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Intramuscular Vitamin D2 in Patients With Systemic Sclerosis Not Responding to Oral Supplementation: A Retrospective Observational Case Series

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Abstract

Background

This study aimed to evaluate changes in serum 25-hydroxyvitamin D (25(OH)D) levels following intramuscular (IM) ergocalciferol in patients with systemic sclerosis (SSc) and persistently low levels (<30 ng/mL) despite at least six months of oral cholecalciferol supplementation. Clinical outcomes of SSc were not assessed.

Methodology

This retrospective series included patients with SSc who received IM vitamin D2 after non-response to oral supplementation. Non-response was defined as a serum 25(OH)D level remaining below 30 ng/mL after at least six months of oral cholecalciferol at a dose of 10,000 IU weekly. Serum 25(OH)D was measured before the first injection, two weeks after the first injection, and four weeks after the second injection.

Results

In total, 12 patients were identified, with a mean age of 47.8 years; all were women. Five patients had diffuse cutaneous SSc, while seven had limited cutaneous SSc. The mean disease duration was 17.9 years, with a mean modified Rodnan skin score of 14.9. All patients received two injections of 300,000 IU of ergocalciferol into the anterior gluteus muscle at a 15-day interval. The mean serum 25(OH)D level rose from 12.9 ng/mL before the first injection to 23.1 ng/mL two weeks after the first injection, and to 37.2 ng/mL four weeks after the second injection ($p < 0.001$). Overall, 10 of the 12 patients reached a level of 30 ng/mL or higher. No adverse events were reported during the follow-up period.

Conclusions

In this small retrospective series, IM ergocalciferol increased serum 25(OH)D levels and was not associated with reported adverse events. Prospective controlled studies are needed to confirm these findings.

Categories: Internal Medicine, Allergy/Immunology, Dermatology
Keywords: connective tissue disease, ergocalciferol, intramuscular, systemic sclerosis, vitamin d deficiency

Introduction

Systemic sclerosis (SSc) is a connective tissue disease characterized by the progressive loss of the microvascular bed, leading to fibrotic changes in the affected organs and tissues. Depending on the extent of skin involvement, it can be classified as either limited cutaneous SSc (lcSSc), which is restricted to the face and areas below the elbows and knees, or diffuse cutaneous SSc (dcSSc) [1].

A remarkably high prevalence of vitamin D deficiency has been reported in patients with connective tissue disorders, such as systemic lupus erythematosus, granulomatosis with polyangiitis, and SSc [2,3]. This deficiency could be multifactorial in SSc, where the disease can affect the organs involved in vitamin D metabolism. Endogenous synthesis through skin exposure to sunlight is the main source of vitamin D; dietary consumption serves as another source [4]. In the epidermis, 7-dehydrocholesterol (or provitamin D3) transforms into previtamin D3 after exposure to UV rays, particularly UVB [5,6]. Previtamin D3 is converted to vitamin D3 (cholecalciferol) through a heat-dependent reaction. Additionally, ergocalciferol is absorbed from food in the digestive tract [4], especially in the small intestine [7]. Dietary sources include supplements and foods such as milk, dairy products, fish, meat, poultry, eggs, and sweets [8]. Cholecalciferol and ergocalciferol enter the bloodstream and are stored in the liver as 25-hydroxyvitamin D (25(OH)D) after hydroxylation by the liver's 25-alpha-hydroxylase. To produce the biologically active form of vitamin D, 25(OH)D undergoes a second hydroxylation in various tissues by 1-alpha-hydroxylase, resulting in the

formation of 1,25-dihydroxyvitamin D (calcitriol or 1,25(OH)2D) [9,10].

