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Original article

Efficacy of plain cholecalciferol versus ergocalciferol in raising serum vitamin D level in Thai female healthcare workers

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ABSTRACT

Objectives: To compare the efficacy of cholecalciferol and ergocalciferol in raising 25-hydroxyvitamin D (25(OH)D) level in Thai female healthcare workers.
Methods: A randomized control trial was conducted in healthy female healthcare workers. Randomization allocated the participants into vitamin D2 group (N = 43), receiving ergocalciferol 20,000 IU weekly and vitamin D3 group (N = 40), receiving cholecalciferol 1000 IU daily for 12 months. Venous blood sample was collected at baseline, 6 and 12 months for serum 25(OH)D, parathyroid hormone and calcium. Compliance was also assessed.
Results: The mean age of the participants was 50.6 ± 9.9 and 50.9 ± 8.4 years in vitamin D2 and D3 groups (P = 0.884). The mean 25(OH)D levels were 16.91 ± 6.07 ng/mL and 17.62 ± 4.39 ng/mL (P = 0.547), respectively. Both groups had significant improvement in 25(OH)D level at 6 months (from 16.91 ± 6.07 to 21.67 ± 5.11 ng/mL and 17.62 ± 4.39 to 26.03 ± 6.59 ng/mL in vitamin D2 and D3 group). Improvement was significantly greater with cholecalciferol (P = 0.018). The level plateaued afterwards in both groups. Only cholecalciferol could increase 25(OH)D in participants without vitamin D deficiency (6.88 ± 4.20 ng/mL increment). Compliance was significantly better in vitamin D2 group (P = 0.025).
Conclusions: Daily cholecalciferol supplementation resulted in a larger increase in serum 25(OH)D level during the first 6 months comparing to weekly ergocalciferol. While vitamin D3 could increase serum 25(OH)D level in all participants, vitamin D2 could not do so in participants without vitamin D deficiency.

1. Introduction

Vitamin D has long been recognized as an important nutrient for musculoskeletal health [1]. The main function of vitamin D is to regulate calcium and phosphate balance through regulation of intestinal absorption and renal resorption, maintain bone health, and to modulate muscle function via vitamin D receptors on muscle fibers [2]. Vitamin D deficiency has been shown to be associated with osteoporosis and falling in the elderly, which in turn, lead to occurrence of fragility fractures [3,4]. Optimization of vitamin D and calcium intake, likewise, can reduce fall and fracture rate [5,6]. Recently, its increasing documented effects on extra-skeletal tissues has even drawn more attention [7]. Despite the renowned effect on health, vitamin D deficiency is still very common worldwide [8,9]. Regardless of its sunny climate, a study in Singapore found a surprising prevalence of vitamin D inadequacy of 92% in patients with hip fractures [10]. Studies in Thai population revealed a prevalence of vitamin D inadequacy varying from 50.9 to 78.4% [11,12]. An unpublished data from the Police General Hospital situated in Bangkok, Thailand found an even higher number of 86%.

There are diverse sources of vitamin D. Ergocalciferol (vitamin D2) is produced from ergosterol found in plants and fungi when they are exposed to UV radiation [13]. Cholecalciferol (vitamin D3) is formed when 7-dehydrocholesterol, a form of pre-vitamin D3 in animal skins is stimulated by UV radiation [14]. Human body gains both vitamin D2 and vitamin D3 from various sources; for example, being exposed to sunlight, and dietary intake of vitamin D2 rich plants and fungi and vitamin D3 from meat, fish and egg, also other fortified food. Another source of vitamin D is vitamin D supplements, which are available in both vitamin D2 and vitamin D3 forms.

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Vitamin D2 and D3 differ in their side chains. Hypothetically, they are metabolized and used in the body in the same way [15–17]. While their metabolic pathways are identical, there are evidences suggesting the different efficacy of vitamin D2 and vitamin D3 in raising serum level of 25(OH)D, which is the most commonly used marker of vitamin D status, making vitamin D3 more efficient than vitamin D2, and have better impact on health [18,19]. However, the results from previous studies are still conflicting. Most studies comparing the two forms of vitamin D reveal that vitamin D3 is more potent than vitamin D2 [18–20]. Several studies, on the other hand, point out they are equally effective [21,22].

