Published in final edited form as:
Endocr Pract. 2009 ; 15(2): 95–103.

EVALUATION OF VITAMIN D REPLETION REGIMENS TO CORRECT VITAMIN D STATUS IN ADULTS

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Abstract

Objective—To determine the efficacy and safety of commonly prescribed regimens for the treatment of vitamin D insufficiency.

Methods—We performed a retrospective analysis of 306 consecutive patients who were prescribed ergocalciferol (vitamin D_2) for correction of vitamin D insufficiency at the Atlanta Veterans Affairs Medical Center between February 2003 and May 2006. Serum levels of parathyroid hormone, 25-hydroxyvitamin D (25-OHD), and calcium were compared before and after treatment with ergocalciferol. Patients who did not have a 25-OHD determination (n = 41) were excluded from analysis. Vitamin D deficiency, insufficiency, and sufficiency were defined as a serum 25-OHD level of <20 ng/mL, 21 to 29 ng/mL, and ≥30 ng/mL, respectively.

Results—We identified 36 discrete prescribing regimens. The 3 most common regimens were ergocalciferol 50,000 IU once weekly for 4 weeks followed by 50,000 IU once monthly for 5 months (n = 48); ergocalciferol 50,000 IU once monthly for 6 months (n = 80); and ergocalciferol 50,000 IU 3 times weekly for 6 weeks (n = 27). Each of these 3 treatments significantly increased serum 25-OHD (P<.01), but vitamin D sufficiency was achieved in only 38%, 42%, and 82% of study subjects, respectively. Regimens with >600,000 IU of ergocalciferol given for a mean of 60 ± 40 days achieved sufficiency in 64% of cases, without vitamin D toxicity.

Conclusion—In this study, regimens that contained at least 600,000 IU of ergocalciferol appeared to be the most effective in achieving vitamin D sufficiency. Guidelines for the treatment of vitamin D insufficiency in healthy adults should be developed.

INTRODUCTION

There is increased awareness for the high prevalence of vitamin D insufficiency in the general population of the United States. Vitamin D insufficiency is associated with an increased risk for several medical conditions, including osteoporotic fractures (1), falls (2), cancer (3,4),

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DISCLOSURE
The authors have no conflicts of interest to disclose.

diabetes (5), and hypertension (6). Several protocols have been published for correction of the vitamin D status in specific patient populations, including those with cystic fibrosis (7), chronic kidney disease (8), hyperparathyroidism (9), osteoporosis (10), and pregnancy (11). Nevertheless, no universally accepted method has been advocated for correction of vitamin D insufficiency in healthy ambulatory adults. Some examples of published regimens for the correction of vitamin D status in healthy adults include 50,000 IU of ergocalciferol once a week for 8 weeks (12) or 50,000 IU of ergocalciferol twice a week for 5 weeks (13). Furthermore, there are limited data to evaluate the efficacy of various methods of correction of vitamin D status in adults.

The recommended adequate intakes of vitamin D published by the Institute of Medicine (400 to 600 IU or 10 to 15 μg daily) for most adults are inadequate to maintain or correct vitamin D status in vitamin D-insufficient adults (14). The amount of vitamin D needed for correction of vitamin D insufficiency in a reasonable duration of time has generally been available only by prescription in the United States as ergocalciferol (vitamin D_2) (14). Now, however, vitamin D can be found in 1,000-, 2,000-, 5,000-, 10,000-, and 50,000-IU capsules (15). Although some evidence indicates that cholecalciferol (vitamin D_3) may be more bioavailable than ergocalciferol (16), it is not widely available by prescription in the United States. There also has been concern that correction of vitamin D insufficiency may result in vitamin D toxicity, but data are limited regarding the potential of vitamin D supplementation to cause vitamin D toxicity. Vitamin D supplementation is believed to be safe under a daily dose of 10,000 IU (17).