Many factors can contribute to vitamin D deficiency in SSc patients. First, dermal fibrous thickening and capillary damage may impact the conversion of 7-dehydrocholesterol to previtamin D3. Serum levels of 25(OH)D were inversely correlated with skin thickness and were significantly lower in patients with dcSSc compared to lcSSc [11]. Second, vascular damage, nerve dysfunction, smooth muscle atrophy, and intestinal wall fibrosis can lead to hypomotility and small intestinal bacterial overgrowth, resulting in subclinical malabsorption of nutrients and vitamins [12,13]. Third, physical impairment associated with a sedentary lifestyle reduces exposure to sunlight. It has also been suggested, though not confirmed, that lower serum levels of vitamin D correlate with SSc severity or activity [2,14-16]. Conversely, recent experiments on mouse cells have demonstrated that vitamin D possesses a direct antifibrotic action. It inhibits the production of transforming growth factor beta 1, a pro-fibrotic cytokine, as well as the synthesis of collagen I and collagen III in mesenchymal multipotent cells while increasing the expression of anti-fibrotic factors such as matrix metalloproteinase 8 [17]. Hence, it remains unclear whether hypovitaminosis D is a risk factor or a consequence of SSc [11].

The oral route is considered the most common way of vitamin D supplementation [18]. However, in the patients included in this series, oral cholecalciferol at a dose of 10,000 IU weekly for at least six months did not correct their low serum 25(OH)D levels. Many studies have analyzed the frequent vitamin D deficiency in SSc [2,11,14,15,19]. However, to our knowledge, no prior study has specifically evaluated intramuscular (IM) vitamin D supplementation in SSc patients with persistently low 25(OH)D despite oral supplementation. Here, we report a retrospective series of patients with SSc and low vitamin D not responding to oral supplementation, who received IM vitamin D. The objective of this study was to evaluate changes in serum 25(OH)D levels following IM ergocalciferol in patients with SSc and persistently low levels (<30 ng/mL) despite at least six months of oral cholecalciferol supplementation. Clinical outcomes of SSc were not assessed.

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Materials And Methods

Study design and patients

This retrospective study included patients evaluated at the Department of Dermatology, Hôtel-Dieu de France Hospital, Beirut, Lebanon, between 2018 and 2022. We included patients who met the following criteria: (i) SSc diagnosis according to the American College of Rheumatology (ACR)/European Alliance of Associations for Rheumatology (EULAR) 2013 classification [1]; (ii) age between 30 and 65 years; (iii) subclinical serum 25(OH)D level <30 ng/mL after at least six months of oral cholecalciferol at a dose of 10,000 IU weekly; and (iv) administration of IM vitamin D during the study period.

Non-response to oral supplementation was defined as a serum 25(OH)D level <30 ng/mL after at least six months of oral cholecalciferol at a dose of 10,000 IU weekly. The same oral dose was used for all patients. Adherence to oral supplementation was assessed by questioning patients at each follow-up visit when vitamin D levels did not improve. The duration of oral supplementation ranged from six to eight months, depending on the timing of each patient's next scheduled consultation. Oral cholecalciferol was discontinued during the IM treatment period.

Data collection

The following data were retrieved from the patients' files: age; sex; SSc type; disease duration; modified Rodnan skin score; dose and duration of oral vitamin D3 supplementation; serum levels of 25(OH)D before, during, and after IM injection of vitamin D2; serum levels of calcium, phosphorus, and parathormone after IM injection; the posology of IM vitamin D2; and the report of any systemic side effects or reactions at the injection site. Of note, skin thickness was evaluated during the patient's examination using the modified Rodnan skin score, grading 17 areas (left and right fingers, dorsum of hands, forearms, upper arms, feet, legs, and thighs; and face, chest, and abdomen) from 0, where skin has normal thickness and mobility, to 4, where skin is thick and impossible to pinch. The higher the score, the greater the disease severity [20].

Study protocol

All patients received two injections of 300,000 IU of ergocalciferol (vitamin D2) into the anterior gluteus muscle at a 15-day interval (Stérogyl 15 "H"; 600,000 IU/1.5 mL; Desma Pharma, France). For each injection, a new ampoule was opened, and half of its volume (0.75 mL, corresponding to 300,000 IU) was drawn and injected immediately. The remaining volume was discarded after the injection and was not stored for later use. Each patient therefore received two separate ampoules.

Blood samples were drawn at three time points. The first sample was drawn three to five days before the first injection, after at least six months of oral supplementation, to measure the baseline serum 25(OH)D level.