With the unarguable importance of vitamin D and the worldwide prevalence of vitamin D deficiency, it is of utmost importance to identify the most effective form of vitamin D available for supplements. Although vitamin D2 has long been prescribed in various hospital in Thailand, plain vitamin D3 has recently become available in Thailand in 2021. Therefore, the aim of this randomized controlled trial is to determine the efficacy of plain vitamin D2 capsule and plain vitamin D3 tablet in raising the level of serum total 25(OH)D in Thai women.

2. Methods

2.1. Participants

A randomized control trial was performed in healthy female healthcare workers in Police General Hospital, Thailand. The inclusion criteria were adult female aged 25–65 years without history of osteoporosis or fragility fractures as defined by fractures from a simple fall. The exclusion criteria were prescription of vitamin D or calcium supplement within the past year, history of anti-osteoporotic medication use, including hormonal replacement therapy, and prescription of anticonvulsants or steroids. Underlying medical conditions that could affect bone metabolism; for example, hypocalcemia, hypercalcemia, uncontrolled hyperthyroidism, hypogonadism, primary hyperparathyroidism, growth hormone deficiency, acromegaly, hemochromatosis and chronic liver diseases, hematological disorders, renal disorders including chronic kidney disease, and autoimmune disorders, were also excluded. Underlying diseases and past medical history were obtained from interview and confirmed by thorough search of the electronic database including the ICD-10 and narrative records. Other medical conditions including type 2 diabetes, hypertension and dyslipidemia were also investigated from the diagnosis on electronic database which was later confirmed with laboratory and physical examination findings and prescription of medication specific for each disease. Type 2 diabetes mellitus diagnosis when hemoglobin A1c was more than or equal to 6.5% or fasting blood glucose was more than or equal to 126 mg/dL. Hypertension was diagnosed when blood pressure was more than 140/90 mmHg on 2 measurements. Dyslipidemia was diagnosed when low-density lipoprotein was more than or equal to 190 mg/dL or Thai CV Risk Score over 10% in non-diabetic individuals or LDL of more than or equal to 100 mg/dL in diabetic patients.

The estimated sample size was calculated based on a study Lehmann et al [23] by testing 2 independent means (two-tailed test) using the following formula.

$$n_1 = \frac{\left(z_{1-\frac{\alpha}{2}} + z_{1-\beta}\right)^2 \left[\sigma_1^2 + \frac{\sigma_2^2}{r}\right]}{\Delta^2}$$

$$r = \frac{n_2}{n_1}, \Delta = \mu_1 - \mu_2$$

The estimated sample size was 30 in each group. Adding 25% drop out rate gave a total of 38 participants per group. All patients agreed to participate in the study and provided written informed consent.

A total of 86 female healthcare providers in Police General Hospital were recruited. Computer blocked randomization (Block size = 8) was performed to divide them into 2 groups with 43 participants in Vitamin D2 group and 40 in vitamin D3 group. The randomization sequence was generated using an online program. The research was reviewed by Police General Hospital ethical committee (COA 121/2564). This trial was also registered and approved by Thai Clinical Trials Registry (TCTR), the national representatives of World Health Organization International Clinical Trials Registry Platform (WHO ICRTP) Registry Network. The TCTR identification number is TCTR20221127002 (https://www.thaiclinicaltrials.org/show/TCTR20221127002).

2.2. Procedures

Vitamin D2 group received 20,000 IU of ergocalciferol, British Dispensary Health Care Company Limited (Thailand) weekly, while vitamin D3 group received a 1000 IU tablet of plain cholecalciferol (NatD, Mega Life Sciences Limited (Thailand)) daily which is equivalent to 7000 IU of cholecalciferol per week. This dose of plain cholecalciferol tablet was chosen in this experiment as it was the only available form of plain vitamin D3 supplement available in hospitals in Thailand at the time we started the experiment. The participants received the same supplementation throughout the study period of one year from May 2021 to May 2022. They were asked not to take other additional vitamin D or calcium. Participants initially completed a baseline questionnaire about their underlying diseases, current medication, and previous history of vitamin D and calcium supplementation. Venous blood sample was collected and assessed for serum total 25(OH)D level, intact parathyroid hormone (PTH), inorganic phosphate, total calcium, alkaline phosphatase, creatinine and albumin.

