The Use of Stratified Vitamin D2 Supplementation Regimen for Restoring and Maintaining Sufficient Vitamin D Level

Aasis Unnanuntana MD, MSc*, Pojchong Chotiyarnwong MD, PhD*

* Department of Orthopaedic Surgery, Siriraj Hospital, Mahidol University, Bangkok, Thailand

Background: *With no standard guideline for treating hypovitaminosis D using ergocalciferol, a stratified vitamin D2 supplementation protocol was developed.*

Objective: *To determine the success rate of the protocol for attaining vitamin D sufficiency and to identify factors that associate with the success of correcting low vitamin D status.*

Material and Method: *Medical records of patients who sought treatment at the Siriraj Metabolic Bone Disease Clinic between March 2012 and December 2014 were retrospectively reviewed. All patients who had serum 25-hydroxyvitamin D (25(OH)D) levels available at both baseline and three months post-treatment were included. Treatment protocol according to 25(OH)D level was, as follows: 60,000, 40,000, 20,000, and 0 IU per week for patients with baseline serum 25(OH)D level of less than 20, 20 to less than 30, 30 to 40, and more than 40 ng/mL, respectively.*

Results: *Two hundred and forty-three patients entered the study and 187 patients (77%) had serum 25(OH)D level 30 ng/mL or more, after treatment with our stratified vitamin D2 supplementation protocol. This proportion increased to 98.4% when 20 ng/mL was used as the cut-off value for adequate vitamin D status. In addition, we found body mass index (BMI) and baseline vitamin D level to be associated with attainment of vitamin D sufficiency status after treatment with our vitamin D2 supplementation protocol.*

Conclusion: *Our stratified vitamin D2 supplementation protocol was effective in attaining vitamin D sufficiency status in approximately 77% of patients. Since baseline vitamin D level and BMI were found to be two important factors that influence the success of treating hypovitaminosis D, these two factors should be considered before and during treatment for low vitamin D level.*

Keywords: *Vitamin D2, Ergocalciferol, Vitamin D deficiency, Vitamin D insufficiency, Hypovitaminosis D, 25-hydroxyvitamin D*

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Prevalence of vitamin D insufficiency in Thais from Chailurkit et al study recently was 45.2%[1]. Several guidelines recommend maintaining serum 25-hydroxyvitamin D (25(OH)D) level of 30 ng/mL or more to maximize the benefit of both skeletal and non-skeletal roles of vitamin D[2-4]. There are two formulations of vitamin D supplementation: vitamin D2 (ergocalciferol) and vitamin D3 (cholecalciferol). Although both formulations are effective in correcting low serum vitamin D level, it has been suggested that vitamin D3 is more stable and the amount required to correct low serum vitamin D status is much less than that of vitamin D2[5]. Accordingly, vitamin D3 supplementation is widely used and easily found in many stores of some countries, such as the United States, India, Japan, Europe, and Canada[6]. The recommended daily vitamin D3 supplement for the general population is approximately 600 to 800 IU per day and 1,000 to 2,000 IU per day for adult patients at high risk of vitamin D deficiency[4].

Given the limited availability of vitamin D3 in Thailand, vitamin D2 is widely used for restoring and maintaining sufficient vitamin D level. Although there are several guidelines for vitamin D2 supplementation[7,8], those regimens were developed in Western countries and may not be applicable to an Asian population. Regarding differences between Caucasians and Asians in body fat composition[9] and fat intake[10], we speculated that vitamin D2 supplementation regimens used in Western countries might yield a different response in the Asian population. Therefore, our institution (Faculty of Medicine Siriraj Hospital) set up a guideline (Siriraj orthopaedic vitamin D2 supplementation regimen) to correct low vitamin

Correspondence to:

Chotiyarnwong P; Department of Orthopaedic Surgery, Siriraj Hospital, Mahidol University, 2 Wang Lang Road, Bangkok 10700, Thailand.
Phone: +66-2-4197529, Fax: +66-2-4128172
E-mail: pojchong@hotmail.com

D status and to maintain serum 25(OH)D level of 30 ng/mL or more. The Siriraj orthopaedic vitamin D2 supplementation regimen is further described in the Material and Method section (Table 1).

