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Clinical Research Article

Effect of Vitamin D Supplementation on Muscle Function in Patients With I131-Induced Hypothyroidism: A Pilot Randomized Trial

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Abstract

Background: There is a lack of data regarding the effect of vitamin D supplements in patients with I131-induced hypothyroidism. The primary aim of this study was to investigate the effect of vitamin D supplements on muscle function, and the secondary aim was to observe the effect on body composition, insulin resistance, and quality of life (QOL) in patients with I131-induced hypothyroidism.

Methods: In this pilot randomized placebo-controlled trial, patients with I131-induced hypothyroidism on a stable dose of levothyroxine were enrolled and allocated into 2 groups to receive oral vitamin D 20 000 IU weekly or placebo for 24 weeks. Baseline biochemical values, body composition, handgrip strength, the 5 times sit-to-stand test (5TSTS), homeostatic model assessment for insulin resistance (HOMA-IR), and QOL were measured before intervention and after 3 and 6 months in both groups. Mixed model regression analysis was used to compare the outcomes between the 2 groups. Significance was set at P value of $< .05$.

Results: There were 20 participants in each group. The time taken for 5TSTS in the vitamin D group was significantly lower than the placebo group at 3 ($P = .032$) and 6 months ($P = .006$). Other outcomes, including handgrip strength, body composition, HOMA-IR, and QOL, showed no significant difference between the 2 groups.

Conclusion: A supplement of vitamin D2 at 20 000 IU per week for 24 weeks could help improve performance in 5TSTS in patients with I131-induced hypothyroidism.

Key Words: I131-induced hypothyroidism, vitamin D supplement, handgrip strength, 5 times sit to stand test, insulin resistance

Abbreviations: 5TSTS, 5 times sit-to-stand test; FT4, free thyroxine; HOMA-IR, homeostatic model assessment of insulin resistance; QOL, quality of life; SF-36, 36-item Short Form Health Survey; TSH, thyrotropin (thyroid stimulating hormone); VDR, vitamin-D-specific nuclear receptor.

Hypothyroidism often occurs following radioactive iodine (I131) therapy for hyperthyroidism in clinical practice. Untreated I131-induced hypothyroidism can lead to symptoms such as muscle weakness, fatigue, weight gain, decreased muscle mass, altered fat mass, increased insulin resistance, and abnormal blood lipid levels [1]. The standard treatment for I131-induced hypothyroidism involves administering replacement doses of thyroid hormones to maintain levels within the normal range.

Muscle weakness affects up to 80% of patients with hypothyroidism, leading to functional limitations such as impaired stair climbing, difficulty rising from a seated position, and lifting objects [2]. The mechanism involves the atrophy of type 2 (fast-twitching) muscle fibers and an increase in the number of type 1 (slow-twitching) muscle fibers [2]. After receiving thyroid hormone replacement, muscle symptoms often improve within 6 months to 1 year [3]. Nevertheless, significant functional impairment may persist in 40% of patients, even with adequate thyroid hormone treatment [4]. Untreated hypothyroidism may lead to modest weight gain related to insulin resistance [5]. However, one study revealed no significant weight change after the initiation of thyroid hormone therapy [6]. Regarding quality of life (QOL), multiple symptoms of hypothyroidism can impair a patient's health status and QOL [7]. Levothyroxine replacement may improve QOL scores; however, QOL might not always return to normal, even upon normalization of thyrotropin (TSH) levels [8].

Vitamin D deficiency has been associated with the atrophy of type 2 muscle fibers, leading to impaired muscle function [9]. A study found that elderly individuals treated with vitamin D over a period of 3 to 6 months experienced an increase in type 2 muscle fibers [10]. In prediabetic patients, those with low vitamin D levels exhibited higher insulin resistance compared to those with high vitamin D levels. Another study

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demonstrated that high-dose vitamin D administration could reduce the degree of insulin resistance [11, 12]. Similarly, low vitamin D levels were associated with low QOL, while vitamin D supplementation had a positive effect on QOL [13, 14].