The participants were followed up at 6 and 12 months for assessment of compliance and side effects. Serum total 25(OH)D, calcium, phosphate and PTH were also measured by a same validated machine at Police General Hospital. Serum 25(OH)D and PTH were analyzed by chemiluminescent microparticle immunoassay (CMIA) on Architect I2000SR analyzer (Abbott Laboratories Limited, USA). The study flowchart is shown in Fig. 1.

The trial will be single-blinded. The data analyst will be blinded as the group to which the participants are allocated are assigned by codes.

The primary outcome was the level of serum 25(OH)D after supplementation of vitamin D2 or D3. The secondary outcomes were the efficiency of vitamin D supplementation in participants with different baseline serum 25(OH)D and compliance to each type of dosing.

2.3. Statistical analysis

Mann-Whitney test and chi-square test will be used to compare the baseline characteristics of the 2 groups. Serum 25(OH)D level, PTH and total calcium at follow up visits were compared using *t* test. Compliance was measured as medication possession ratio (MPR) using the following formula [24].

$$\text{MPR} = \frac{\textit{Sum of days' supply for all fills in period}}{\textit{Number of days in period}} \text{ x } 100\%$$

MPR was compared using Wilcoxon test. Subgroup analysis in participants with and without vitamin D deficiency was performed.