In the current study, we sought to determine which vitamin D repletion regimens were in use at a large academic-affiliated Veterans Affairs Medical Center (VAMC). We were interested in determining the physician practice patterns in treatment of vitamin D insufficiency. We also wished to evaluate the efficacy and safety of several commonly prescribed vitamin D repletion regimens.

PATIENTS AND METHODS

Study Subjects and Protocol

We received approval by the Emory University Institutional Review Board and the Atlanta Research and Development Committee to conduct this study. This was a retrospective review of 306 consecutive patients who were prescribed ergocalciferol at the Atlanta VAMC between February 2003 and May 2006. We examined the medical records of patients who were prescribed vitamin D through the Atlanta VAMC pharmacy, which dispenses all prescription medications to all patients seen at the Atlanta VAMC. We recorded demographic information for each study subject; the amount of vitamin D prescribed; the study subject's 25-hydroxyvitamin D (25-OHD) and parathyroid hormone (PTH) levels before and after treatment with vitamin D; basic laboratory values including total calcium, albumin, and creatinine; and the specialty of the prescribing physician. Levels for 25-OHD were determined by Quest liquid chromatography-mass spectrometry (83%) or Diasorin radioimmunoassay (17%) during the study period. Vitamin D sufficiency was defined as 25-OHD ≥30 ng/mL, and toxicity was defined as 25-OHD >150 ng/mL or a calcium level 1.0 mg/dL above the reference range (or both findings) (14). Patients were excluded from the study if no documentation of vitamin D prescription could be found in patient records or if the medical records were restricted from review.

Statistical Analysis

We used Microsoft Excel 2003 (Seattle, Washington) and SAS version 9.1 (SAS Institute, Cary, North Carolina) to conduct our statistical analysis. Descriptive statistics were used for

demographic and laboratory data. To compare differences by analysis of variance in the vitamin D repletion regimens, we used "PROC GLM" (general linear models procedure) in SAS to produce least squares means. To compare the association of serum 25-OHD changes with PTH changes, we used a linear regression with log-transformed dependent and independent variables to account for nonnormality. We tested for interaction by specialty of the prescribing physician (mainly endocrinologists, nephrologists, or primary care physicians) ($P<.10$ was considered significant) and controlled for season of final 25-OHD, initial PTH, serum creatinine, and initial 25-OHD as covariates ($P<.05$ was considered significant). In addition to treatment regimen, we also tested total dose of vitamin D received, rapidity of repletion, timing of dose (monthly, weekly, daily, and so forth), and dosing regimen (using the 4 most common methods) as potential exposure variables, with vitamin D sufficiency as the outcome variable. Only total dose was significant for achieving vitamin D sufficiency. We also tested the effect of initial 25-OHD in the model; it was not significant at the 5% level.

To determine the relative efficacy of different amounts of vitamin D on correcting vitamin D insufficiency, we used "PROC LOGISTIC" (logistic procedure) in SAS to calculate odds ratios to compare 3 total amounts of vitamin D used in the repletion regimen (≤300,000 IU, 300,001 to 599,999 IU, and ≥600,000 IU), with ≥600,000 IU as the reference group.

RESULTS

Study Subjects

Patients who had prescriptions for vitamin D filled by the Veterans Affairs (VA) pharmacy but did not have a 25-OHD determination were excluded from analysis; thus, 265 of the original 306 patients were eligible for the study. The large majority of patients were male, typical of the patient population within the VA system. The mean age of the study population was 67 ± 12 years. In 174 patients, 25-OHD was determined both before and after vitamin D repletion. The various reasons for determining the 25-OHD included evaluations for osteoporosis, chronic kidney disease, and myalgias. Patients who had a 25-OHD determination as part of a work-up for malabsorptive disorders were excluded from the study.