The rationale of our regimen was adapted from studies by Holick[7] and Malabanan et al[8]. These studies showed that treatment of vitamin D deficiency in the United States required 50,000 IU of vitamin D2 per week for 8 to 16 weeks and 50,000 IU of vitamin D2 every two to four weeks for maintenance to avoid deficiency. In Thailand, vitamin D2 is available only in 20,000 IU capsules, therefore, our regimen started from a dose of vitamin D2 20,000 IU per week for maintenance for those who had sufficient 25(OH)D level, but not more than 40 ng/mL, and 60,000 IU per week for those who had 25(OH)D level less than 20 ng/mL. Patients who had 25(OH)D level between 20 and 30 ng/mL were given vitamin D2 40,000 IU per week.

The objectives of the present study were to: 1) determine the success rate of our stratified vitamin D2 supplementation regimen in restoring and maintaining normal vitamin D status in orthopaedic patients, and 2) identify factors that associate with the success of correcting low serum vitamin D level.

Material and Method

After receiving approval from the Siriraj Institutional Review Board (SIRB), we retrospectively reviewed medical records of patients who sought treatment at the Siriraj Metabolic Bone Disease Clinic between March 2012 and December 2014. Since being established in March 2012, the Siriraj Metabolic Bone Disease Clinic has evaluated and treated 513 patients. In response to the high prevalence of hypovitaminosis D in this patient population, we implemented the Siriraj orthopaedic vitamin D2 supplementation regimen in October 2012 to treat the low vitamin D status, a simple and easy-to-use method for all levels of physicians and nurses. We included all patients aged more than 18 years and had both baseline and post-treatment serum 25(OH)D levels available. Exclusion criteria were patients who received vitamin D2 supplementation before implementation of the Siriraj orthopaedic vitamin D2 supplementation regimen; patients with medical problems that affect vitamin D absorption and metabolism, such as short bowel syndrome, chronic kidney disease, and granulomatous disorders; patients who received anticonvulsants, rifampicin, cholestyramine, and/or antiretrovirals; and patients who received additional vitamin D in calcium or multivitamin supplementation (defined as receiving vitamin D of 400 IU/day or more in calcium or multivitamin formulations).

The Siriraj orthopaedic vitamin D2 supplementation regimen

Patients with low vitamin D levels were divided into either the deficiency or insufficiency groups based on serum 25(OH)D level. Vitamin D deficiency was defined as serum 25(OH)D level of less than 20 ng/mL, with vitamin D insufficiency defined as serum 25(OH)D level ranging from 20 to less than 30 ng/mL[2]. Treatment included prescribing vitamin D2 60,000 and 40,000 IU per week for patients diagnosed with vitamin D deficiency and insufficiency, respectively. For patients with sufficient vitamin D status, vitamin D2 20,000 IU was given every week for those with serum 25(OH)D levels between 30 and 40 ng/mL, and no additional vitamin D2 supplementation for patients who had baseline serum 25(OH)D level above 40 ng/mL (Table 1). Serum 25(OH)D level was repeated at approximately three months after treatment. The objective was to maintain serum 25(OH)D level within the range of 30 to 50 ng/mL[11].

Data collection

Patient demographic data and risk factors for osteoporosis were collected from the metabolic bone disease registry. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters. Patients who took calcium or multivitamin formulations containing trace amounts of vitamin D (<400 IU/day) were also noted. Bone mineral density (BMD) and basic metabolic laboratory results were taken and recorded. BMD was obtained by dual energy

Table 1. Siriraj orthopaedic vitamin D2 supplementation regimen to achieve normal vitamin D level

Baseline serum 25(OH)D level (ng/mL)	Dosage of vitamin D2 supplementation (international units, IU)
<20 ng/mL	60,000 IU/week
20 to <30 ng/mL	40,000 IU/week
30 to 40 ng/mL	20,000 IU/week
>40 ng/mL	No additional vitamin D supplementation

X-ray absorptiometry (DXA) of the L_2 to L_4 lumbar spine, femoral neck, and total hip. The lowest T-score among the three sites was selected.