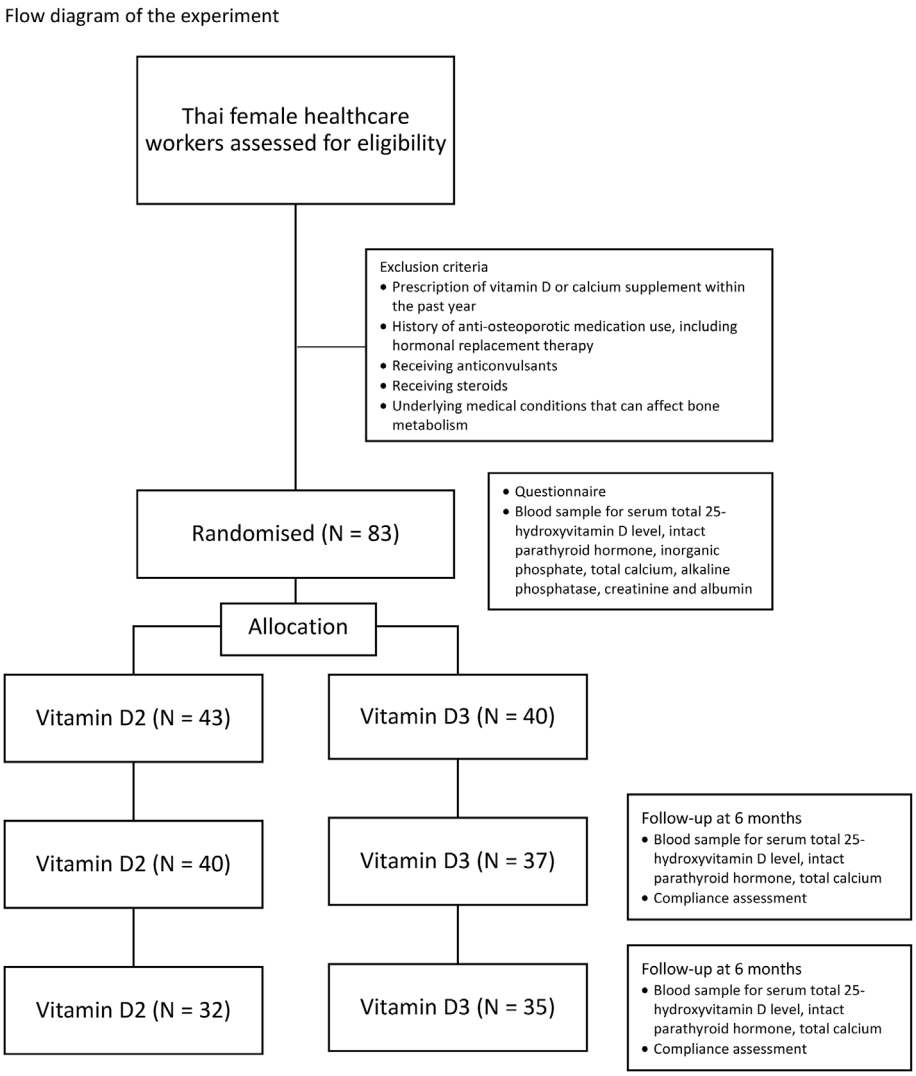

Fig. 1. Flow diagram of the experiment.

According to the Endocrine Society's definition, vitamin D deficiency was defined as serum 25(OH)D below 20 ng/mL, and vitamin D insufficiency was defined 25(OH)D of 20 ng/mL to less than 30 ng/mL [25]. All data was analyzed using an intention-to-treat analysis. All statistical calculation was performed by Stata, version 13.0; StataCorp LLC, College Station, TX, United States.

3. Results

3.1. Characteristics of the participants

The baseline characteristics of the participants were the same in both groups as shown in Table 1. The mean age of the participants was 50.6 ± 9.9 and 50.9 ± 8.4 years in vitamin D2 and vitamin D3 groups respectively (P = 0.884). There were 5 (11.63%) participants with hypertension in vitamin D2 group and 5 (12.5%) in vitamin D3 group (P = 0.903). There were numerically more participants with underlying hypertension and dyslipidemia in the vitamin D3 group, but did not achieve statistical significance (2.32% vs 7.5% with type II diabetes mellitus (P = 0.271) and 16.28% vs 30% with dyslipidemia (P = 0.137)).

3.2. Serum biomarkers at baseline and follow-up visits

3.2.1. Initial visit

As shown in Tables 1 and 2, the baseline 25(OH)D level in all participants was 17.26 ± 5.31 ng/mL. The mean 25(OH)D levels of the vitamin D2 and D3 groups were 16.91 ± 6.07 ng/mL and 17.62 ± 4.39 ng/mL (P = 0.547). All except one participant had 25(OH)D level below 30 ng/mL and 57 (68.67%) had 25(OH)D level below 20 ng/mL. The proportion of participants with 25(OH)D level below 30 ng/mL and 20 ng/mL were the same in both groups (97.6% and 69.8% in vitamin D2 group and 100% and 70% in vitamin D3 group, respectively). Parathyroid hormone, calcium, alkaline phosphatase, creatinine and albumin level were the same in both groups. Inorganic phosphate level was higher in vitamin D2 group (3.74 ± 0.43 vs. 3.51 ± 0.48 mg/dL (P = 0.022)).

3.2.2. Six-month follow-up

At 6 months, 40 and 37 participants from vitamin D2 and D3 groups came for a follow-up visit. The reasons for drop out was redeployment to different provinces in 5 participants, and resignation from work in another. Both groups had significant improvement in 25(OH)D level at 6 months, rising from 16.91 ± 6.07 to 21.67 ± 5.11 ng/mL in vitamin D2 group and from

Table 1
Baseline characteristics of the participants.

	Groups			
	Total (N = 83)	Vitamin D2 (N = 43)	Vitamin D3 (N = 40)	
Variables	(Mean ± SD or N (%))	(Mean ± SD or N (%))	(Mean ± SD or N (%))	P
Age, yr	50.77 ± 9.14	50.63 ± 9.91	50.93 ± 8.37	0.884
Hypertension	10 (12.0%)	5 (11.6%)	5 (12.5%)	0.903
Diabetes mellitus	4 (4.8%)	1 (2.3%)	3 (7.5%)	0.271
Dyslipidemia	19 (22.9%)	7 (16.3%)	12 (30%)	0.137
25(OH)D < 20 ng/mL	57 (68.7%)	29 (67.4%)	28 (70%)	0.802
25(OH)D < 30 ng/mL	82 (98.8%)	42 (97.7%)	40 (100%)	0.332
Cr, mg/dL	0.77 ± 0.24	0.82 ± 0.43	0.63 ± 0.39	0.264
ALP, U/L	66.72 ± 22.03	63.64 ± 23.87	70.03 ± 19.63	0.189
Phosphate, mg/dL	3.63 ± 0.47	3.74 ± 0.43	3.51 ± 0.48	0.022
Albumin, g/dL	4.88 ± 2.35	5.07 ± 2.54	4.69 ± 2.87	0.197

25(OH)D, 25-hydroxyvitamin D; Cr, creatinine; ALP, alkaline phosphatase.