Prescribed Vitamin D Treatment Regimens

We found 36 discrete modalities of vitamin D repletion regimens (Table 1). The prescribed dose of ergocalciferol ranged from 400 IU to 50,000 IU, and the frequency of dosing ranged from twice daily to once monthly. The mean duration for all vitamin D repletion regimens was 116 ± 62 days, with a range of 7 to 196 days. Patients given more than 600,000 IU of vitamin D had repletion within a mean of 60 ± 40 days. The 3 most common prescribing modalities were ergocalciferol 50,000 IU once weekly for 4 weeks followed by 50,000 IU once monthly for 5 months (total of 450,000 IU) (treatment 1, n = 48); ergocalciferol 50,000 IU once monthly for 6 months (total of 300,000 IU) (treatment 2, n = 80); and ergocalciferol 50,000 IU 3 times weekly for 6 weeks (total of 900,000 IU) (treatment 3, n = 27). We also examined a popular regimen recommended by Malabanan et al (12)—ergocalciferol 50,000 IU per week for 8 weeks—as treatment 4 (total of 400,000 IU). Treatment 4 also included all regimens that totaled 400,000 IU of ergocalciferol given within an 8-week period.

Treatments 1 and 2 are the recommendations from the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF KDOQI) for treating vitamin D insufficiency in patients with chronic kidney disease. Treatment 1 is recommended for patients with an initial 25-OHD value ranging from 5 to 15 ng/mL, and treatment 2 is recommended for patients with initial 25-OHD levels ranging from 16 to 30 ng/mL (8). Treatments 3 and 4 are regimens commonly prescribed by endocrinologists at our medical center (in 74% and 64% of cases,

respectively). Of the 265 patients included in this study, 66% had both pretreatment and posttreatment 25-OHD levels.

Efficacy of Vitamin D Repletion Regimens

Treatments 1, 2, and 3 resulted in a statistically significant increase in serum 25-OHD ($P<.01$) (Table 2). Treatments 1, 2, and 3 corrected vitamin D deficiency (25-OHD <20 ng/mL) in 55%, 86%, and 95% of cases and corrected vitamin D insufficiency (25-OHD <30 ng/mL) in 38%, 42%, and 82% of cases, respectively. Serum PTH and calcium levels were not significantly affected by any of these 3 prescribing modalities. Patients who received treatment 4 did not have a statistically significant increase in 25-OHD or decrease in PTH. Only 4 patients (50%) in this group reached a 25-OHD level >20 ng/mL, and only 1 patient (13%) reached a 25-OHD concentration ≥30 ng/mL.

Physician Preference for Vitamin D Treatment Regimen

Treatments 1 and 2 were predominantly prescribed by nephrologists. The mean serum creatinine level was significantly higher in these patients. Treatments 3 and 4 were favored by endocrinologists, and a larger percentage of women were prescribed treatment 3 (26%) in comparison with treatments 1 and 2 (4%) or treatment 4 (14%).

Effect of Total Vitamin D Dose on Vitamin D Status

We evaluated the effects of total ergocalciferol dose on changes in 25-OHD, PTH, and calcium. The patients were classified into 3 groups based on total dosage of ergocalciferol: ≤300,000 IU; 300,001 to 599,999 IU; and ≥600,000 IU. All total doses of vitamin D increased 25-OHD significantly ($P<.01$). Vitamin D sufficiency (25-OHD ≥30 ng/mL) was most frequently achieved when patients received ≥600,000 IU of vitamin D (64%). With use of the total amount of ≥600,000 IU of vitamin D as the reference group, the odds ratios of remaining vitamin D insufficient despite treatment were as follows: 7.3 (95% confidence interval, 3.9 to 13.8; $P<.001$) for patients receiving ≤300,000 IU of vitamin D and 3.2 (95% confidence interval, 1.6 to 6.4; $P = .56$) for patients receiving 300,001 to 599,999 IU of vitamin D (Table 3). Serum PTH and calcium levels were not significantly changed in any of these groups.

