Volume 4 | Issue 3 | 2024

ISSN | 2771-019X

Journal of
Clinical & Medical Images
Case Reports

Open Access |Short review

Mini-review: Vitamin D toxicity: Diagnosis, management, and treatment

***Corresponding Author:** Afshan Davari*

Email: Afshan.davari@gmail.com

Amir Reza Bahadori[1]; Sara Mohammadian[2]; Afshan Davari[3]*

[1]Shiraz University of Medical Sciences, Shiraz, Fars, Iran.

[2]Medical Faculty, Tehran Branch, Islamic Azad University, Kazerun, Iran.

[3]Medical Colleges, Tehran University of Medical Sciences, Tehran, Iran.

Abstract

Vitamin D is a fat soluble vitamin which is mandatory for human health. Vitamin D absorption depends on intact ileum, pancreatic secretions and bile emulsification. Malabsorption syndromes with steatorrhea like cystic fibrosis and celiac disease, poor diet, insufficient sun exposure, Chronic Kidney Disease (CKD), and advanced liver disease can cause vitamin D deficiencies. Thus, many individuals used vitamin D supplement. Unmonitored and self-prescribed consumption of vitamin D supplements and granulomatous disease (1-alpha hydroxylase production by epithelioid macrophages) could lead to vitamin D toxicity. Therefore, suitable management of that is literally important for physicians.

Received: Apr 16, 2024

Accepted: Jun 03, 2024

Published Online: Jun 10, 2024

Cite this article: Bahadori AR, Mohammadian S, Davari A. Mini-review: Vitamin D toxicity: Diagnosis, management, and treatment. J Clin Med Images Case Rep. 2024; 4(3): 1690.

Introduction

Vitamin D, a fat-soluble vitamin, is synthesized in the skin through exposure to ultraviolet B-light radiation [1]. Factors such as limited sun exposure and dietary deficiencies contribute to low vitamin D status among many individuals, across all age groups and geographic locations [2,3], and due to its association with many diseases, supplementing with vitamin D to restore body reserves is highly important [4]. Yet, concurrently, we are observing an increase in reports of toxicity associated with this vitamin as well [5]. Possible reasons for this incident include the over-the-counter status of the drug in most countries [6,7], incorrect dosage prescription [8], companies' errors in producing supplements with vitamin D higher than the reported limit in their product [9], alongside fortification of food with vitamin D [5]. Symptoms of vitamin D toxicity are diverse and include neuropsychiatric, cardiovascular, gastrointestinal, and renal manifestations [10] that typically occur with vitamin D levels exceeding 375 nmol/l [11]. This toxicity related to vitamin D involves heightened absorption of calcium from the intestines, resulting in hypercalcemia. Additionally, an excess of vitamin D can stimulate bone resorption, leading to further elevation of calcium levels [12]. Herein, the objective of this study is to examine the clinical symptoms of vitamin D toxicity and strategies for managing it through a review of case reports of vitamin D toxicity.

Vitamin D toxicity

Vitamin D is a fat soluble prohormone that is mandatory for human health. it has two main forms, D_2 and D_3. D_2 (ergocalciferol) is obtained from the ingestion of plants, fungi and yeast while D_3 (ergocalciferol) is obtained from exposure of skin to the sun (UVB), ingestion of fish, milk and plants [13,14]. This fat-soluble vitamin that is transported to the liver via chylomicrons. Both forms are converted to 25-OH D3 (storage form) by the enzyme 25-hydroxylase in the liver and to the active form $1,25\text{-}(OH)_2D_3$ (calcitriol) by the enzyme 1 alpha-hydroxylase in PCT cells of the kidney [15-18].

Renal 1-hydroxylase, which determines the conversion rate of vitamin D into its active form, is regulated by PTH, FGF23, calcium and phosphate levels. Hypocalcemia, hypophosphatemia and elevated PTH stimulate vitamin D activation while FGF23 inhibits it [17-19].