Despite appropriate treatment with thyroid hormone, some patients continue to experience persistent symptoms. Implementing vitamin D supplementation may contribute to the improvement of these residual symptoms. Currently, there have been no studies on the effects of vitamin D supplements on muscle strength in patients with I131-induced hypothyroidism. Therefore, this study aimed to investigate the effects of vitamin D supplementation compared to a placebo on muscle function in patients with I131-induced hypothyroidism, with secondary outcomes that included body composition, insulin resistance, and QOL.

Methods

This placebo-controlled randomized trial was conducted between January 2023 and December 2023, at Maharaj Nakorn Chiang Mai Hospital, a tertiary care hospital. The research protocol complied with the ethical standards and was approved by Research Ethics Committee Faculty of Medicine, Chiang Mai University (Ethical No. MED-2565-09285). The trial was registered in the Thai Clinical Trials Registry with the registration number TCTR202 30107005.

Study Setting and Eligibility

Eligible patients were aged between 18 and 70 years, diagnosed with I131-induced hypothyroidism, and undergoing thyroid hormone replacement therapy. Patients were required to exhibit normal thyroid hormone levels and to have maintained a stable replacement dose for at least 6 months. Exclusion criteria included patients with thyroid cancer, as well as those with chronic conditions, such as cerebrovascular disease, end-stage renal disease (estimated glomerular filtration rate < 60 mL/min/1.73 m^2), diabetes mellitus, muscle weakness, chronic depression, cancer, liver disease (Child-Pugh class B or C), and gastrointestinal disorders causing malabsorption. Additionally, individuals with abnormal levels of calcium and phosphate, pregnant women, those already receiving vitamin D and calcium supplementation, and those taking thiazide medication were excluded.

Study Design and Randomization

Eligible patients were invited to enroll in the study, during which research staff explained the research details, safety information, and addressed any questions or concerns. Written informed consent and baseline measurements were obtained from patients at the time of enrollment. Baseline data, including age, gender, weight, height, body mass index, waist circumference, dose of I131 received during hyperthyroidism treatment, duration of hyperthyroidism since diagnosis, duration of thyroid hormone replacement therapy before enrolling in the study, sitting blood pressure, lean body mass, and fat mass, were collected. Baseline laboratory tests, including free thyroxine (FT4), TSH, serum calcium, serum phosphate, serum albumin, serum creatinine, fasting plasma glucose, and fasting insulin, were retrieved prior to the study. Muscle function and QOL assessments were also conducted at baseline. Vitamin D levels were checked as a baseline before disclosing the results. Participants were randomly assigned in a 1:1 ratio using the www.randomization.com program. The enrollment, allocation, and baseline data collection processes were conducted by a physician (S.M.) who was not involved in the outcome assessment process. Therefore, the patients and the assessors were blinded to the study. The patients were divided into 2 groups: the first group received a weekly dose of 20 000 IU of vitamin D capsules combined with a carrier consisting of gelatin and vegetable oil (produced by The British Dispensary [L.P.] Co., Ltd), and the second group received a visually identical placebo capsule made of starch (produced by the Faculty of Pharmacy, Chiang Mai University). The dosage of vitamin D supplementation adhered to the recommended daily intake according to National Institutes of Health (NIH) guidelines, which advise not exceeding 4000 IU per day for individuals aged 18 to 70 [15]. The dosage provided in the study, 20 000 IU per week (equivalent to 2857 IU/day), was within the specified limits. In the event of vitamin D toxicity, characterized by an elevated serum calcium level beyond the normal range, the recommended course of action included discontinuing vitamin D medication and administering treatment for hypercalcemia in accordance with medical guidelines [16].

Participants from both groups underwent serial follow-up assessments of muscle function, body composition, QOL assessment and biochemical tests, including FT4, TSH, serum calcium, serum phosphate, serum albumin, serum creatinine, fasting plasma glucose, and fasting insulin, at 3 and 6 months.

Assessment of Outcomes

Muscle function was assessed using handgrip strength and the 5 times sit-to-stand test (5TSTS). Handgrip strength was measured using the Jamar handgrip dynamometer, with measurements recorded in kilograms. The assessment was conducted 3 times on the preferred side, and the highest recorded result was documented.

The 5TSTS involved instructing the patient to stand up and sit down 5 times as quickly as possible upon the examiner's cue of "Go." The patient utilized a free-standing chair positioned against a wall, maintaining arms folded across the chest and back against the chair. The time taken to complete the task was recorded. The test necessitated a standard chair, a stopwatch, and clear instructions [17].