The second sample was drawn two weeks after the first injection, before the second injection, to measure the serum 25(OH)D level. The third sample was drawn four weeks after the second injection, corresponding to six weeks after the first injection, to measure serum 25(OH)D, calcium, phosphorus, and parathormone levels. Serum calcium, phosphorus, and parathormone were not measured at baseline.

Safety was assessed at each follow-up visit, namely, at the time of the second injection (two weeks after the first injection) and four weeks after the second injection. At each visit, patients were actively questioned about systemic symptoms suggestive of hypercalcemia or vitamin D toxicity (nausea, vomiting, constipation, abdominal pain, polyuria, polydipsia, fatigue, and confusion) and about local reactions at the injection site (pain, swelling, erythema, or induration). These findings were documented in the patients' medical files. The total safety follow-up period was therefore four weeks after the second injection.

Laboratory measurements

According to the manufacturer's protocol, serum 25(OH)D was measured on peripheral blood samples by the Liaison® chemiluminescence immunoassay (DiaSorin Inc., Italy). All patients with levels below 30 ng/mL were considered to have a poor vitamin D status, without subdividing them into deficiency and insufficiency ranges. The reference ranges of our laboratory were 2.10-2.55 mmol/L for serum calcium, 0.81-1.45 mmol/L for serum phosphorus, and 6.3-36.8 pg/mL for parathormone.

Statistical analysis

Statistical analysis was performed using SPSS version 29.0.2 (IBM Corp., Armonk, NY, USA). Quantitative variables were described as mean ± standard deviation (SD), and qualitative variables as numbers. Serum 25(OH)D levels before the first IM injection, two weeks after the first IM injection, and four weeks after the second IM injection were compared using repeated-measures analysis of variance (ANOVA), as the same patients were measured at three time points. Normality was assessed with the Shapiro-Wilk test, and sphericity with Mauchly's test. When sphericity was violated, the Greenhouse-Geisser correction was applied. Pairwise comparisons were performed with the Bonferroni post hoc test and reported as mean differences with 95% confidence intervals (CIs). Effect sizes were reported as eta squared (η^2) for the overall model and Cohen's d for pairwise comparisons. Because of the small sample size, the Friedman test, followed by Wilcoxon signed-rank tests with Bonferroni correction, was used as a sensitivity analysis. P-values <0.05 were considered significant.

Ethical considerations and patient consent

This is a retrospective analysis of data collected during routine clinical care. The administration of IM ergocalciferol and the scheduled blood sampling were part of standard clinical practice and were not performed for research purposes. No research-specific procedure was performed, and all data were anonymized before analysis. All patients first gave written informed consent for treatment. When data were later collected retrospectively, a second written informed consent for publication was obtained from all 12 included patients. This consent covered the use of their anonymized clinical data in a retrospective research publication.

Results

Of 36 patients with SSc screened, 30 were between 30 and 65 years old. Overall, 20 patients had serum 25(OH)D levels <30 ng/mL, of whom 16 remained below this level after at least six months of oral supplementation, which invariably consisted of weekly 10,000 IU cholecalciferol capsules. Four of these 16 patients declined injectable therapy; therefore, 12 patients who received IM vitamin D were included (Figure *1*). All were women, with a mean age of 47.8 ± 8.4 years. Five had dcSSc, and seven had lcSSc. The mean disease duration was 17.9 ± 6.8 years.