Serum 25(OH)D level and all other tests were measured at the central laboratory of our hospital. Renal function was estimated by calculating the estimated glomerular filtration rate (eGFR, mL/minute/1.73 m^2), according to Cockroft-Gault equation: GFR = (140 - age in years) x (weight in kg/serum creatinine in mg/dL) x (1 in men or 0.85 in women)[12]. Serum concentration of 25(OH)D was measured by electrochemiluminescence binding assay on cobas e411 analyzer (Roche Diagnostics GmBH, Mannheim, Germany). Intraassay coefficient of variation percent (%CV) was 7.8% at 6.76 ng/mL and 1.7% at 67.0 ng/mL. Interassay %CV was 10.7% at 6.76 ng/mL and 2.2% at 67.0 ng/mL.

Statistical analysis

To determine an adequate sample size, the percentage of patients who achieved vitamin D sufficiency after vitamin D2 supplementation was used as the primary outcome variable. From a previous study, 56% of patients attained sufficient vitamin D status with their prescribed ergocalciferol regimen[13]. On the basis of that study, we calculated the sample size by using one proportion confidence interval formula at a confidence interval of 95% (95% CI) and an allowable rate of 7% (relative error 12.5%). Accordingly, a sample size of 194 patients was calculated for the present study. However, we increased the sample size by approximately 20% to compensate for anticipated incomplete patient records. As such, a sample size of at least 233 patients was required for the present study.

Descriptive statistics were presented as mean ± standard deviation (SD) for continuous variables and frequencies and percentages for categorical variables. Differences in baseline demographic data and clinical characteristics among the three vitamin D groups were evaluated using one-way analysis of variance (ANOVA) for continuous variables and Chi-square or Fisher's exact test for categorical variables. To evaluate factors that associated with the success of correcting low serum vitamin D level, patients were divided into two groups based on attainment of vitamin D status, as follows: achieved vitamin D sufficiency or not achieved vitamin D sufficiency. Group differences among continuous variables between these two groups were reported by mean ± standard deviation and evaluated using unpaired Student's t-test. Discrete and categorical variables were evaluated using Chi-square or Fisher's exact test. Unadjusted odds ratios (OR) and their respective 95% CI were calculated to assess the magnitude of the association. All hypotheses were evaluated using two-tailed test, with statistical significance set at alpha equal to 0.05. Multiple comparisons were adjusted using the Bonferroni method.

Following the initial analysis, a multivariable logistic regression model was created to evaluate independent associations of each potential explanatory variable and attainment of vitamin D sufficiency. For the model, variables with a univariate significance level of 0.25 or less were considered to be clinically relevant and were eligible for inclusion in the model. Using a forward stepwise procedure, variables that failed to achieve a *p*-value of 0.15 or less were removed from the final model. Given the explanatory nature of the analyses, 0.15 was selected as the threshold for retention in the final model; however, statistical significance was still set at *p*-value of less than 0.05. Beta coefficients, Exp(B), and their respective 95% confidence intervals were reported for the final regression model. All analyses were performed using SPSS version 18.0 (SPSS Inc., Chicago, IL, USA).

Results

Five hundred thirteen patients were treated at the Siriraj Metabolic Bone Disease Clinic during the study period. Of the 513 patients, 270 patients were excluded from the study, as follows, 128 patients for having received vitamin D2 supplementation prior to implementation of the Siriraj orthopaedic vitamin D2 supplementation regimen, 72 patients for not having both baseline and post-treatment serum 25(OH)D levels recorded and available, 59 patients for having taken additional vitamin D3 supplementation of 400 IU/day or more, and 11 patients for having underlying medical diseases that affect vitamin D absorption and metabolism. Of 513 patients, 243 patients met the inclusion criteria and were included in the present study.

Most patients were female (92.2%), with an average age of 71.6 years. Of the 243 patients, 95 patients (39.1%) were diagnosed with vitamin D deficiency, 66 patients (27.2%) had vitamin D insufficiency, and 82 patients (33.7%) had vitamin D sufficiency. When comparing demographic data and clinical characteristics of all patients based on baseline vitamin D status (Table 2), patients with vitamin D deficiency had significantly higher BMI than the other two groups ($p = 0.029$). Patients with baseline

vitamin D sufficiency reported a history of vitamin D supplementation (<400 IU per day) via dietary intake at a rate higher than the other two groups ($p = 0.002$). Although serum calcium was statistically significantly different between the three groups, the mean serum calcium in all groups remained within normal range (9.1±0.5, 9.1±0.7, and 9.3±0.4 mg/dL for deficiency, insufficiency, and sufficiency groups, respectively). Therefore, the difference in serum calcium level between the three groups appeared to have no clinical significance. There were no differences in the proportion of subjects diagnosed with osteopenia and/or osteoporosis, baseline eGFR results, or other basic metabolic laboratory results among the three patient groups.