Table 2
Serum total 25-hydroxyvitamin D, total calcium and intact parathyroid hormone level at baseline, 6 months and 12 months.

Variables	Groups			
	Total (N = 83)	Vitamin D2 (N = 43)	Vitamin D3 (N = 40)	
	(Mean ± SD or N (%))	(Mean ± SD or N (%))	(Mean ± SD or N (%))	P
Initial visit				
25(OH)D, ng/mL	17.26 ± 5.31	16.91 ± 6.07	17.62 ± 4.39	0.547
Calcium, ;mg/dL	8.98 ± 1.00	8.91 ± 1.36	9.06 ± 0.35	0.513
PTH, ;pg/mL	69.71 ± 33.36	66.42 ± 31.21	73.25 ± 35.59	0.355
6 months				
25(OH)D, ng/mL	23.76 ± 6.23	21.67 ± 5.11	26.03 ± 6.59	0.002
Calcium, ;mg/dL	8.99 ± 0.04	9.06 ± 0.29	8.93 ± 0.32	0.063
PTH, pg/mL	64.95 ± 28.32	59.82 ± 22.83	70.50 ± 32.68	0.099
1 year				
25(OH)D, ng/mL	24.14 ± 6.04	21.76 ± 4.78	26.32 ± 6.29	0.002
Calcium, ;mg/dL	9.54 ± 0.37	9.62 ± 0.27	9.48 ± 0.43	0.123
PTH, ;pg/mL	79.53 ± 33.91	78.99 ± 30.06	80.03 ± 37.52	0.902

25(OH)D, 25-hydroxyvitamin D; PTH, parathyroid hormone.

17.62 ± 4.39 to 26.03 ± 6.59 ng/mL in vitamin D3 group. The 25(OH)D level was significantly higher in vitamin D3 group (P = 0.002), so did the improvement in 25(OH)D level (4.68 ± 7.33 ng/mL in vitamin D2 group vs 8.46 ± 6.31 ng/mL in vitamin D3 group (P = 0.018)). A total of 2 (5%) and 23 (57.5%) of participants in vitamin D2 group had 25(OH)D levels greater than 30 and 20 ng/mL, respectively. In contrast, 9 (24.3%) and 28 (75.7%) of the vitamin D3 group had 25(OH)D levels above 30 ng/mL and 20 ng/mL. Parathyroid hormone and calcium levels were not different between the 2 groups. The data was shown in Table 2 and Fig. 2. There was no reported side effect of the vitamin D supplement.

3.2.3. *Twelve month follow-up*

At 12 months, 10 more healthcare workers dropped out from the study due to redeployment in 8, and unable to visit the hospital in 2 of them, leaving 35 healthcare workers in vitamin D3 and 32 in vitamin D2 group. None of the participants who previously drooped out at 6 months came back into the study. Vitamin D3 group had higher 25(OH)D levels (21.76 ± 4.78 ng/mL vs 26.32 ± 6.29 ng/mL (P = 0.002)). Both groups however, did not show significant improvement from the 6-month visit. Altogether, there were 2 (6.3%) participants in vitamin D2 group and 8 (22.9%) in vitamin D3 group with 25(OH)D levels above 30 ng/mL. The number of participants with 25(OH)D level above 20 ng/mL was 21 (65.6%) in vitamin D2 group and 28 (80%) in vitamin D3 group. Again, parathyroid hormone and calcium levels were the same in both groups. The results were in Table 2 and Fig. 2. There was no side effect of the vitamin D.