Bioelectrical impedance analysis was conducted using the Tanita BC-545 N body composition analyzer (Tanita Cooperation, Tokyo, Japan) to assess fat mass and lean body mass. The measuring current was standardized at 50 Hz, and patient age, sex, and height were input manually. Patients were instructed to stand barefoot, wear loose clothing, and remain still during the measurement process. The machine's software was utilized to calculate the percentage of body fat. Dual-energy x-ray absorptiometry measurements were employed to validate the contact electrode system of this body composition analyzer, with results demonstrating a satisfactory correlation for fat mass [18].

Homeostatic model assessment for insulin resistance (HOMA-IR) was used as an index for insulin resistance, calculated using the formula: fasting insulin (microU/L) $\times$ fasting glucose (nmol/L)/22.5.

QOL assessments were conducted using the Thai version of the 36-item Short Form Health Survey (SF-36) questionnaire, consisting of 8 aspects, as follows: *Physical Function*, which

assesses the ability to perform various physical activities; *Role Physical*, which measures the ability to perform physical activities related to roles or responsibilities; *Bodily Pain*, which measures the level of pain experienced; *General Health*, which assesses the general health of the individual; *Vitality*, which measures liveliness and mental readiness; *Social Functioning*, which assesses the ability to perform social activities; *Role Emotional*, which measures the ability to perform emotional or mental activities related to roles or responsibilities; and *Mental Health*, which assesses overall mental health [19].

Assay Methods

Serum FT4 (RRID:AB_3095310; normal reference range, 0.93–1.71 ng/dL), and TSH (RRID: RRID:AB_3095311; normal reference range, 0.27–4.2 μIU/mL) were measured by electrochemiluminescence assay (ECLIA) (Elecsys FT4 IV, TSH assay, Roche Diagnostics GmbH, Mannheim, Germany) with intra- and inter-assay variation of 1.9% to 8.2%. Insulin level (RRID:AB_2756877; normal reference range, 2.6-24.9 mU/L) was measured by electrochemiluminescence assay (ECLIA) (Elecsys Insulin assay, Cobas e411 analyzer, Roche Diagnostics GmbH, Mannheim, Germany) with intra- and inter-assay variation of 1.9% to 3.7%. Vitamin D level (RRID:AB_2909604; normal reference range, 30-50 ng/mL) was measured by electrochemiluminescence binding assay (Elecsys Vitamin D total III, Roche Diagnostics GmbH, Mannheim, Germany) with intra- and inter-assay variation of 2.4% to 8.5%.

Statistical Analysis

Data were analyzed using STATA (Stata Corp., College Station, TX, USA). Categorical variables were presented as frequency and percentage. Continuous variables with a normal distribution were presented as mean and SD, while non-normally distributed continuous variables were presented as median and interquartile range. Comparison between groups for categorical variables was performed using the Fisher exact test, and for continuous variables, the Student *t* test was utilized for normally distributed variables, while the Mann-Whitney U test was used for non-normally distributed variables. Changes in muscle function, body composition, HOMA-IR, and QOL scores between the vitamin D and placebo groups at 3 and 6 months were analyzed using linear mixed model analysis, adjusted for unequal baseline. Results were presented as mean difference and 95% CI. All analyses were conducted according to the intention-to-treat principle and the result were considered significant if the Bonferroni-corrected *P* value was $< .05$. The sample size for this study was not calculated, as it was a pilot study.

Results

We recruited participants by searching for individuals who could join the research project at the scheduled outpatient department appointments in the Endocrine Clinic. The details of the research project were provided, and a total of 54 individuals were eligible to participate. However, 14 individuals opted not to join the research, citing the inability to attend the scheduled appointments.

A total of 40 participants with I131-induced hypothyroidism were included in the study. Twenty participants were assigned to the vitamin D group, while another 20 participants were allocated to the placebo group. All 40 patients completed the treatment period (Fig. 1). Participants in both groups exhibited similarities in demographic, anthropometric, and laboratory data, except for age. In the vitamin D group, the average age was higher than in the placebo group (53.2 ± 2.0 years vs 45.7 ± 2.7 years). Both groups predominantly consisted of female participants. There was no significant difference in baseline biochemical tests, including vitamin D levels, handgrip strength, 5TSTS, and QOL scores between the groups. Baseline characteristics are presented in Table 1.