Furthermore, vitamin D plays a significant role in bone mineralization, muscle function, cell differentiation, malignancy prevention, immune system, and so on. Since covid-19 pandemic many articles illustrated that vitamin d can enhance immune system and plays an important role among viruses. Therefore, many physicians recommend individuals to use supplement that contain vitamin D [20-25].

The principal function of vitamin D is to increase intestinal absorption of calcium (through an active transcellular pathway) and phosphate [17]. Also, by maintaining calcium balance, Vitamin D facilitates mineral deposition in the bone matrix. Also, the principal function of vitamin D is to increase intestinal absorption of calcium (through an active transcellular pathway) and phosphate. As well, by maintaining calcium balance, Vitamin D facilitates mineral deposition in the bone matrix, thus vitamin D is literally mandatory for human skeletal firmness and osteoporosis prevention [20,26].

On the hand, many studies depicted that vitamin D could prevent many gene mutations in different types of malignancy such as lung, and breast, thus a great number of oncologists recommend individuals to use vitamin D [27,28]. In addition, vitamin D could reduce prevalence of Major Depressive Disorder (MDD) among society, especially in women mental health [29,30], also J.E. Lavigne et al. illustrated that sufficient serum level of vitamin d would reduce level of attempt of suicide [30]. Therefore, due to recommendation of many physicians, power of media, and a huge number of advertisements many individuals use vitamin D supplements [3,31,32].

Furthermore, a great number of pharmaceuticals companies produced different kinds of supplement which contain different amount of vitamin D, such as; calcium – D tablets, pearl vitamin D 50,000, daily tablet of vitamin D 1000, and so on [33]. As a result of that, a huge number of people use vitamin D supplements regularly without any monitoring or prescription [6,34]. Thus, chronic vitamin D toxicity was reported in several case reports articles [31,32,35]. And also, acute vitamin D toxicity which mainly occurred owing to attempt of suicide or miss use of ampule vitamin D 300,000 is literally rare [36].

Previous studies illustrated that vitamin D levels for adults should be between 30 pg/ml and 60 pg/ml, vitamin D level between 21 pg/ml and 29 pg/ml categorized as an insufficient level, less than 20 pg/ml called deficient, and the serum level above of 150 pg/ml is categorized as a toxic level. Also, adult individuals regularly allowed to use 600 IU/day vitamin D [31,37-39].

Patients who come with vitamin d toxicity might initially present nausea, vomiting, sensorium, confusion, polyuria, dehydration, and headache [32,40] after that in clinical finding might have presented other sever complications. It could depict Acute Kidney Injury (AKI), pancreatitis, cardiac arrhythmia, electrolyte imbalance, and hypercalcemia [31,40-42].

Diagnosis of vitamin D toxicity is based on the clinical manifestation of hypercalcemia along with high serum level of calcium, diminished serum level of PTH, and exceed of 150 pg/ml serum level of vitamin D [3,31,40,41]. As well, when a patient with high serum level of vitamin D presented in emergency room several laboratory data such as a Complete Blood Count (CBC), Blood Urea Nitrogen (BUN), creatinine, Para-Thyroid Hormone (PTH), calcium, phosphor, sodium, magnesium, urine analysis, amylase, lipase, LDH, creatine kinase (CPK), Vessels Blood Gas (VBG), vitamin D level must monitor regularly [18,31,40,43,44]. Also, electrocardiogram (ECG) for evaluation of QT interval, ST segment conditions, and cardiac arrhythmias is literary mandatory [45]. Moreover, for role outing brain tumors, brain MRI highly suggested [3,46].