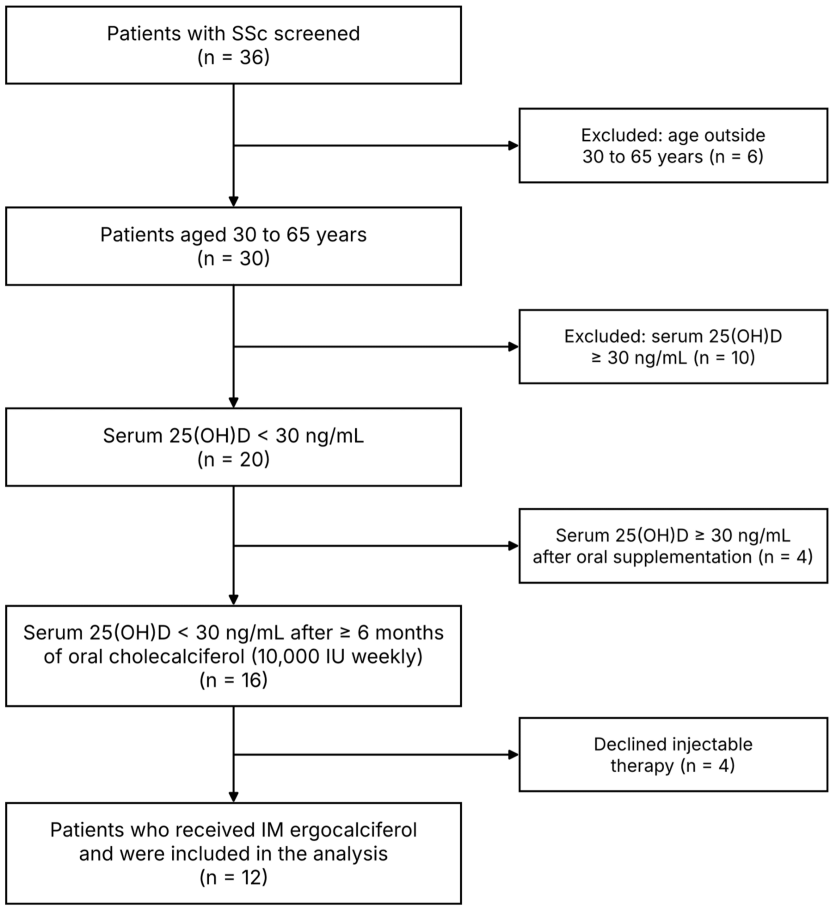


FIGURE 1: Flow diagram of patient selection.

SSc: systemic sclerosis; 25(OH)D: 25-hydroxyvitamin D; IM: intramuscular

Table *1* displays the patients' characteristics and the serum levels of 25(OH)D during treatment.

Patient	Age (years)	Sex	SSc type	Disease duration (years)	Modified Rodnan skin score	Previous cure with oral vitamin D3 (cholecalciferol)		Serum level of 25(OH)D (ng/mL)		
						Dose (IU/week)	Duration (months)	Before the first IM injection	2 weeks after the first IM injection	4 weeks after the second IM injection
1	50	F	Systemic	17	22	10.000	6	12	27	41
2	54	F	Localized	21	12	10.000	6	09	21	47
3	62	F	Systemic	30	28	10.000	6	14	23	34
4	41	F	Localized	10	8	10.000	6	12	30	47
5	49	F	Localized	18	10	10.000	6	21	29	36
6	60	F	Localized	25	13	10.000	6	10	21	45
7	40	F	Systemic	15	18	10.000	6	12	25	39
8	43	F	Systemic	17	20	10.000	6	11	21	31
9	51	F	Localized	28	15	10.000	6	6	15	29
10	35	F	Systemic	12	12	10.000	8	18	22	32
11	49	F	Localized	13	8	10.000	6	15	21	29
12	39	F	Localized	9	13	10.000	7	15	22	36
Mean ± SD	47.8 ± 8.4	-	-	17.9 ± 6.8	14.9 ± 6.0	-	6 ± 0.6	12.9 ± 4.0	23 ± 4.1	37.1 ± 6.6

TABLE 1: Patients' characteristics and serum levels of 25(OH)D before the first IM injection, two weeks after the first IM injection, and four weeks after the second IM injection of ergocalciferol.