After prescribing our stratified vitamin D2 supplementation regimen, 187 patients (76.9%) had serum 25(OH)D level of 30 ng/mL or more. Four patients had 25(OH)D level greater than 50 ng/mL after treatment; however, these patients were asymptomatic. Mean serum calcium for these four patients was 9.6 mg/dL, ranging from 9.3 to 10.2 mg/dL. Fifty-six patients (23.0%) still had 25(OH)D level of less than 30 ng/mL after three months of vitamin D2 supplementation. When 20 ng/mL was used as a cut-off value for adequate vitamin D status, our regimen demonstrated an ability to restore serum vitamin D sufficiency in up to 98.4% of patients (Table 3). When evaluating the success of our vitamin D2 supplementation regimen based on baseline serum vitamin D level, we found that patients in vitamin D deficiency group had the lowest number of patients who achieved vitamin D sufficiency after treatment. The percentage of patients who achieved vitamin D sufficiency status were 63.2%, 80.3%, and 90.2% for vitamin D deficiency, insufficiency, and sufficiency, respectively ($p = 0.019$ between deficiency and insufficiency groups, and $p<0.001$ between deficiency

Table 2. Demographic data and baseline clinical characteristics of study subjects

Clinical variables	Overall (n = 243)	Vitamin D deficiency (25(OH)D <20 ng/mL) (n = 95)	Vitamin D insufficiency (25(OH)D 20 to <30 ng/mL) (n = 66)	Vitamin D sufficiency (25(OH)D ≥30 ng/mL) (n = 82)	*p*-value
Average age* (years)	71.6±11.2	71.9±12.5	70.8±9.4	72.0±11.5	0.761
Female, n (%)	224 (92.2)	90 (94.7)	59 (89.4)	79 (91.5)	0.442
BMI* (kg/m^2)[a]	23.4±4.1	24.2±4.4	22.9±4.1	22.7±3.8	0.029
History of, n (%)					
Steroid use	33 (13.8)	10 (10.8)	10 (15.4)	13 (16.0)	0.547
Vitamin D supplementation[a]	101 (42.3)	29 (30.9)	26 (40.6)	46 (56.8)	0.002
Proton pump inhibitor use	75 (31.4)	29 (31.2)	21 (32.3)	25 (30.9)	0.981
Smoking	6 (2.5)	2 (2.2)	2 (3.1)	2 (2.5)	0.935
Alcohol consumption	3 (1.3)	1 (1.1)	2 (3.1)	0 (0)	0.247
Chemotherapy	16 (6.7)	7 (7.5)	3 (4.6)	6 (7.4)	0.734
Bisphosphonate use	62 (25.9)	17 (18.3)	21 (32.3)	24 (29.6)	0.091
Fall	94 (40.2)	37 (41.1)	22 (34.4)	35 (43.8)	0.508
Bone mineral density, n (%)	(n = 230)	(n = 88)	(n = 63)	(n = 79)	0.092
Normal (T-score ≥ -1)	13 (5.7)	9 (10.2)	3 (4.8)	1 (1.3)	
Osteopenia (T-score between -1 and -2.5)	80 (34.8)	33 (37.5)	22 (34.9)	25 (31.6)	
Osteoporosis (T-score ≤ -2.5)	137 (59.6)	46 (52.3)	38 (60.3)	53 (67.1)	
Laboratory tests*					
eGFR (mL/minute/1.73 m^2)	55.3±24.5	58.6±28.0	57.1±21.7	51.2±21.6	0.061
Total calcium (mg/dL)[a]	9.2±0.6	9.1±0.5	9.1±0.7	9.3±0.4	0.027
Albumin (g/dL)	4.1±1.7	3.9±0.6	4.4±3.0	4.1±0.4	0.170
Phosphate (mg/dL)	3.5±0.5	3.5±0.6	3.5±0.5	3.5±0.5	0.938
Parathyroid hormone (pg/mL)	51.8±20.0	51.0±23.6	55.1±15.6	49.9±18.3	0.275
25(OH)D (ng/mL)[a]	25.3±10.7	15.3±4.3	25.0±3.1	37.1±7.2	<0.001
BUN (mg/dL)	15.2±6.8	14.8±6.7	14.9±5.2	16.0±7.7	0.424
Creatinine (mg/dL)	1.0±1.1	0.8±0.4	1.0±1.5	1.07±1.2	0.275