Vitamin D toxicity is very important and we should proceed treatment in rapidly. Many studies suggested that hydration is quite important in these patients and 3 lit/ day hydration with normal saline serum were recommended [8,44,47]. Also, K. Feghali et al. in their study mention that for electrolyte imbalance and AKI condition in hypervitaminosis D, dialysis could be a suitable treatment [6]. Furthermore, hypercalcemia which induced by vitamin D is life threatening and its treatment is vital [48,49]. Many studies mention that calcitonin, diuretic, bisphosphonate, glucocorticoids, Denosumab, and Zoledronic Acid would be a suitable treatment for hypercalcemia which induced by hypervitaminosis D [39,47]. In addition, in the case of high serum level of creatinine, instead of bisphosphonates, denosuman could be a great option for reducing serum calcium level [39,47,50]. Furthermore, after patient treatment, they should use calcium and vitamin D restricted diet [48,51]. Also, the patients should avoid expose to sun light or use of vitamin D – calcium supplements [31,51].

Conclusion

Vitamin D supplement ought to use under prescription of physicians with serum level monitoring, thus it could prevent hypervitaminosis D and their life threatening future conditions.

References

1. Saponaro F, Saba A, Zucchi R. An update on vitamin D metabolism. International journal of molecular sciences. 2020; 21(18): 6573.
2. Amrein K, Scherkl M, Hoffmann M, Neuwersch-Sommeregger S, Köstenberger M, Tmava Berisha A, et al. Vitamin D deficiency 2.0: an update on the current status worldwide. European journal of clinical nutrition. 2020; 74(11): 1498-513.
3. Giustina A, Bouillon R, Binkley N, Sempos C, Adler RA, Bollerslev J, et al. Controversies in vitamin D: a statement from the third international conference. Journal of Bone and Mineral Research Plus. 2020; 4(12): e10417.
4. Reid IR. What diseases are causally linked to vitamin D deficiency? Archives of Disease in Childhood. 2016; 101(2): 185-9.
5. Taylor PN, Davies JS. A review of the growing risk of vitamin D toxicity from inappropriate practice. British journal of clinical pharmacology. 2018; 84(6): 1121-7.
6. Feghali K, Papamarkakis K, Clark J, Malhotra N, Stoddart L, Osakwe I. Vitamin D toxicity managed with peritoneal dialysis. Case Reports in Endocrinology. 2021; 2021.
7. Wani M, Wani I, Banday K, Ashraf M. The other side of vitamin D therapy: a case series of acute kidney injury due to malpractice-related vitamin D intoxication. Clinical nephrology. 2016; 86(5): 236.
8. Misgar RA, Sahu D, Bhat MH, Wani AI, Bashir MI. Vitamin D toxicity: a prospective study from a tertiary care centre in Kashmir Valley. Indian journal of endocrinology and metabolism. 2019;

23(3): 363-6.

9. Kara C, Gunindi F, Ustyol A, Aydin M. Vitamin D intoxication due to an erroneously manufactured dietary supplement in seven children. Pediatrics. 2014; 133(1): e240-e4.

10. Marcinowska-Suchowierska E, Kupisz-Urbańska M, Łukaszkiewicz J, Płudowski P, Jones G. Vitamin D toxicity–a clinical perspective. Frontiers in endocrinology. 2018; 9: 357018.

11. Zittermann A, Prokop S, F Gummert J, Borgermann J. Safety issues of vitamin D supplementation. Anti-Cancer Agents in Medicinal Chemistry (Formerly Current Medicinal Chemistry-Anti-Cancer Agents). 2013; 13(1): 4-10.

12. Vogiatzi MG, Jacobson-Dickman E, DeBoer MD, Drugs, Society TCoTPE. Vitamin D supplementation and risk of toxicity in pediatrics: a review of current literature. The Journal of Clinical Endocrinology & Metabolism. 2014; 99(4): 1132-41.

13. Raymond-Lezman JR, Riskin SI. Benefits and risks of sun exposure to maintain adequate vitamin D levels. Cureus. 2023; 15(5).

14. Rebelos E, Tentolouris N, Jude E. The role of vitamin D in health and disease: a narrative review on the mechanisms linking vitamin d with disease and the effects of supplementation. Drugs. 2023; 83(8): 665-85.

15. Bikle DD. Vitamin D: Newer concepts of its metabolism and function at the basic and clinical level. Journal of the Endocrine Society. 2020; 4(2): bvz038.

