kiki Kogyo 5101, Japan). The maximum of three measurements was recorded in kilogram force on both sides (14).

Leg extension power (LEP)

Explosive leg extension power (LEP) was measured with the Nottingham Power Rig (15). The subject, in a seated position with folded arms and a 90-degree knee angle at the start, pushed a large foot pedal as hard and fast as possible, setting a flywheel in motion. The best of seven measurements was recorded (in Watts, W) on both sides. A resting interval of 30 seconds was allowed between attempts.

Timed “Get Up and Go” test (TGUG)

Functional mobility was quantified by the timed “Get Up and Go” test (16, 17). In this test, the time taken by an individual to stand up from a standard arm chair (with a built-in timer), walk a distance of 3 meters, turn, walk back to the chair and sit down again is recorded. The subject walked through the test once before being timed, in order to become familiar with it. If a participant used a walking-aid in everyday life, this was also used in the test.

Modified Cooper test (COOP)

The Modified Cooper test (COOP) (18) is a test in which the maximum walking distance (in meters) achieved in 2 minutes is recorded. In older people, it is used as a measurement of overall mobility. The participant is instructed to walk as fast as possible without starting to run, and was taken through the distance before being timed. A walking aid was allowed.

Habitual physical activity

Habitual physical activity was measured with a physical activity questionnaire for the elderly (19). This was an interview-administered instrument. Activities in three domains (household, sports, leisure time) were determined and combined to create an overall physical activity score.

Laboratory analyses

Non-fasting blood samples were drawn at baseline and 6 months to determine 25OHD, 1,25(OH)₂D, calcium, albumin, alkaline phosphatase, phosphate and creatinine.

Statistical analyses

In the Intention to Treat analysis, we included all women tested at 6 months. For the Per Protocol analysis, subjects were excluded if they met the following criteria: baseline 25OHD <20 nmol/L or >50 nmol/L, a compliance of vitamin D/placebo treatment <70%, did not take calcium tablets and had a dietary intake of calcium