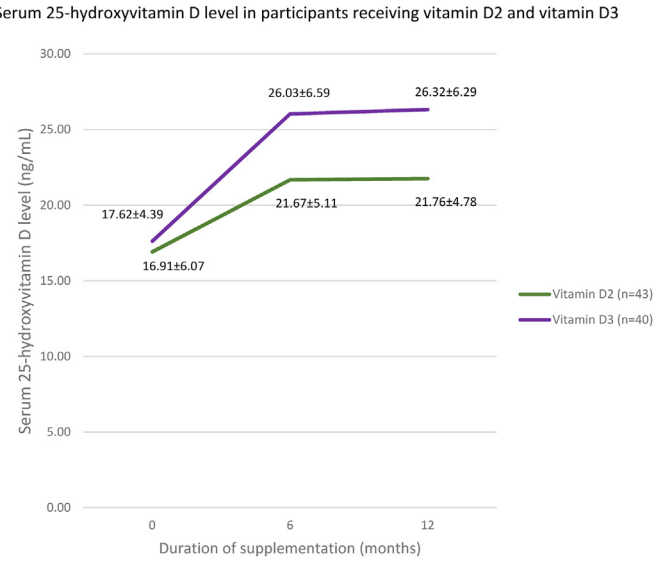

Fig. 2. Serum 25-hydroxyvitamin D level in participants receiving vitamin D2 and vitamin D3.

3.3. *Improvement in 25(OH)D level in participants with and without vitamin D deficiency*

The majority of participants had vitamin D deficiency, involving 29 (67.44%) in vitamin D2 group and 28 (70%) in vitamin D3 group.

The mean 25(OH)D level in these participants were 13.52 ± 3.66 ng/mL and 15.36 ± 3.00 ng/mL in vitamin D2 and D3 groups, respectively (P = 0.030). The improvement in 25(OH)D level was 7.29 ± 7.12 ng/mL and 9.05 ± 6.91 mg/mL in vitamin D2 and D3 groups. The difference between groups however, did not bear statistical significance (P = 0.360). Neither group showed improvement in 25(OH)D levels during the third visit.

Changes in 25(OH)D level showed a different pattern in participants without vitamin D deficiency. The average level of serum 25(OH) D was 23.94 ± 3.36 ng/mL and 22.90 ± 1.65 ng/mL in vitamin D2 and vitamin D3 groups, respectively (P = 0.339). There was an improvement in 25(OH)D level in vitamin D3 group during the 6-month visit to 29.91 ± 4.77 ng/mL (mean improvement 6.88 ± 4.20). Such increase was not observed in the vitamin D2 group (mean improvement of −0.74 ± 4.21 ng/mL). There was no noticeable change in 25(OH)D level from the second to the third visit in both groups. The trend in vitamin D improvement in each subgroups are in Fig. 3.

3.4. Compliance

MPR was significantly higher in vitamin D2 group during both follow-up visits. The average MPR at 6 months was 0.95 ± 0.08 and 0.81 ± 0.14 in vitamin D2 and D3 group, respectively (P < 0.001)). The mean MPR at 12 months was 0.96 ± 0.10 and 0.88 ± 0.15 (P = 0.025).

4. Discussion

While vitamin D is vital for musculoskeletal health, vitamin D inadequacy is common worldwide [7,26]. The prevalence of serum 25(OH)D level below 12 ng/mL in the United States, Canada and Europe ranged from 5.9 to 13%, while vitamin D insufficiency ranged from 24 to 40.4% [26]. Asia, Africa, and the Middle East had been consistently described as areas with highest prevalence of vitamin D inadequacy with a prevalence of vitamin D deficiency of as high as 66% in Indian adults [27–29].