16. El-Sharkawy A, Malki A. Vitamin D signaling in inflammation and cancer: Molecular mechanisms and therapeutic implications. Molecules. 2020; 25(14): 3219.

17. Haussler MR, Whitfield GK, Kaneko I, Haussler CA, Hsieh D, Hsieh J-C, et al. Molecular mechanisms of vitamin D action. Calcified tissue international. 2013; 92: 77-98.

18. Bikle DD. Vitamin D metabolism, mechanism of action, and clinical applications. Chemistry & biology. 2014; 21(3): 319-29.

19. Al-Ishaq RK, Kubatka P, Brozmanova M, Gazdikova K, Caprnda M, Büsselberg D. Health implication of vitamin D on the cardiovascular and the renal system. Archives of physiology and biochemistry. 2021; 127(3): 195-209.

20. Kazemian E, Pourali A, Sedaghat F, Karimi M, Basirat V, Sajadi Hezaveh Z, et al. Effect of supplemental vitamin D3 on bone mineral density: a systematic review and meta-analysis. Nutrition reviews. 2023; 81(5): 511-30.

21. Rizwan M, Cheng K, Gang Y, Hou Y, Wang C. Immunomodulatory Effects of Vitamin D and Zinc on Viral Infection. Biological Trace Element Research. 2024: 1-17.

22. Moukayed M. A narrative review on the potential role of vitamin D3 in the prevention, protection, and disease mitigation of acute and long COVID-19. Current nutrition reports. 2023; 12(2): 215-23.

23. Mobarak S, Salasi M, Hormati A, Khodadadi J, Ziaee M, Abedi F, et al. Evaluation of the effect of sofosbuvir and daclatasvir in hospitalized COVID-19 patients: a randomized double-blind clinical trial (DISCOVER). Journal of Antimicrobial Chemotherapy. 2022; 77(3): 758-66.

24. Tabatabaii SA, Taghizadeh-Behbahani A, Khanbabaee G, Alibakhshi M, Bahadori AR, Farahbakhsh N. Patient-Reported Outcomes and Healthcare Practices: A Retrospective Analysis of Cystic Fibrosis Management During the COVID-19 Pandemic. Archives of Pediatric Infectious Diseases. 2024(In Press).

25. Fallahi MJ, Lankarani KB, Honarvar B, Jalalpour AH, Shamsnia SA, Peiravi M, et al. Pulmonary Manifestations and their Determinants in Long Covid Patients: A Retrospective Cohort Study after One Year Follow-Up, From Iran. 2023.

26. Christakos S, Li S, DeLa Cruz J, Verlinden L, Carmeliet G. Vitamin D and bone. Bone Regulators and Osteoporosis Therapy. 2020: 47-63.

27. Miao D, Goltzman D. Mechanisms of action of vitamin D in delaying aging and preventing disease by inhibiting oxidative stress. Vitamins and hormones. 121: Elsevier; 2023. p. 293-318.

28. Markowska A, Antoszczak M, Kojs Z, Bednarek W, Markowska J, Huczyński A. Role of vitamin D3 in selected malignant neoplasms. Nutrition. 2020; 79: 110964.

29. Maharlouei N, Kasraei H, Shaygani F, Bahadori AR, Khonyagar S, Reyhani Z, et al. The 8th International Conference on Women's Health; Women's Mental Health. Women's Health Bulletin. 2020; 7(1): 58-61.

30. Lavigne JE, Gibbons JB. The association between vitamin D serum levels, supplementation, and suicide attempts and intentional self-harm. Plos one. 2023; 18(2): e0279166.

31. Bhat JR, Geelani SA, Khan AA, Roshan R, Rathod SG. Vitamin D toxicity due to self-prescription: A case report. Journal of Family Medicine and Primary Care. 2022; 11(4): 1561-3.

32. Galior K, Grebe S, Singh R. Development of vitamin D toxicity from overcorrection of vitamin D deficiency: a review of case reports. Nutrients. 2018; 10(8): 953.