The time taken to perform the 5TSTS was significantly shorter in the vitamin D group compared to the placebo group at both 3 months (mean difference −1.12 seconds, 95% CI −2.03 to −0.21, $P = .032$) and 6 months (mean difference −1.71 seconds, 95% CI −2.85 to −0.57, $P = .006$). There was no statistically significant change in handgrip strength observed at 3 months and 6 months in the vitamin D group compared to the placebo group. Data are presented in Table 2 and Fig. 2.

For secondary outcomes, there were no statistically significant differences in blood pressure, serum calcium, albumin, phosphate, creatinine, fasting insulin, fasting blood glucose, FT4, TSH, HOMA-IR, fat mass, lean body mass, and SF-36 at both 3 months and 6 months. Additionally, no occurrences of hypercalcemia or any complications were reported during the study. Data are presented in the Supplementary Table [20].

Discussion

This randomized placebo-controlled trial assessed the effect of vitamin D supplementation on muscle function, body composition, insulin resistance index, and QOL in post-I131-induced hypothyroidism patients receiving a stable dose of thyroid hormone replacement. Intriguingly, higher muscle function, as measured by 5TSTS, was observed in the vitamin D-treated group compared to the placebo-treated group at 3 and 6 months of therapy. However, there were no statistically significant differences between the 2 groups in the effects of changes in handgrip strength, fat mass, lean body mass, HOMA-IR, and SF-36 QOL score at both 3 and 6 months. Baseline vitamin D levels in both groups were comparable, with a mean level of 24 ng/mL, defined as "no vitamin D insufficiency" according to World Health Organization definition [21]. Hence, the positive effect of vitamin D observed in the present study may not be solely attributable to vitamin D deficiency but rather to the direct effect of vitamin D itself on improving muscle function.

In both clinical and research contexts, the handgrip dynamometer is commonly used to evaluate muscle strength and mobility, while the 5TSTS is frequently employed to assess functional lower limb strength and balance. A quicker completion time of the 5TSTS suggests enhanced postural balance and muscle strength [22]. Nevertheless, there has been controversy surrounding the utilization of the handgrip dynamometer for assessing overall muscle strength. Additionally, the assumption that a decline in handgrip strength correlates with a decrease in lower limb strength, knee extensor strength, and/or knee flexor strength remains uncertain [23]. Changes in handgrip strength may not adequately account for alterations in lower limb strength. Consequently, handgrip strength may not be an appropriate tool for assessing strength changes