The prevalence of vitamin D deficiency in female healthcare workers in our study was 68.7%, which was higher than general Thai population which varied from 5.7% to 43.1% [12,30–33]. The discrepancy could be explained by older participants in our study and also their habitat. Our participants were healthcare workers working in the center of Bangkok are unarguably in a municipal area, in which habitants generally show lower level of serum 25(OH)D compared to the countryside [12]. Our result was more consistent with a systematic review involving 19,083 healthcare workers with an average serum 25(OH)D level of 24.44 ± 4.4 ng/mL and a prevalence of vitamin D deficiency ranging from 43% in nurses and healthcare employees to 72% in healthcare students [34]. Funaki et al [35] demonstrated a prevalence of vitamin D deficiency as high as 92.7% in female healthcare workers in Japan during COVID-19. A recent study in Thai orthopedic surgeons also found the vitamin D deficiency in 72% of the participants [36]. The nature of the career therefore, largely explained the surprisingly high numbers of vitamin D inadequacy in our study. The tasks of healthcare workers involve mainly indoor activities and long working hours which prohibit them from outdoor recreational activities during daytime. Moreover, out study was also conducted during the COVID-19 pandemic, which restricted social gatherings and activities. This finding strongly suggests that education on hypovitaminosis D along with promotion of self-awareness of the condition is necessary in healthcare workers. Proper screening strategy and appropriate intervention should also be implemented to avoid long-term consequences of vitamin D deficiency.

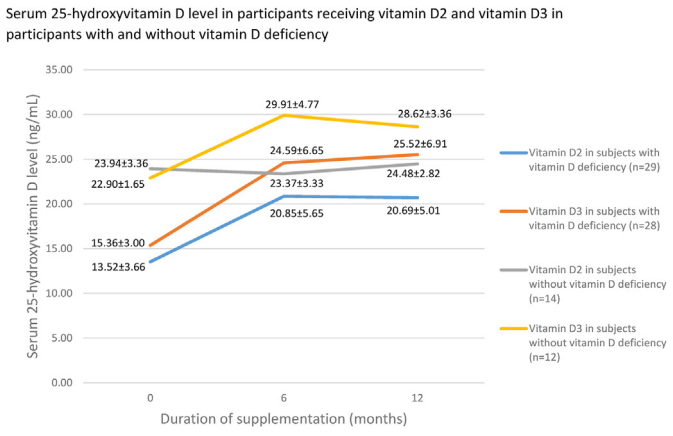

Fig. 3. Serum 25-hydroxyvitamin D level in participants receiving vitamin D2 and vitamin D3 in participants with and without vitamin D deficiency.

Vitamin D3 could raise serum 25(OH)D levels significantly more than vitamin D2 during the first 6 months with 8.46 ± 6.31 ng/mL improvement with vitamin D3 and 4.68 ± 7.33 ng/mL with vitamin D2. While both forms of supplementation have the same activating pathway, it is hypothesized that their differences are due to unequal affinity of the 2 forms of vitamin D for VDR [37]. It is also proposed that vitamin D3 is more preferable as a substrate for 25-hydroxylase in the liver [38]. Furthermore, degradation of vitamin D3 requires an additional step to that of vitamin D2 [37]. These mechanisms, combined, could make vitamin D3 more efficient than vitamin D2 in raising serum 25(OH)D levels. Another study in Thai population found a tendency, but without statistical significance, toward a higher increase in serum 25(OH)D when using a multivitamin supplement which included equivalent dose on vitamin D3 compared to vitamin D2 [39]. The follow-up time in the study was only 3 months. The number of participants was small. Moreover, the study was conducted in young participants. A systematic review and meta-analysis by Tripkovic et al [16] confirms that vitamin D3 leads to greater change in serum 25(OH)D concentration. However, the study was subjected to high between-study heterogeneity, variety in study designs, vitamin D dosing regimens, short follow up time and small sample sizes.