25(OH)D = 25-hydroxyvitamin D; BMI = body mass index; eGFR = estimated glomerular filtration rate; BUN = blood urea nitrogen

* Data presented as mean ± standard deviation unless otherwise specified

[a] *p*-value less than or equal to 0.05 indicates statistical significance

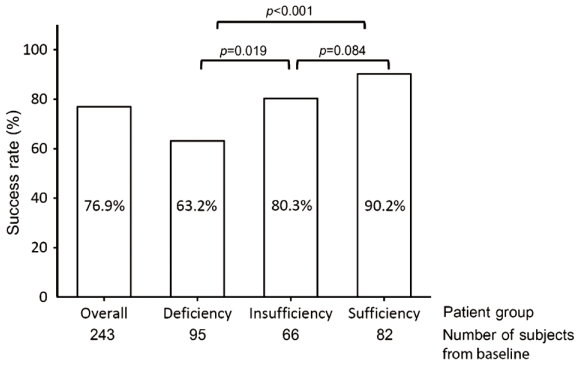

Fig. 1 Percentage of patients who achieved vitamin D sufficiency status (25(OH)D ≥30 ng/mL) after treatment with a stratified vitamin D2 supplementation regimen for 3 months. Comparisons between groups were performed using Chi-square test.

and sufficiency groups). There was no statistically significant difference between vitamin D insufficiency and sufficiency groups ($p = 0.084$) (Fig. 1). If patients presenting with a sufficient level (>30 ng/mL) of 25(OH)D at baseline were excluded from analysis after three months, this left 161 patients for continued evaluation of the effectiveness of our supplementation regimen. After three months of stratified vitamin D2 supplementation, 113 of 161 patients (70.1%) achieved 25(OH)D level to sufficiency status, 44 patients (27.3%) were classified as having vitamin D insufficiency (20 to <30 ng/ml) and 4 patients (2.5%) were vitamin D deficient ($p = 0.027$) (Table 3).

When evaluating the relationship between each clinical variable and the success of achieving vitamin D sufficiency status (25(OH)D of 30 ng/mL or more), three variables were found to be associated with attainment of vitamin D sufficiency status after treatment with our D2 supplementation regimen with significance level of 0.25 or less: BMI, eGFR, and baseline vitamin D level. As such, these three variables were included in multiple logistic regression analysis. By using forward stepwise multivariate logistic regression to identify factors that associate with success of achieving vitamin D sufficiency status (25(OH)D of 30 ng/mL or more), the model showed that only baseline vitamin D level and BMI were statistically associated with attainment of vitamin D sufficiency status after treatment with our vitamin D2 supplementation regimen (Table 4). The beta coefficient (B) of baseline vitamin D level was 0.092. This indicates that the higher the baseline vitamin D level is, the greater the chance of achieving vitamin D sufficiency status after treatment. The beta coefficient of BMI was -0.132, which implies that an increasing BMI is associated with a lower chance of achieving vitamin D sufficiency status after treatment with our stratified vitamin D2 supplementation regimen.

Table 3. Number of patients who attained different vitamin D cut-off levels after treatment with Siriraj orthopaedic vitamin D2 supplementation regimen

Serum 25(OH)D level after treatment	Number of patients (%) (n = 243)	Excluded patient with sufficient vitamin D level at baseline (%) (n = 161)
<20 ng/mL	4 (1.6)	4 (2.5)
20 to 29 ng/mL	52 (21.4)	44 (27.3)
30 to 50 ng/mL	183 (75.3)	111 (68.9)
>50 ng/mL	4 (1.6)	2 (1.2)

Table 4. Factors associated with success of achieving vitamin D sufficiency after treatment with Siriraj orthopaedic vitamin D2 supplementation regimen