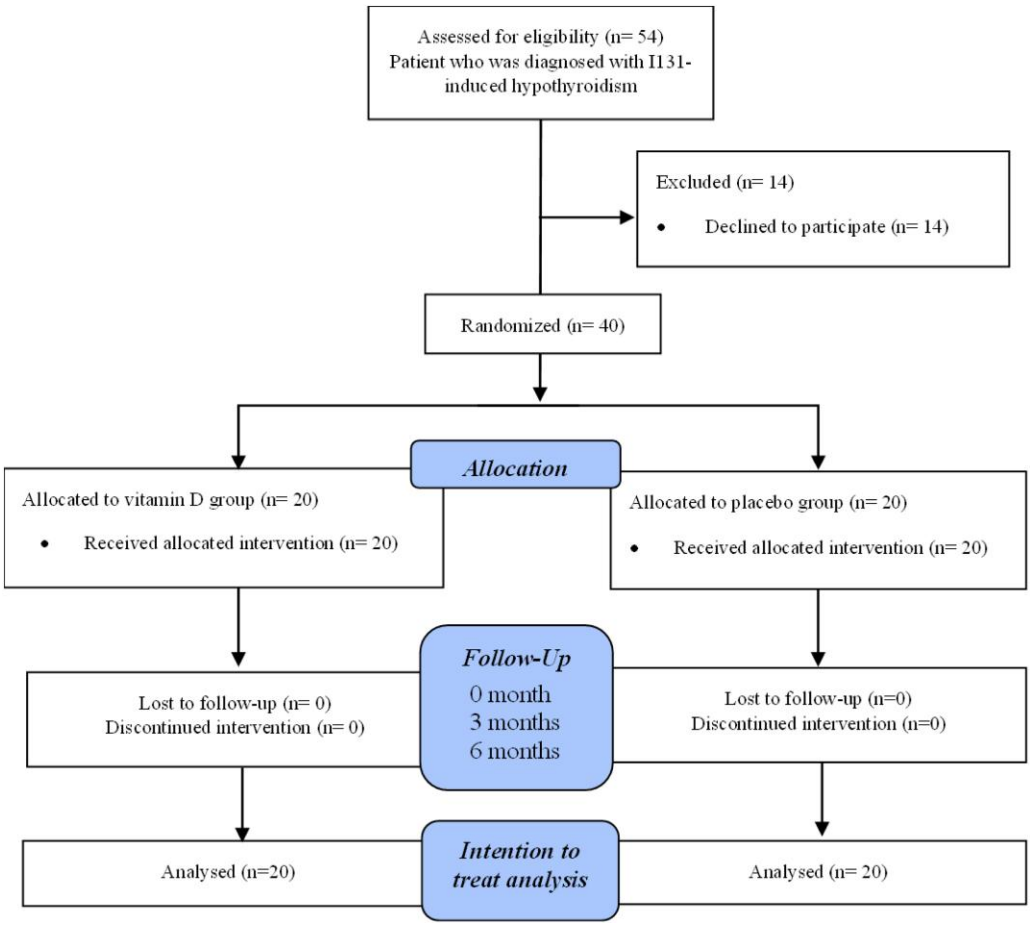

Figure 1. Study flow diagram.

across various body regions [24]. This could elucidate the findings of this study, which demonstrated a significant improvement only in the 5TSTS following vitamin D replacement therapy, without a corresponding change in handgrip strength.

The mechanism of hypothyroid myopathy involves the atrophy of type 2 (fast-twitching) muscle fibers and an increase in the number of type 1 (slow-twitching) muscle fibers [2]. Furthermore, hypothyroid myopathy involves the accumulation of glycosaminoglycans in the muscles, a reduction in myosin ATPase activity, and a decrease in ATP turnover within muscle fibers [25-27]. The mechanism underlying the impact of vitamin D on muscle strength and function in I131-induced hypothyroidism patients is not fully understood. However, recent research has provided increasing evidence supporting the role of vitamin D in both muscles and the central nervous system. The active form of vitamin D, 1,25-dihydroxy vitamin D, binds to vitamin-D-specific nuclear receptors (VDR) in muscle tissue, which subsequently triggers de novo protein synthesis and muscle cell growth through the activation of mitogen-activated protein kinase (MAPK) signaling pathways [28, 29]. This action of vitamin D is thought to contribute to improved muscle strength and function. Furthermore, VDRs have been identified in certain areas of the brain, particularly in the cortical, subcortical, and spinal motor zones. This evidence suggests that vitamin D may influence the cerebral processes related to maintaining postural balance, as indicated by the improvement seen specifically in the 5TSTS test following vitamin D therapy in this study. However, the exact mechanisms through which vitamin D affects the central nervous system and muscle function, ultimately leading to improved balance, remain subjects of ongoing research [30].

To date, there has been no randomized placebo-controlled trial investigating the effects of vitamin D supplementation on muscle function specifically in I131-induced hypothyroidism. However, data on this issue have been reported in certain populations, such as postmenopausal and elderly individuals. A systematic review and meta-analysis of randomized controlled trials found that vitamin D supplementation improved handgrip strength in postmenopausal women, although insignificant results were demonstrated in terms of mobility. Conversely, in community-dwelling older persons, another meta-analysis of randomized controlled trials found that vitamin D treatment did not improve sarcopenia indicators and may even harm some aspects of physical performance [31]. It is important to note the existing controversy regarding the effects of vitamin D supplementation on muscle function. Outcomes may vary depending on different populations, underlying diseases, and doses of vitamin D treatment.