Effect of 25-OHD Increase on PTH and Vitamin D Status

We created 4 quartiles based on percentage increase of 25-OHD. Quartiles 1 through 4 consisted of those patients with greater than a 200% increase in 25-OHD, those with a 90% to 200% increase, those with a 33% to 89% increase, and those with less than a 33% increase in 25-OHD, respectively. There were significantly more patients in quartile 4 who received a lower total dose of vitamin D ($P = .008$). In addition, those patients in quartiles 1 and 4 were more likely to have been prescribed vitamin D by a nephrologist ($P = .002$). Patients in the first 2 quartiles (indicating the greatest increase in 25-OHD) had higher final 25-OHD values and had more study subjects reach vitamin D sufficiency (Table 4). Although not statistically significant, a trend existed toward a lower body mass index in quartile 1, the subset of patients with the most robust increase in mean 25-OHD levels. This quartile also had the highest percentage of patients receiving ≥600,000 IU of vitamin D.

Vitamin D Toxicity and Hypercalcemia

In this study, there were no cases of vitamin D toxicity. In all 4 treatment regimens analyzed, the mean corrected calcium from before to after treatment with ergocalciferol differed no more than 0.2 mg/dL (Table 2). Posttreatment 25-OHD levels ranged from 7 to 100 ng/mL, and corrected calcium values ranged from 7.8 to 11.7 mg/dL (reference range, 8.5 to 10.9).

DISCUSSION

In our study, we sought to determine the physician practice patterns in correction of vitamin D insufficiency at a large VA tertiary care hospital. We have determined that no standard regimen exists for correction of vitamin D insufficiency in our hospital. Although most of the regimens increased the mean 25-OHD levels, the majority of the regimens did not achieve vitamin D sufficiency (25-OHD values ≥30 ng/mL). We also found that PTH levels do not consistently decrease after treatment of vitamin D insufficiency. Review of all the prescribed regimens in our hospital disclosed no case of vitamin D toxicity.

No international standard has been established for vitamin D sufficiency, and some studies suggest 30 ng/mL should be the minimal level for sufficiency (18,19). Most experts agree that vitamin D deficiency is defined as serum 25-OHD <20 ng/mL. Studies have demonstrated that serum 25-OHD levels of 30 to 32 ng/mL result in maximal suppression of PTH, optimal intestinal calcium absorption, and prevention of fractures (1,20-22). Higher levels of 25-OHD may be necessary for other extraskeletal benefits, such as the prevention of cancer (4). Therefore, we and other investigators suggest that vitamin D sufficiency be defined as serum 25-OHD ≥30 ng/mL (16).

The Institute of Medicine recommends that most adults and children consume 200 to 600 IU of vitamin D daily; however, this recommendation assumes that the individual is vitamin D sufficient initially. Several randomized placebo-controlled trials of calcium and vitamin D have demonstrated that taking 800 IU or less of vitamin D daily does not achieve sufficiency (as defined by 25-OHD ≥30 ng/mL) (17,23). Much higher doses of vitamin D are necessary to correct vitamin D insufficiency. For most healthy adults, however, no standard repletion regimen is available. Malabanan et al (12) reported that ergocalciferol in a dosage of 50,000 IU once a week for 8 weeks (treatment 4 in our study) was an effective regimen to improve vitamin D status and decrease PTH levels in patients managed in an osteoporosis clinic in Boston. Their definition of vitamin D sufficiency, however, was a 25-OHD level >20 ng/mL. Of the 35 subjects in their study who received that treatment regimen, only 21 (60%) had posttreatment 25-OHD levels >30 ng/mL, a proportion similar to that seen in our review.

We found that the total dose of vitamin D was more predictive of vitamin D sufficiency rather than the frequency of dosing. This finding is consistent with a study by Ish-Shalom et al (24), who examined a dosage of vitamin D_3 of 90,000 IU given during a period of 56 days as a daily, weekly, or monthly dose and found that all regimens were equally efficacious. This result suggests that the frequency of dosing may not matter as much as the total dose administered over time. Nevertheless, our study differs in that we administered vitamin D_2, and we assessed the outcome in patients who generally received vitamin D therapy for a longer period.