Factors	B (SE)	Exp(B)	95% CI for Exp(B)		*p*-value
			Lower	Upper	
Baseline vitamin D level	0.092 (0.02)	1.097	1.053	1.142	<0.001
Body mass index (BMI)	-0.132 (0.05)	0.877	0.802	0.958	0.003
eGFR	-0.007 (0.01)	0.993	0.980	1.007	0.324
Constant	2.640 (1.16)	14.013			0.023
$R^2 = 0.25$ (Nagelkerke)					

B = beta coefficient; SE = standard error; eGFR = estimated glomerular filtration rate; Exp(B) = odds ratio
p-value less than or equal to 0.05 indicates statistical significance

Discussion

The majority of ergocalciferol regimens to correct serum vitamin D level were developed and used in Western countries. The overall success rate of vitamin D sufficiency attainment (defined as 25(OH) D of 30 ng/mL or more) of these regimens has been moderate (Table 5). Given that vitamin D absorption depends on food intake and Asian food generally contains less fat than Western food, a different ergocalciferol regimen should then be explored.

Our vitamin D2 supplementation regimen differs from other ergocalciferol regimens that our regimen is stratified, with vitamin D2 supplement amount being based on each patient's baseline vitamin D level, instead of using a fixed dose for all patients, as reported by previous investigators[13-16]. By using our stratified vitamin D2 supplementation regimen, we were able to correct and/or maintain serum 25(OH)D level above 30 ng/mL in approximately 77% of patients. Similar to our results, Mastaglia et al[15] found that administering vitamin D2 70,000 IU/week for three months was effective in raising 25(OH)D levels to 34 ng/mL or higher in 75% of postmenopausal osteopenic/osteoporosis women. Vande Griend et al[13] found that 58% of patients who received a loading dose of vitamin D2 50,000 to 100,000 IU/week for two to six months attained vitamin D sufficiency. High variability in the success of achieving vitamin D sufficiency results from several factors, including baseline vitamin D level, patient comorbidity and BMI, and duration of vitamin D treatment. We recommend against single-fixed dosing for all status levels of hypovitaminosis D, given the increased potential for hypervitaminosis D, Vitamin D toxicity is rare, even 200,000 IU per week of vitamin D2 supplementation for two months[5] or when a daily dosage of 10,000 IU vitamin D3 is given for up to four months[17].

Although many studies have attempted to evaluate the effectiveness of vitamin D2 supplementation, none have attempted to identify factors that associate with success of treating low serum vitamin D status with vitamin D2. Our study found that baseline vitamin D and BMI are statistically significantly associated with success of achieving vitamin D sufficiency. This finding confirmed our belief that treatment of low vitamin D status should be stratified, based on baseline 25(OH)D level. It is clear from our findings that patients with a lower vitamin D level require a larger amount of vitamin D supplementation than those with a higher baseline vitamin D level. Regarding BMI, our study found that patients in the vitamin D deficiency group had significantly higher BMI than patients in the other two groups. This result was similar to several previous studies, all of which demonstrated that obese individuals have lower circulating vitamin D concentrations than non-obese individuals[18]. Because vitamin D is fat-soluble and adipose tissue is a major vitamin D storage site, it is possible that vitamin D bioavailability is reduced in obese patients due to increased uptake in adipose tissue[19].

Table 5. Summary of effectiveness of treatment for hypovitaminosis D with ergocalciferol (vitamin D2)

Authors	Journal (year)	Type of study	Regimen (number of subjects)	Duration of treatment	Target level (ng/mL)	Attainment rate (%)*
Mastaglia, et al.[15]	Eur J Clin Nutr (2006)	Prospective	Ergocalciferol 35,000 IU/week (n = 13) Ergocalciferol 70,000 IU/week (n = 12)	3 months	34	50% for 35,000 IU/week 75% for 70,000 IU/week
Binkley, et al.[14]	J Clin Endocrinol Metab (2011)	Prospective	Ergocalciferol 1,600 IU/day (n = 16) or the equivalent of 50,000 IU/month (n = 16)	12 months	30	75% for 1,600 IU/day 75% for 50,000 IU/month
Vande Griend, et al.[13]	Pharmacotherapy (2012)	Retrospective	Ergocalciferol 50,000 to 100,000 IU/week (n = 412)	60 to 180 days	30	58%
Sansanayudh, et al.[16]	Int J Clin Pharm (2014)	Prospective	Ergocalciferol 20,000 IU/week (n = 30) Ergocalciferol 40,000 IU/week (n = 30)	8 weeks	30	33.3% for 20,000 IU/week 60% for 40,000 IU/week
Present study		Retrospective	Ergocalciferol 60,000 IU/week for D deficiency (n = 95) Ergocalciferol 40,000 IU/week for D insufficiency (n = 66) Ergocalciferol 20,000 IU/week or no supplement for D sufficiency (n = 82)	3 months	30	63.2% in the D deficiency group 80.3% in the D insufficiency group 90.2% the D sufficiency group