The strengths of this study include that it is the first randomized placebo-controlled trial to investigate the effects of vitamin D supplementation on muscle function in I131-induced hypothyroidism patients. Additionally, all enrolled participants completed follow-up visits without any missing data, ensuring robust data collection.

Table 1. Baseline characteristics

Baseline characteristics	Vitamin D group (N = 20)	Placebo group (N = 20)	*P* value
Demographic data			
Female, n (%)	18 (90)	16 (80)	.376
Age, years (mean ± SD)	53.2 ± 2.0	45.7 ± 2.7	.034
Weight, kg (mean ± SD)	60.3 ± 2.3	65.2 ± 3.1	.223
BMI, kg/m^2 (mean ± SD)	24.7 ± 0.9	25.1 ± 0.9	.789
Waist circumference, cm (mean ± SD)	80.6 ± 2.4	81.3 ± 2.5	.845
I131 dose, mci (mean ± SD)	12.4 ± 2.0	11.3 ± 1.1	.643
Time since diagnosis, months (mean ± SD)	148.1 ± 22.1	130.1 ± 18.9	.543
Time since LT4 initiation, months (mean ± SD)	85.7 ± 14.6	68.3 ± 13.8	.396
SBP, mmHg (mean ± SD)	127.9 ± 4.0	123.9 ± 2.8	.421
DBP, mmHg (mean ± SD)	79.6 ± 2.1	76.5 ± 2.2	.325
Biochemical data			
25(OH)D, ng/mL (mean ± SD)	24.3 ± 1.7	24.2 ± 1.4	.962
Calcium, mg/dL (mean ± SD)	9.2 ± 0.0	9 ± 0.1	.263
Albumin, g/dL(mean ± SD)	4.3 ± 0.0	4.4 ± 0.0	.358
Phosphate, mg/dL (mean ± SD)	3.2 ± 0.1	3.1 ± 0.1	.716
Creatinine, mg/dL (mean ± SD)	0.7 ± 0.0	0.7 ± 0.0	.842
Fasting insulin, mU/L (mean ± SD)	12.6 ± 2.1	9.4 ± 1.1	.203
Fasting plasma glucose, mg/dL (mean ± SD)	86.9 ± 2.7	83.8 ± 2.3	.399
HOMA-IR (mean ± SD)	2.8 ± 0.5	2 ± 0.2	.142
FT4, ng/dL (mean ± SD)	1.4 ± 0.0	1.3 ± 0.0	.664
TSH, uIU/mL (mean ± SD)	2.0 ± 0.2	1.6 ± 0.2	.294
Body composition			
Lean body mass, kg (mean ± SD)	37.2 ± 0.5	38.5 ± 0.5	.121
Fat mass, % (mean ± SD)	33.2 ± 1.8	35 ± 2.4	.539
Muscle strength			
Hand grips, kg (mean ± SD)	22.6 ± 1.3	25.9 ± 1.4	.101
Five times chair stand test, sec (mean ± SD)	11.6 ± 0.8	10.9 ± 0.5	.489
SF-36, points (mean ± SD)			
PF: physical functioning	75 ± 3.8	82 ± 2.9	.154
RP: role physical	73.7 ± 8.0	70 ± 8.8	.754
BP: bodily pain	59.6 ± 4.1	70 ± 5.2	.129
GH: general health	57.4 ± 3.8	57 ± 3.8	.941
VT: vitality	63.7 ± 3.1	64 ± 3.9	.960
SF: social functioning	79.3 ± 3.5	77.5 ± 4.9	.759
RE: role emotional	68.3 ± 8.8	68.3 ± 10.1	.999
MH: mental health	72.4 ± 3.1	73.2 ± 3.8	.874

Abbreviations: 25(OH)D, 25-hydroxyvitamin D; BMI, body mass index; FT4, free thyroxine; HOMA-IR, homeostatic model assessment of insulin resistance; LT4, levothyroxine; TSH, thyrotropin (thyroid stimulating hormone).