SSc: systemic sclerosis; IM: intramuscular; F: female; SD: standard deviation

Serum 25(OH)D levels were normally distributed at the three time points (Shapiro-Wilk test, $p = 0.94$, 0.27, and 0.23, respectively). Mauchly's test showed that the assumption of sphericity was violated ($W = 0.33$, $\chi^2(2) = 11.16$, $p = 0.004$); therefore, the Greenhouse-Geisser correction was applied ($\varepsilon = 0.60$). The repeated-measures ANOVA showed a significant difference between serum 25(OH)D levels across the three time points ($F(1.20, 13.15) = 87.5$, $p < 0.001$, $\eta^2 = 0.81$). The mean increase was 10.2 ng/mL (95% CI = 7.0 to 13.4; $p < 0.001$; $d = 2.6$) between baseline and two weeks after the first injection, 24.3 ng/mL (95% CI = 17.3 to 31.2; $p < 0.001$; $d = 2.9$) between baseline and four weeks after the second injection, and 14.1 ng/mL (95% CI = 9.3 to 18.9; $p < 0.001$; $d = 2.4$) between two weeks after the first injection and four weeks after the second injection (Figure *2*). All observed effect sizes were large according to Cohen [21]. These results were confirmed by the Friedman test ($\chi^2(2) = 24.0$, $p < 0.001$), and all pairwise Wilcoxon signed-rank comparisons remained significant after Bonferroni correction ($p < 0.01$). Serum 25(OH)D increased in every patient at each time point, and 10 of the 12 patients reached a level of 30 ng/mL or higher four weeks after the second injection.

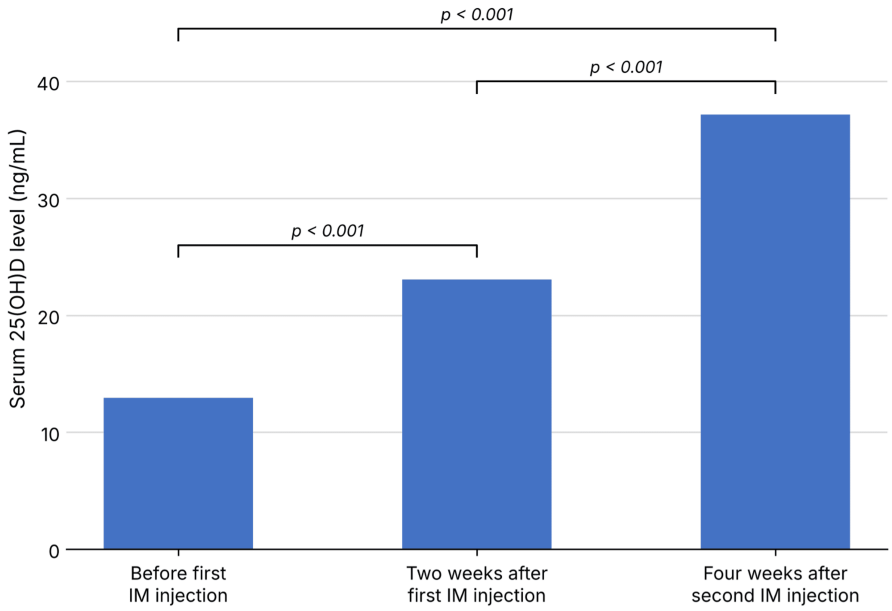


FIGURE 2: Mean serum 25(OH)D levels before the first ergocalciferol injection, two weeks after the first IM injection, and four weeks after the second IM injection, in the 12 patients.

Repeated-measures ANOVA with Greenhouse–Geisser correction and Bonferroni post hoc test; F(1.20, 13.15) = 87.5, p < 0.001.

ANOVA: analysis of variance; 25(OH)D: 25-hydroxyvitamin D; IM: intramuscular

Serum calcium, phosphorus, and parathormone levels, measured four weeks after the second injection, were within the reference ranges in all 12 patients. No adverse events, either systemic or at the injection site, were reported during the follow-up period.

Discussion

We report the changes in serum 25(OH)D levels and the tolerance of IM ergocalciferol in a small series of patients with SSc and a low vitamin D level refractory to oral supplementation. To our knowledge, this is the first report of IM vitamin D supplementation in patients with a connective tissue disease and a low vitamin D status refractory to oral supplementation. Such a route of administration was reported in vitamin D-deficient diabetic patients [22]. We first applied it to one patient in 2018; the biochemical response and the absence of adverse events in this patient led us to use the same treatment in other patients.