Both regimens of supplementation, 20,000 IU of vitamin D2 weekly, and 1000 IU of vitamin D3 daily could not further raise serum 25(OH)D level after 6 months, giving the final serum 25(OH)D level of 21.76 ± 4.78 ng/mL and 26.32 ± 6.29 ng/mL after 12 months of supplementation, which was adequate in non-osteoporotic women with a general recommendation of keeping serum 25(OH)D level above 20 ng/mL. The level, however, was still below the recommended value by various national and international practice guidelines of 30 ng/mL for osteoporosis patients with a recommended daily dose of vitamin D3 of 600–1200 IU, depending on age group and varying between guidelines [40–43]. Moreover, studies have also proposed a serum 25(OH)D level of 30 ng/mL as the most advantageous for multiple health outcomes in healthy adults [44,45]. According to Thai national guideline in osteoporosis, 600–800 IU of vitamin D3 daily or 20,000 IU of vitamin D2 per week is recommended for non-pharmacologic treatment of osteoporosis in Thailand [40]. However, our study clearly revealed neither vitamin D2 and vitamin D3 of the recommended dosage would be sufficient to achieve the desired level of serum 25(OH)D, especially with 20,000 IU of weekly vitamin D2 which only achieved 25(OH)D levels above 20 ng/mL in 65.6% of the participants and above 30 ng/mL in only 24.3% by the end of the study. Our finding was consistent with previous studies in Thai population which demonstrated that 40,000–60,000 IU a week of

ergocalciferol were needed to achieve a normal level of serum 25(OH)D, while 20,000 IU could merely maintain serum 25(OH)D level around 20 ng/mL [46,47]. Therefore, higher doses of vitamin D than previously stated in the guidelines is needed, and serial serum sampling for 25(OH)D level is required to titrate the dose of vitamin D supplementation. If retesting of serum 25(OH)D is not available, more than 1000 IU of daily cholecalciferol supplementation or more than 20,000 IU of weekly ergocalciferol may be an option to raise 25(OH)D to above 30 ng/mL.

Subgroup analysis of showed that vitamin D2 and D3 supplementation could increase serum 25(OH)D better in participants who had vitamin D deficiency than those with only vitamin D insufficiency. In subjects with serum 25(OH)D level below 20 ng/mL, both regimens could increase serum 25(OH)D during the first 6 months. In contrast, when only participants with 25(OH)D above 20 ng/mL were considered, supplementation of 20,000 IU of vitamin D2 per week could not increase serum 25(OH)D level in any visits. However, vitamin D3 could still improve serum 25(OH)D level by 6.88 ± 4.20 ng/mL, which was slightly lower than those with vitamin D deficiency. This finding also confirmed that vitamin D3 are more effective than vitamin D2 in raising 25(OH)D levels, particularly in women with vitamin D insufficiency. Again, even in participants who were no vitamin D deficient at baseline, 1000 IU of cholecalciferol daily could not provide the desired level of serum 25(OH)D of over 30 ng/mL.

Compliance is undeniably essential in treatment of chronic diseases, and are often attenuated in the elderly [24,48,49]. In our study, compliance was significantly higher with weekly vitamin supplementation than in daily doses. The MPR in vitamin D3 group improved slightly in the last visit as we emphasized its importance during the second visit. Our finding was consistent with several previous studies which found that patients comply more to less frequent dosing [49–51].

To date, our research is the first to study compare supplementation of vitamin D3 and vitamin D2 in Thai healthcare workers, who are at surprisingly high risk of vitamin D deficiency and insufficiency. Moreover, there has been no study in Thailand using plain vitamin D3 since it has only become available in hospitals in Thailand in 2020. The main limitation of this study is in its small sample size and that the participants are from only 1 institution. Further study with more diverse groups of healthcare workers and specific serum 25(OH)D2 and 25(OH)D3 quantification are of interest.

5. Conclusions

Most Thai female healthcare workers were vitamin D deficient. Comparing to 20,000 IU of weekly ergocalciferol, 1000 IU of daily cholecalciferol supplementation resulted in a larger increase in serum 25(OH)D level during the first 6 months, but both failed to continue raising serum 25(OH)D afterwards. While vitamin D3 could increase serum 25(OH)D level in all participants, vitamin D2 could not do so in participants without vitamin D deficiency. Compliance was better with weekly than daily dosing.

CRediT author statement

Tanawat Amphansap: Conceptualization, Data collection, Data curation, Writing-review & editing. **Atiporn Therdyothin**: Methodology, Data collection, Formal analysis, Writing-original draft, Project administration. **Nitirat Stitkitti**: Methodology, Data collection. **Lertkong Nitiwarangkul**: Formal analysis. **Vajarin Phiphobmongkol**: Conceptualization.

Conflicts of interest

The authors declare no competing interests.

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