However, some limitations should be acknowledged. No significant differences were observed between the groups in terms of secondary outcomes, including body composition, insulin resistance markers, and QOL scores, after vitamin D supplementation. These findings could be attributed to the small sample size, which may have lacked the power to detect significant differences, and the relatively short follow-up period. However, to ensure that the study has sufficient statistical power to interpret the results, we conducted a backward calculation for power analysis which indicated a power of > 80%. Future research with a larger sample size and longer follow-up duration is warranted. Furthermore, some experts have proposed that vitamin D insufficiency should be defined as a vitamin D level < 30 ng/mL, which differs from World Health Organization criteria [32]. Therefore, future studies may include participants with vitamin D levels above 30 ng/mL to confirm whether the observed positive results are solely due to the effect of vitamin D supplementation rather than the correction of vitamin D deficiency. Also, vitamin D levels at the end of follow-up period (6 months) were not measured in this study. Additionally, the SF-36 questionnaire was used to assess QOL instead of the thyroid-specific patient-reported outcome (ThyPRO) questionnaire, which is specific for patients with benign thyroid diseases. Although the ThyPRO questionnaire has been translated into Thai, further research is needed to establish its construct validity by comparing responses of patients

Table 2. Primary and secondary outcomes compared between groups at 3 and 6 months[a]

Outcome	Vitamin D group (N = 20) (mean ± SD)	Placebo group (N = 20) (mean ± SD)	Vitamin D vs placebo, mean difference (95% CI)	*P* value
Primary outcomes				
Hand grips (kg)				
3 months	23.23 ± 0.95	23.83 ± 0.95	−0.08 (−1.48 to 1.66)	.999[b]
6 months	25.19 ± 1.05	24.07 ± 1.05	1.81 (0.08 to 3.54)	.080[b]
Five times sit to stand test (sec)				
3 months	9.92 ± 0.55	10.70 ± 0.55	−1.12 (−2.03 to −0.21)	.032[b]
6 months	9.52 ± 0.50	10.89 ± 0.50	−1.71 (−2.85 to −0.57)	.006[b]
Secondary outcomes				
Lean body mass (kg)				
3 months	38.25 ± 0.89	39.12 ± 0.89	0.31 (−2.29 to 2.91)	.816
6 months	36.71 ± 1.28	41.00 ± 1.28	−3.11 (−6.55 to 0.33)	.077
Fat mass (%)				
3 months	31.01 ± 2.12	34.96 ± 2.12	−1.10 (−5.57 to 3.36)	.628
6 months	34.09 ± 1.67	32.93 ± 1.67	4.00 (−1.23 to 9.24)	.134
Waist circumference (cm)				
3 months	80.97 ± 2.53	82.47 ± 2.53	−1 (−5.98 to 3.98)	.694
6 months	81.45 ± 3.07	78.13 ± 3.07	3.81 (−3.14 to 10.77)	.283
HOMA-IR				
3 months	2.53 ± 0.36	1.82 ± 0.36	−0.32 (−0.90 to 0.26)	.285
6 months	3.11 ± 0.35	2.12 ± 0.35	−0.045 (−0.74 to 0.65)	.899
SF- 36 (points)				
−PF: physical functioning				
3 months	75.96 ± 2.82	82.28 ± 2.82	−1.75 (−7.42 to 3.92)	.546
6 months	79.46 ± 3.02	80.03 ± 3.02	4 (−4.41 to 12.41)	.352
−RP: role physical				
3 months	73.75 ± 7.67	77.49 ± 7.67	−12.5 (−33.51 to 8.51)	.244
6 months	70.00 ± 7.78	66.24 ± 7.78	−5 (−26.02 to 16.02)	.641
−BP: bodily pain				
3 months	68.63 ± 3.97	73.26 ± 3.97	3.65 (−5.45 to 12.75)	.432
6 months	67.93 ± 3.57	70.21 ± 3.57	6 (−5.52 to 17.52)	.308
−GH: general health				
3 months	56.66 ± 3.63	59.94 ± 3.63	−2.7 (−10.46 to 5.06)	.496
6 months	57.11 ± 3.80	58.61 ± 3.80	−0.925 (−9.36 to 7.51)	.830
−VT: vitality				
3 months	62.56 ± 3.36	64.93 ± 3.36	−1.25 (−9.68 to 7.18)	.771
6 months	63.81 ± 3.25	63.93 ± 3.25	1 (−7.46 to 9.46)	.817
−SF: social functioning				
3 months	80.63 ± 4.54	82.98 ± 4.54	−1.75 (−15.91 to 12.41)	.809
6 months	81.26 ± 4.40	83.11 ± 4.40	−1.25 (−15.46 to 12.96)	.863
− RE: role emotional				
3 months	66.49 ± 8.24	77.05 ± 8.24	−16.46 (−39.24 to 6.32)	.157
6 months	71.26 ± 8.08	68.71 ± 8.08	−3.35 (−27.30 to 20.60)	.784
−MH: mental health				
3 months	73.80 ± 3.39	73.59 ± 3.39	2.6 (−4.63 to 9.83)	.481
6 months	74.00 ± 3.22	70.99 ± 3.22	5.4 (−1.90 to 12.70)	.147