The most efficient replacement therapy has been the subject of debate for years [23]. If a choice can be made, recent guidance prefers vitamin D3 to vitamin D2 for oral supplementation [24]. Equal efficacy and safety were shown in daily, weekly, or monthly dosing regimens [25]. Compared to the IM route, higher and earlier peaks are observed with the oral route [26,27]. Compared to IM cholecalciferol, lower peaks were seen with IM ergocalciferol. For our patients, ergocalciferol was the only IM vitamin D available. The total dose was divided into two injections of 300,000 IU each, given 15 days apart, to reduce the risk of side effects. Each injection was prepared from a new ampoule.

IM vitamin D injections have shown promising results. In healthy Korean adults with vitamin D deficiency, a single injection of 200,000 IU of vitamin D3 raised, within 12 weeks, the 25(OH)D levels above 20 ng/mL and 30 ng/mL in around 90% and 50% of individuals, respectively [28]. Moreover, 10 adults with a variety of past and present medical conditions received 600,000 IU of IM vitamin D3; blood samples showed a peak of 25(OH)D at four weeks for most participants, and the levels were still remarkably higher than baseline at 24 weeks [18]. Similarly, Wylon et al. compared the pharmacokinetic evolution of a single 100,000 IU IM dose of cholecalciferol to that of an 84-day oral supplementation; serum 25(OH)D level peaked one week after the first dose of oral cholecalciferol and four weeks after the IM injection. Unlike the IM route, the fast rise with the oral route was transitory. The sustained levels following IM injection were explained by a delayed release along with the storage capacity of vitamin D in the adipose tissue [26]. Likewise, Gupta et al. compared the mean serum 25(OH)D levels in two healthy groups with vitamin D deficiency. Overall, 20 received 60,000 IU of cholecalciferol weekly for five weeks, and 20 others received a single IM injection of 300,000 IU of

cholecalciferol. At 12 weeks, levels were significantly higher in the second group (25.46 ± 1.37 vs. 16.66 ± 1.36 ng/mL; $p < 0.001$), showing a sustained increase from baseline [12].

The strengths of this study include its focus on a population with persistently low vitamin D despite oral supplementation, which has not been previously reported in SSc, the uniform treatment protocol applied to all patients, and the complete 25(OH)D data at all three time points.

The limitations of this study include a retrospective observation with a small sample size, a short follow-up, and restricted clinical data. Although the poor vitamin D status was subclinical, we thought, based on literature data on the possible interaction between low vitamin D and disease status, that rapidly raising the level would be theoretically beneficial. We have investigated the improvement of vitamin D levels only, without other scleroderma-related manifestations, which would have carried more weight in this study. Furthermore, the patients were not thoroughly investigated for the precise cause of low vitamin D, such as abnormal gastrointestinal absorption, renal disease, menopausal status, concomitant medication, or poor drug compliance.

In addition, the absence of a control group does not allow the observed increase to be attributed with certainty to IM ergocalciferol. A selection bias is also possible, as only patients who accepted injectable therapy were included, and four patients declined it. Although oral cholecalciferol was discontinued during IM therapy, adherence to prior oral supplementation was self-reported and not objectively verified, which may have contributed to the initial lack of response. Safety was assessed through adverse events reported during a short follow-up, and serum calcium, phosphorus, and parathormone were measured only after treatment, which did not allow comparison with baseline values. All patients were women treated at a single center, which limits the generalizability of our findings. Finally, higher doses of oral vitamin D are recommended in patients with malabsorption, such as after bariatric surgery; up to 6,000 IU of daily vitamin D3 is preferred to up to 50,000 IU of vitamin D2 three times weekly [29]. This approach was not tested in our patients, and the present data do not allow any comparison between IM and high-dose oral supplementation.