For healthy adults, universal guidelines that are effective in raising 25-OHD levels to the currently accepted definition of vitamin D sufficiency (>30 to 32 ng/mL) have not been published. The National Kidney Foundation has published guidelines (NKF KDOQI) for the correction of vitamin D insufficiency in patients with chronic kidney disease (8). These guidelines base the treatment of vitamin D on the severity of vitamin D insufficiency (severe, <5 ng/mL; moderate, 5 to 15 ng/mL; and mild, 16 to 30 ng/mL). Vitamin D repletion with orally administered ergocalciferol for 6 months is recommended, with loading doses of 50,000 IU weekly for 12 weeks and then once monthly for severe vitamin D insufficiency; 50,000 IU weekly for 4 weeks and then monthly for moderate vitamin D insufficiency; and 50,000 IU monthly for mild vitamin D insufficiency. In our study, treatments 1 and 2 reflect the NKF KDOQI guidelines for vitamin D repletion in severe and moderate vitamin D insufficiency, respectively. Because there was no change in PTH levels in either treatment group, these modalities may be insufficient to correct secondary hyperparathyroidism. Conflicting reports

have been published about vitamin D sufficiency and its effects on serum PTH in patients with chronic kidney disease. Some studies suggest that vitamin D repletion with ergocalciferol may lower PTH levels in stages 3 or 4 chronic kidney disease (glomerular filtration rate 30 to 59 and 15 to 29 mL/min, respectively) (25,26), whereas others do not (27). Few reports are available about the effect of cholecalciferol on PTH, but it has been demonstrated to increase 25-OHD concentrations and to cause a trend in lowering PTH (28). Only a small majority of patients achieved vitamin D sufficiency in our study; this outcome perhaps explains why a decrease in PTH was not seen after treatment.

Large oral or parenteral doses of vitamin D_3 (cholecalciferol) have been shown to increase and sustain higher 25-OHD levels. A single 100,000-IU oral dose of vitamin D_3 yielded 60% higher 25-OHD levels at 5 weeks in comparison with placebo (mean, 14.2 and 7.7 ng/mL, respectively) (29). An annual 600,000-IU intramuscular injection yielded sustained improvement in 25-OHD levels >20 ng/mL at 4 and 12 months in conjunction with a modest decrease in PTH value (30). In Argentinean children, a single 150,000-IU oral dose of ergocalciferol safely maintained 25-OHD levels at a mean of 18.7 ng/mL but did not improve serum PTH concentrations (31). Additionally, a 10-day high-dose course of ergocalciferol (50,000 IU daily) showed sustained elevation in 25-OHD levels at 4 months (32).

Ergocalciferol (vitamin D_2) is the most commonly prescribed form of vitamin D used to treat vitamin D insufficiency in the United States, and it is the only vitamin D that is widely available in the 50,000-IU dose strength. Cholecalciferol (vitamin D_3) is not widely available in strengths higher than 2,000 IU. Some investigators have suggested that cholecalciferol may be more bioavailable than ergocalciferol (33). When given equal molar quantities (approximately 4,000 IU) of vitamin D_2 or D_3 for 14 days, the subjects who consumed vitamin D_3 demonstrated a 1.7-times greater efficacy in raising plasma 25-OHD levels (34). Armas et al (35) demonstrated similar absorption of vitamin D_2 and D_3 in healthy male subjects but noted higher and sustained levels of circulating 25-OHD in the vitamin D_3-receiving group. The differences between ergocalciferol and cholecalciferol may relate to variations in binding to vitamin D-binding protein; however, this hypothesis still remains to be established (33,36). In contrast, Holick et al (37) recently demonstrated that vitamin D_2 and vitamin D_3 were equally efficacious in raising 25-OHD concentrations when given as a daily 1,000-IU dose. This outcome suggests that there may be a difference in vitamin D preparations when given in pharmacologic versus physiologic doses in the resultant increase in 25-OHD levels.