[a]Mixed-model analysis was adjusted for age.
[b]Bonferroni-corrected *P* value.

with benign thyroid diseases with those of a normal population [33]. Evidence suggested a correlation between bone mineral density and handgrip strength, as well as a strong association between bone mineral density and vitamin D levels. However, bone mineral density was not assessed at the baseline in this study.

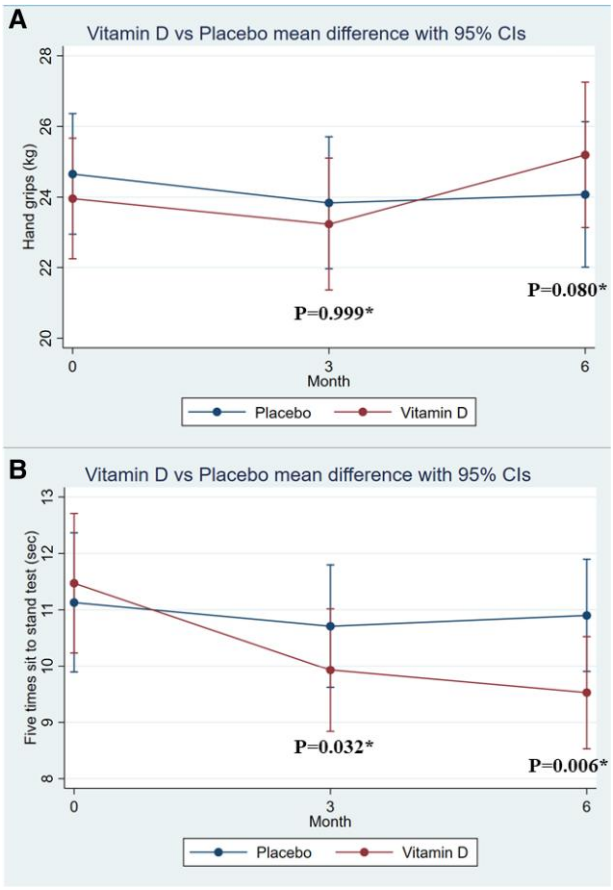

Figure 2. Least square mean change of primary outcome from baseline and at 3 and 6 months comparing between 2 groups. (A) Hand grip strengths (B) Five times sit to stand test. Error bars represented 95% CI. (*Bonferroni-corrected *P* value).

Conclusion

In conclusion, this randomized placebo-controlled trial demonstrated that supplementation with vitamin D2 at a dose of 20 000 IU per week for 24 weeks improved performance in 5TSTS in patients with I131-induced hypothyroidism. However, further research with a larger sample size and longer follow-up period is warranted to confirm these findings and explore additional outcomes.

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Author Contributions

S.M. enrolled and collected baseline characteristics, performed the data analysis, and wrote the first draft of the manuscript. W.M. designed and created the concept of the study, performed the data analysis, and interpreted the data, and was the major contributor in writing and editing the manuscript. P.J., M.P., and P.T. interpreted the data and edited the manuscript.

Disclosures

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

Data Availability

The data that support the findings of this study are available upon request from the authors.

Ethics Approval and Consent to Participate

This study was approved by Faculty of Medicine, Chiang Mai University ethical committee (Ethical No. MED-2565-09285). Written informed consent was obtained from all participants before participating in the study. All methods were carried out in accordance with the Declaration of Helsinki.

Clinical Trial Information

The trial was registered in the Thai Clinical Trials Registry with the registration number TCTR20230107005.

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