Conclusions

In this small retrospective series, IM ergocalciferol was associated with a short-term biochemical response in patients with SSc and a persistently low vitamin D status despite oral supplementation. Serum 25(OH)D increased significantly; 10 of the 12 patients reached a level of 30 ng/mL or higher, and no adverse events were documented during follow-up. Close monitoring of serum 25(OH)D may help determine the frequency of supplementation. This study provides descriptive data that may help generate hypotheses, which should be tested in prospective controlled studies with longer follow-up and assessment of SSc-related outcomes.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Boutros Soutou, Josiane Helou

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Critical review of the manuscript for important intellectual content: Boutros Soutou, Josiane Helou, Maroun Aoun, Farid Mallat, Rita Jabbour

Supervision: Boutros Soutou, Josiane Helou

Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

References

1. van den Hoogen F, Khanna D, Fransen J, et al.: 2013 classification criteria for systemic sclerosis: an American College of Rheumatology/European League against Rheumatism collaborative initiative. Arthritis Rheum. 2013, 65:2737-47. 10.1002/art.38098
2. Giuggioli D, Colaci M, Cassone G, et al.: Serum 25-OH vitamin D levels in systemic sclerosis: analysis of 140 patients and review of the literature. Clin Rheumatol. 2017, 36:583-90. 10.1007/s10067-016-3535-z
3. Diaconu AD, Ostafie I, Ceasovschih A, Șorodoc V, Lionte C, Ancuța C, Șorodoc L: Role of vitamin D in systemic sclerosis: a systematic literature review. J Immunol Res. 2021, 2021:9782994. 10.1155/2021/9782994
4. Kechichian E, Ezzedine K: Vitamin D and the skin: an update for dermatologists . Am J Clin Dermatol. 2018, 19:223-35. 10.1007/s40257-017-0323-8
5. Chen TC, Chimeh F, Lu Z, et al.: Factors that influence the cutaneous synthesis and dietary sources of vitamin D. Arch Biochem Biophys. 2007, 460:213-7. 10.1016/j.abb.2006.12.017
6. Tripkovic L, Lambert H, Hart K, et al.: Comparison of vitamin D2 and vitamin D3 supplementation in raising serum 25-hydroxyvitamin D status: a systematic review and meta-analysis. Am J Clin Nutr. 2012, 95:1357-64. 10.3945/ajcn.111.031070
7. Bikle DD: Vitamin D insufficiency/deficiency in gastrointestinal disorders. J Bone Miner Res. 2007, 22 Suppl 2:V50-4. 10.1359/jbmr.07s208
8. Gannagé-Yared MH, Chemali R, Sfeir C, Maalouf G, Halaby G: Dietary calcium and vitamin D intake in an adult Middle Eastern population: food sources and relation to lifestyle and PTH. Int J Vitam Nutr Res. 2005, 75:281-9. 10.1024/0300-9831.75.4.281
9. Lucas RM, Gorman S, Geldenhuys S, Hart PH: Vitamin D and immunity. F1000Prime Rep. 2014, 6:118. 10.12703/P6-118
10. Wharton B, Bishop N: Rickets. Lancet. 2003, 362:1389-400. 10.1016/S0140-6736(03)14636-3
11. Corrado A, Colia R, Mele A, Di Bello V, Trotta A, Neve A, Cantatore FP: Relationship between body mass composition, bone mineral density, skin fibrosis and 25(OH) vitamin D serum levels in systemic sclerosis. PLoS One. 2015, 10:e0137912. 10.1371/journal.pone.0137912
12. Gupta N, Farooqui KJ, Batra CM, Marwaha RK, Mithal A: Effect of oral versus intramuscular vitamin D replacement in apparently healthy adults with vitamin D deficiency. Indian J Endocrinol Metab. 2017, 21:131-6. 10.4103/2230-8210.196007
13. Marie I, Ducrotté P, Denis P, Menard JF, Levesque H: Small intestinal bacterial overgrowth in systemic sclerosis. Rheumatology (Oxford). 2009, 48:1314-9. 10.1093/rheumatology/kep226