One of the limitations of this study is our lack of data on cholecalciferol. As mentioned previously, ergocalciferol is the only commonly available orally administered vitamin D in the 50,000-IU dose strength. Only 1 patient in our study reached vitamin D sufficiency with use of the vitamin D_2 50,000-IU once weekly regimen; therefore, we are unable to draw conclusions regarding its efficacy. This regimen, however, was devised when the target for 25-OHD was greater than 20 ng/mL; thus, it is likely that this regimen is inadequate. Additionally, we were unable to assess medication compliance in this study. Moreover, because posttreatment 25-OHD levels were determined at variable intervals, we may have missed the peak levels of posttreatment 25-OHD. Finally, we were limited by the number of healthy subjects prescribed ergocalciferol, inasmuch as many study subjects also had chronic kidney disease. Patients with early-stage renal disease should be able to convert vitamin D to 25-OHD. Any alteration of this process, however, has not been well studied.

CONCLUSION

We found that our hospital does not have a standard regimen for treating vitamin D insufficiency. The most effective regimen to correct vitamin D deficiency (25-OHD levels <20 ng/mL) and vitamin D insufficiency (25-OHD <30 ng/mL) was ergocalciferol 50,000 IU 3

times a week for 6 weeks. As expected, only regimens >600,000 IU administered for a mean time of 60 ± 40 days of vitamin D raised 25-OHD levels in the majority of patients but varied in efficacy to correct vitamin D insufficiency. All the prescribed regimens were safe and did not result in vitamin D toxicity. We urge that guidelines for treatment of vitamin D insufficiency be developed for clinical practice to standardize the management of vitamin D insufficiency in healthy adults.

ACKNOWLEDGMENT

All authors contributed to the design of the study, the analysis of the data, and the writing of the manuscript. This work was supported in part by grants from the Atlanta Research and Education Foundation, the Atlanta Veterans Affairs Medical Center, the University Research Committee of Emory University, and the National Institutes of Health (K23AR054334).

Abbreviations

NKF KDOQI, National Kidney Foundation Kidney Disease Outcomes Quality Initiative; 25-OHD, 25-hydroxyvitamin D; PTH, parathyroid hormone; VA, Veterans Affairs; VAMC, Veterans Affairs Medical Center.

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Table 1

Total Dose of Vitamin D and Total Number of Vitamin D Repletion Modalities at the Veterans Affairs Medical Center in Atlanta, Georgia, 2003-2006[a]

Total dose of vitamin D	No.
Vitamin D total unknown	
Ergocalciferol 50,000 IU weekly	3
Ergocalciferol 50,000 IU QD	2
Vitamin D ≤300,000 IU	
Ergocalciferol 50,000 IU once monthly × 1	1
Ergocalciferol 10,000 IU QD × 3 days, then 10,000 IU once a week × 4 wk	2
Ergocalciferol 50,000 IU monthly × 3 mo	1
Ergocalciferol 50,000 IU weekly × 4 wk	5
Ergocalciferol 10,000 IU QD × 28 days	1
Ergocalciferol 50,000 IU weekly × 4 wk, then 50,000 IU monthly × 2 mo	2
2 Ergocalciferol 50,000 IU monthly × 6 mo	80
Ergocalciferol 50,000 IU weekly × 6 wk	1
Ergocalciferol 50,000 IU QD × 3 days, then 50,000 IU weekly × 3 wk	3
Vitamin D 300,001 to 599,999 IU	
4 Ergocalciferol 50,000 IU QD × 3-4 days, then 50,000 IU weekly × 4 wk	4
Ergocalciferol 50,000 IU QD × 7 days	1
4 Ergocalciferol 50,000 IU once a week × 8 wk	8
1 Ergocalciferol 50,000 IU once a week × 4 wk, then 50,000 IU monthly × 5 mo	48
Ergocalciferol 50,000 IU once a week × 4 wk, then 50,000 IU monthly × 4 or 6 mo	7
Ergocalciferol 50,000 IU QD × 7 days, then 50,000 IU weekly × 4 wk	1
4 Ergocalciferol 50,000 IU twice weekly × 4 wk	2
Ergocalciferol 50,000 IU QOD × 21 days	1
Vitamin D ≥600,000 IU	
Ergocalciferol 50,000 IU 3 times a week × 4 wk	3
Ergocalciferol 50,000 IU twice a week × 6 wk, then monthly × 0-3 mo	10
Ergocalciferol 50,000 IU once a week × 12 wk, then monthly × 0-3 mo	9
Ergocalciferol 50,000 IU QD × 14 days	2
Ergocalciferol 50,000 IU QOD × 30 days	1
Ergocalciferol 50,000 IU twice a week × 8 wk, then monthly × 0-4 mo	4