* Percentage of patients who achieved target serum vitamin D concentration or higher at follow-up

The present study has some limitations. First, as with all retrospective studies, it was subject to inherent biases in patient selection. Second, since this study had no control group, it was unclear if these patients would have done better with other fixed vitamin D2 supplementation regimen, or with vitamin D3 supplementation. Third, we did not have accurate information regarding patient dietary intake of vitamin D. In addition, some calcium and multivitamin formulations contain small amounts of vitamin D (D3 of less than 400 IU). We considered this amount of vitamin D to be minimal; as such, patients who took calcium plus vitamin D formulation that did not exceed 400 IU/day were included in the study. Therefore, it is possible that some patients may have received vitamin D supplementation that was higher than planned or expected. Fourth, we did not have data regarding patient compliance. The data described here, however, did reflect a real-world clinical setting in which some patients complied with treatment regimen, while others did not. In addition, previous investigators had demonstrated large between-individual variability in response to equal amounts of vitamin D intake[14]. Therefore, it is not possible to reliably predict or ensure that post-treatment responses in subsequent studies will be the same as the responses we found in the present study. The causes of between-individual variability are unknown, but are likely associated with differences in vitamin D absorption and metabolism. As a result, monitoring of serum 25(OH)D level is necessary for healthcare providers who wish to ensure that their patients achieve optimal vitamin D status.

Conclusion

Given the high prevalence of hypovitaminosis D, patient evaluation and treatment are necessary to prevent complications that arise from low vitamin D levels. The present study clearly demonstrated that the Siriraj stratified vitamin D2 supplementation regimen achieved serum 25(OH)D levels of 20 and 30 ng/mL in 98% and 77% of the overall study population, respectively. In addition, we found that baseline vitamin D level and BMI were two statistically significant factors that associated the success of treating hypovitaminosis D. Thus, these two factors should be considered during treatment of patient with low vitamin D level. Patients with extremely low vitamin D status and high BMI should receive a higher dose of vitamin D supplementation. Our stratified vitamin D2 supplementation regimen is effective and can be safely administered to correct and/or maintain vitamin D sufficiency status.

What is already known on this topic?

Hypovitaminosis D is common in Thais. It can be treated with vitamin D supplementation. Dosage of vitamin D supplementation in general population is 800 IU per day. The potency of vitamin D2 is less than vitamin D3. Vitamin D2 is the only form of native vitamin D supplementation available in Thailand.

What this study adds?

This study proves that a stratified vitamin D2 supplementation protocol is safe and effective in correcting low serum vitamin D level. Factors associated with attainment of vitamin D sufficiency status after treatment with vitamin D2 supplementation are BMI and baseline vitamin D level.

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Potential conflicts of interest

None.

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การใช้วิตามินดี 2 เสริมตามระดับของวิตามินดีในกระแสเลือดเพื่อแก้ไขภาวะวิตามินดีต่ำและรักษาระดับวิตามินดีให้เพียงพอในกระแสเลือด

อาศิส อุนนะนันทน์, โพชฌงค์ โชติญาณวงษ์

ภูมิหลัง: *ในปัจจุบันยังไม่มีมาตรฐานในแนวทางการรักษาภาวะวิตามินดีต่ำโดยการใช้วิตามินดี 2 เสริม คณะผู้นิพนธ์จึงได้พัฒนาแนวทางการรักษาภาวะวิตามินดีต่ำโดยการให้วิตามินดี 2 เสริมตามระดับวิตามินดีในกระแสเลือดของผู้ป่วย*