14. Arnson Y, Amital H, Agmon-Levin N, et al.: Serum 25-OH vitamin D concentrations are linked with various clinical aspects in patients with systemic sclerosis: a retrospective cohort study and review of the literature. Autoimmun Rev. 2011, 10:490-4. 10.1016/j.autrev.2011.02.002
15. Trombetta AC, Smith V, Gotelli E, et al.: Vitamin D deficiency and clinical correlations in systemic sclerosis patients: a retrospective analysis for possible future developments. PLoS One. 2017, 12:e0179062. 10.1371/journal.pone.0179062
16. An L, Sun MH, Chen F, Li JR: Vitamin D levels in systemic sclerosis patients: a meta-analysis . Drug Des Devel Ther. 2017, 11:3119-25. 10.2147/DDDT.S144860
17. Artaza JN, Norris KC: Vitamin D reduces the expression of collagen and key profibrotic factors by inducing an antifibrotic phenotype in mesenchymal multipotent cells. J Endocrinol. 2009, 200:207-21. 10.1677/JOE-08-0241
18. Gorman S, Zafirau MZ, Lim EM, et al.: High-dose intramuscular vitamin D provides long-lasting moderate increases in serum 25-hydroxvitamin D levels and shorter-term changes in plasma calcium. J AOAC Int. 2017, 100:1337-44. 10.5740/jaoacint.17-0087
19. Zhang L, Duan Y, Zhang TP, Huang XL, Li BZ, Ye DQ, Wang J: Association between the serum level of vitamin D and systemic sclerosis in a Chinese population: a case control study. Int J Rheum Dis. 2017, 20:1002-8. 10.1111/1756-185X.12794
20. Clements P, Lachenbruch P, Siebold J, et al.: Inter and intraobserver variability of total skin thickness score (modified Rodnan TSS) in systemic sclerosis. J Rheumatol. 1995, 22:1281-5.
21. Cohen J: Statistical power analysis. Curr Dir Psychol Sci. 1992, 1:98-101. 10.1111/1467-8721.ep10768783
22. Dwivedi A, Gupta B, Tiwari S, Pratyush DD, Singh S, Singh SK: Parenteral vitamin D supplementation is superior to oral in vitamin D insufficient patients with type 2 diabetes mellitus. Diabetes Metab Syndr. 2017, 11 Suppl 1:S373-5. 10.1016/j.dsx.2017.03.019
23. Sanders KM, Seibel MJ: Therapy: new findings on vitamin D3 supplementation and falls - when more is perhaps not better. Nat Rev Endocrinol. 2016, 12:190-1. 10.1038/nrendo.2016.29
24. Camacho PM, Petak SM, Binkley N, et al.: American Association of Clinical Endocrinologists/American College of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis-2020 update. Endocr Pract. 2020, 26:1-46. 10.4158/GL-2020-0524SUPPL
25. Fassio A, Adami G, Rossini M, et al.: Pharmacokinetics of oral cholecalciferol in healthy subjects with vitamin D deficiency: a randomized open-label study. Nutrients. 2020, 12:1553. 10.3390/nu12061553
26. Wylon K, Drozdenko G, Krannich A, Heine G, Dölle S, Worm M: Pharmacokinetic evaluation of a single intramuscular high dose versus an oral long-term supplementation of cholecalciferol. PLoS One. 2017, 12:e0169620. 10.1371/journal.pone.0169620
27. Yu SB, Lee Y, Oh A, Yoo HW, Choi JH: Efficacy and safety of parenteral vitamin D therapy in infants and children with vitamin D deficiency caused by intestinal malabsorption. Ann Pediatr Endocrinol Metab. 2020, 25:112-7. 10.6065/apem.1938142.071
28. Choi HS, Chung YS, Choi YJ, Seo DH, Lim SK: Efficacy and safety of vitamin D(3) B.O.N intramuscular injection in Korean adults with vitamin D deficiency. Osteoporos Sarcopenia. 2016, 2:228-37. 10.1016/j.afos.2016.09.004
29. Mechanick JI, Apovian C, Brethauer S, et al.: Clinical Practice Guidelines for the Perioperative Nutrition, Metabolic, and Nonsurgical Support of Patients Undergoing Bariatric Procedures - 2019 update:

Cosponsored by American Association of Clinical Endocrinologists/American College of Endocrinology, the Obesity Society, American Society for Metabolic & Bariatric Surgery, Obesity Medicine Association, and American Society of Anesthesiologists - executive summary. Endocr Pract. 2019, 25:1346-59. 10.4158/GL-2019-0406