Total dose of vitamin D	No.
Ergocalciferol 50,000 IU twice a week × 16 wk	1
3 Ergocalciferol 50,000 IU 3 times a week × 6 wk	27
Ergocalciferol 50,000 IU 3 times a week × 6 wk with daily supplements	5
Ergocalciferol 50,000 IU twice a week × 10 wk	4
Ergocalciferol 50,000 IU QD × 21 days	4
Ergocalciferol 50,000 IU QD × 3 days, then 50,000 IU 3 times a week × 6 wk	1
Ergocalciferol 50,000 IU 3 times a week × 8 wk	4
Ergocalciferol 50,000 IU twice a week × 12 wk	3
Ergocalciferol 50,000 IU QD × 60 days	1
Ergocalciferol 50,000 IU 3 times a week × 10-12 wk	2
Ergocalciferol 50,000 IU QOD × 2-6 mo	4

[a] QD = every day; QOD = every other day. Numbers preceding entries denote the 4 most common prescribing modalities (see text for further information).

Table 2

Effect of the Most Common Ergocalciferol Regimens Prescribed at Our Medical Center to Treat Vitamin D Insufficiency on Serum 25-Hydroxyvitamin D, Parathyroid Hormone, and Corrected Calcium[a]

Factor	Treatment			
	1 (n = 48)	2 (n = 80)	3 (n = 27)	4 (n = 14)
Age, y: No. (%)				
<55	10 (21)	5 (6)	9 (33)	5 (36)
55-64	15 (31)	25 (31)	8 (30)	3 (21)
65-75	11 (23)	20 (25)	3 (11)	4 (29)
>75	12 (25)	30 (38)	7 (26)	2 (14)
Male sex, No. (%)	46 (96)	77 (96)	20 (74)	12 (86)
Body mass index, kg/m^2 (SD)	29.4 (6.5)	29.7 (7.8)	27.5 (7.2)	26.9 (4.5)
Creatinine, mg/dL (SD)	2.6 (1.4)	2.4 (1.2)	1.1 (0.6)	1.2 (0.6)
Prescribing service, No. (%)				
Nephrology	39 (81)	63 (79)	1 (4)	1 (7)
Internal medicine	8 (17)	13 (16)	2 (7)	2 (14)
Endocrinology	1 (2)	4 (5)	20 (74)	9 (64)
Other	0 (0)	0 (0)	4 (15)	2 (14)
25-Hydroxyvitamin D (ng/mL)				
Pretreatment (SD)	11 (5)	21 (5)	17 (7)	14 (5)
Posttreatment (SD)	25 (12)	30 (12)	46 (19)	21 (8)
P value (paired *t* test)	**<.01**	**<.01**	**<.01**	.07
Correction of vitamin D deficiency >20 ng/mL, No. (%)	16 (55)	43 (86)	21 (95)	4 (50)
Correction of vitamin D insufficiency ≥30 ng/mL, No. (%)	11 (38)	21 (42)	18 (82)	1 (13)
No. (%)[b]	29 (60)	50 (63)	22 (81)	8 (57)
Parathyroid hormone (pg/mL)				
Pretreatment (SD)	194 (167)	143 (71)	103 (72)	111 (35)
Posttreatment (SD)	193 (157)	147 (77)	77 (36)	101 (42)
P value (paired *t* test)	.95	.55	.14	.46
Normal posttreatment PTH	4 (15)	8 (13)	10 (59)	1 (17)
No. (%)[b]	27 (56)	60 (75)	17 (63)	6 (43)
Corrected calcium (mg/dL)				