33. Bano A, Abrar S, Brilli E, Tarantino G, Bugti AA, Fabbrini M, et al. A comparative absorption study of sucrosomial® orodispersible vitamin D3 supplementation vs. a reference chewable tablet and soft gel capsule vitamin D3 in improving circulatory 25 (OH) D levels in healthy adults with vitamin D deficiency—Results from a prospective randomized clinical trial. Frontiers in Nutrition. 2023; 10.

34. Billington EO, Burt LA, Rose MS, Davison EM, Gaudet S, Kan M, et al. Safety of high-dose vitamin D supplementation: secondary analysis of a randomized controlled trial. The Journal of Clinical Endocrinology & Metabolism. 2020; 105(4): 1261-73.

35. Silva C, Fung AW, Masson V, Assen K, Ward V, McKenzie J, et al. Vitamin D toxicity from an unusual and unexpected source: a report of 2 cases. Hormone Research in Paediatrics. 2023; 96(3): 332-40.

36. Asif A, Farooq N. Vitamin D toxicity. StatPearls [Internet]: StatPearls Publishing; 2023.

37. Giustina A, Bouillon R, Dawson-Hughes B, Ebeling PR, Lazaretti-Castro M, Lips P, et al. Vitamin D in the older population: a consensus statement. Endocrine. 2023; 79(1): 31-44.

38. Sarma A. Vitamin D toxicity presenting with altered sensorium and hypercalcaemia. Indian Journal of Anaesthesia. 2020; 64(10): 909-11.

39. Motlaghzadeh Y, Bilezikian JP, Sellmeyer DE. Hypercalcemia due to vitamin D toxicity. Feldman and Pike's Vitamin D. 2024: 625-50.

40. Lee JP, Tansey M, Jetton JG, Krasowski MD. Vitamin D toxicity: a 16-year retrospective study at an academic medical center. Laboratory medicine. 2018; 49(2): 123-9.

41. Muneer S, Siddiqui I, Majid H, Zehra N, Jafri L, Khan AH. Practices of vitamin D supplementation leading to vitamin D toxicity: Experience from a Low-Middle Income Country. Annals of Medicine and Surgery. 2022; 73: 103227.

42. Batman A, Saygili ES, Yildiz D, Sen EC, Erol RS, Canat MM, et al. Risk of hypercalcemia in patients with very high serum 25-OH vitamin D levels. International journal of clinical practice. 2021; 75(7): e14181.

43. Zhang H, Jiang Y, Shi N, Lu Y-Q. Serum vitamin D levels and acute kidney injury: a systemic review and meta-analysis. Scientific Reports. 2022; 12(1): 20365.

44. Lim K, Thadhani R. Vitamin D toxicity. Brazilian Journal of Nephrology. 2020; 42: 238-44.

45. Condoleo V, Pelaia C, Armentaro G, Severini G, Clausi E, Cassano V, et al. Role of vitamin D in cardiovascular diseases. Endocrines. 2021; 2(4): 417-26.

46. Norlin M. Effects of vitamin D in the nervous system: Special focus on interaction with steroid hormone signalling and a possible role in the treatment of brain cancer. Journal of neuroendocrinology. 2020; 32(1): e12799.

47. MM Basso S, Lumachi F, Nascimben F, Luisetto G, Camozzi V. Treatment of acute hypercalcemia. Medicinal Chemistry. 2012; 8(4): 564-8.

48. Sohn J-T. Toxic Dose of Vitamin D-Induced Hypercalcemia. American Journal of Therapeutics. 2022; 29(3): e368-e9.

49. Schlingmann KP. Vitamin D–dependent Hypercalcemia. Endocrinology and Metabolism Clinics. 2021; 50(4): 729-42.

50. Walker MD, Shane E. Hypercalcemia: a review. JAMA. 2022; 328(16): 1624-36.

51. Ramasamy I. Vitamin D metabolism and guidelines for vitamin D supplementation. The Clinical Biochemist Reviews. 2020; 41(3): 103.