วัตถุประสงค์: *เพื่อประเมินอัตราความสำเร็จของการเข้าถึงระดับวิตามินดีในกระแสเลือดที่เพียงพอโดยการใช้แนวทางการรักษาภาวะวิตามินดีต่ำโดยการให้วิตามินดี 2 เสริมตามระดับวิตามินดีในกระแสเลือดของผู้ป่วย และสืบหาปัจจัยที่มีความสัมพันธ์กับความสำเร็จในการแก้ไขระดับวิตามินดีในกระแสเลือดต่ำ*

วัสดุและวิธีการ: *การศึกษาแบบย้อนหลังจากข้อมูลการรักษาของผู้ป่วยที่เข้ารับการรักษาที่คลินิกโรคกระดูกทางเมตะบอลิกของโรงพยาบาลศิริราชระหว่างเดือนมีนาคม พ.ศ. 2555 ถึง ธันวาคม พ.ศ. 2557 ในผู้ป่วยทุกรายที่มีการส่งตรวจระดับวิตามินดี (25-hydroxyvitamin D) ในกระแสเลือดทั้งก่อนและ 3 เดือนหลังการรักษา แนวทางการแก้ไขภาวะวิตามินดีต่ำและรักษาระดับวิตามินดีให้อยู่ในระดับปกติโดยการให้วิตามินดี 2 เสริมตามระดับวิตามินดีในกระแสเลือดเป็นดังนี้ ให้วิตามินดี 2 เสริมขนาด 60,000, 40,000, 20,000 และ 0 หน่วยสากลต่อสัปดาห์ สำหรับผู้ป่วยที่มีระดับวิตามินดีในกระแสเลือดในระดับที่น้อยกว่า 20, 20 ถึงน้อยกว่า 30, 30 ถึง 40 และมากกว่า 40 นาโนกรัมต่อมิลลิลิตร ตามลำดับ*

ผลการศึกษา: *จากผู้ป่วยที่เข้าร่วมการศึกษาทั้งหมด 243 ราย พบว่า ผู้ป่วยจำนวน 187 ราย (ร้อยละ 77) มีระดับวิตามินดีในกระแสเลือดอยู่ในระดับที่เพียงพอ (มากกว่าหรือเท่ากับ 30 นาโนกรัมต่อมิลลิลิตร) ภายหลังการรักษาโดยการให้วิตามินดี 2 เสริมตามแนวทางการรักษาภาวะวิตามินดีต่ำโดยการให้วิตามินดี 2 เสริมตามระดับวิตามินดีในกระแสเลือดของผู้ป่วย อย่างไรก็ตามหากใช้ระดับวิตามินดีในกระแสเลือดที่มากกว่าหรือเท่ากับ 20 นาโนกรัมต่อมิลลิลิตร เป็นเกณฑ์ของระดับวิตามินดีในกระแสเลือดที่เพียงพอจะมีผู้ป่วยจำนวนมากถึงร้อยละ 98.4 ที่มีระดับวิตามินดีในกระแสเลือดสูงกว่าระดับดังกล่าวภายหลังการรักษา นอกจากนี้คณะผู้นิพนธ์ยังพบว่าดัชนีมวลกายและระดับวิตามินดีในกระแสเลือดก่อนการรักษามีความสัมพันธ์กับการเข้าถึงระดับวิตามินดีที่เพียงพอภายหลังการรักษาด้วยแนวทางการรักษาภาวะวิตามินดีต่ำโดยการให้วิตามินดี 2 เสริมตามระดับวิตามินดีในกระแสเลือด*

สรุป: *แนวทางการรักษาภาวะวิตามินดีต่ำโดยการให้วิตามินดี 2 เสริมตามระดับวิตามินดีในกระแสเลือดของคณะผู้นิพนธ์ประสบความสำเร็จในการเข้าถึงระดับวิตามินดีในกระแสเลือดที่เพียงพอประมาณร้อยละ 77 ของผู้ป่วยทั้งหมด เนื่องจากดัชนีมวลกายและระดับวิตามินดีในกระแสเลือดก่อนการรักษาเป็นปัจจัยสำคัญสองประการที่มีอิทธิพลต่อความสำเร็จในการรักษาภาวะวิตามินดีต่ำ ดังนั้นแพทย์ผู้ให้การรักษาจะต้องคำนึงถึงปัจจัยสองประการนี้ทั้งในระยะก่อนและระหว่างการรักษาผู้ป่วยที่มีปัญหาวิตามินดีต่ำด้วย*