Factor	Treatment			
	1 (n = 48)	**2 (n = 80)**	**3 (n = 27)**	**4 (n = 14)**
Pretreatment (SD)	9.4 (0.5)	9.5 (0.4)	9.4 (0.5)	9.3 (0.5)
Posttreatment (SD)	9.3 (0.5)	9.4 (0.5)	9.6 (0.8)	9.5 (0.8)
P value (paired *t* test)	.48	.48	.14	.36
No. (%)[b]	36 (75)	75 (94)	21 (78)	9 (64)

[a]Treatment 1 = ergocalciferol 50,000 IU once weekly × 4 weeks, then once monthly × 5 months. Treatment 2 = ergocalciferol 50,000 IU once monthly × 6 months. Treatment 3 = ergocalciferol 50,000 IU 3 times weekly × 6 weeks. Treatment 4 = ergocalciferol 50,000 IU once weekly × 8 weeks or 400,000 IU within 8 weeks. Vitamin D sufficiency was defined as posttreatment 25-hydroxyvitamin D levels ≥30 ng/mL. Normal parathyroid hormone level was defined as <65 pg/mL.

[b]Within each treatment group, the number of pretreatment and posttreatment values obtained for each laboratory variable.

Table 3

Odds Ratios for Remaining Vitamin D Insufficient Based on Total Amount of Vitamin D Prescribed

Amount of vitamin D (IU)	Odds ratio	95% confidence interval	*P* value
≥600,000	1.00	...	Referent
300,001 to 599,999	3.2	1.6-6.4	.56
≤300,000	7.3	3.9-13.8	<.001

Table 4

Patient Characteristics by Quartiles Based on Percentage Increase in 25-Hydroxyvitamin D

Factor	Quartile 1	Quartile 2	Quartile 3	Quartile 4	*P* value
Percent increase in 25-hydroxyvitamin D	>200	90-200	33-89	<33	
No. in quartile	43	43	45	43	
Percentage within each repletion stratification in each quartile					
Received ≤300,000 IU	13	17	38	32	
Received 300,001 to 599,999 IU	28	29	25	18	
Received ≥600,000 IU	38	31	21	10	.008[a]
Nephrology patient, No. (% of quartile)	27 (63)	5 (12)	8 (18)	28 (65)	.002[a]
Percentage in each quartile, by season					
Winter	17	26	23	34	
Spring	27	27	25	22	
Summer	28	17	32	23	
Fall	25	31	22	22	.33[a]
Mean 25-hydroxyvitamin D (ng/mL)					
Initial	10 ± 4	14 ± 5	19 ± 6	21 ± 11	<.001[b]
Follow-up	43 ± 16	34 ± 12	30 ± 10	19 ± 7	<.001[b]
Mean parathyroid hormone (pg/mL)					
Initial	115 ± 57	156 ± 143	119 ± 51	135 ± 81	.78[b]
Follow-up	90 ± 52	134 ± 116	120 ± 62	159 ± 107	.004[b]
Mean body mass index (kg/m^2)	28 ± 8	29 ± 6	29 ± 6	31 ± 7	.08[b]

[a] By χ^2 test.

[b] *P* value for trend.