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PERSPECTIVE

Disease prevention strategies using vitamin D

Sunil J. Wimalawansa

Abstract: During the past 15 years, the biological and scientific knowledge of the pleiotropic properties of vitamin D and its metabolites has expanded beyond the well-understood effects of vitamin D in calcium homeostasis and skeletal health. Many, recently published peer-reviewed articles clinical and epidemiological studies support multiple extra-skeletal beneficial effects of having adequate serum 25 hydroxy vitamin D [25(OH)D] concentrations. However, this knowledge has not translated into clinical practice. Consequently, thousands of people are developing (and existing disease are getting worse) vitamin D deficiency release and complications, otherwise could have been prevented.

Keywords: disease prevention, vitamin D

1 Introduction

Vitamin D deficiency is associated with a wide variety of diseases and disorders, including metabolic ailments, several types of cancer, autoimmune diseases and infections, and increased overall mortality. Ironically, preventing such diseases costs less than 1% of the costs of managing these disorders. Whilst several countries have now come up with locally applicable guidelines, the majority are not. Even among the scientific societies of those countries who published their recommendations and vitamin D guidelines, only a handful of their governments and health departments have accepted as policies and implemented. Thus, the populous are continuing to suffer unnecessarily.

2 Vitamin D deficiency

Vitamin D deficiency is confirmed by having serum 25(OH)D concentration of less than 20 ng/mL (50 nmol/L). Levels between 21 and 30 ng/mL are considered "insufficient" from a physiological point of view, that are required for positively modulating extraskeletal tissues and preventing associated diseases. For the population, the goal is to maintain the serum 25(OH)D concentration above 30 ng/mL (75 nmol/L), ideally between 30 and 60 ng/mL in a longer-term basis.

Based on more than 30,000 recently published vitamin D-related peer-reviewed articles, data strongly suggest an average person to maintain serum 25(OH)D concentrations greater than 30 ng/mL and for high risk groups and vulnerable people to have a higher concentration of more than 40 ng/mL. The latter groups include those with comorbidities, such as obesity, gastrointestinal abnormalities, metabolic disturbances/disorders, and autoimmune disorders. Having such levels is recognized to reduce the risks of contracting diseases and severity of such preventable disorders.

3 Basic facts about vitamin D

Humans are supposed to obtain the majority of requirements from the exposure to ultraviolet -B (UVB) rays following exposer to the sunlight. The remainder will come from dietary intake (and now a day) and from vitamin D or multivitamin supplements. Except for sub-exposed mushrooms that provided vitamin D_2 and oily fish such as mackerel and salmon that provided D_3, the vitamin D coming from the diet is little. The amount and the rate of synthesis of previtamin D in the dermal tissue is based on a number of factors. These include, exposure to sunrays between 10 AM and 3 PM in summer like environments, direct exposure of the adequate surface area of the skin to UVB rays, season of the year (winter vs. summer), closeness to the equator, the lack of air pollution that allows UVB rays reaching the earth surface, *etc*.

4 Groups of people benefits from vitamin D supplements

Because of vitamin D and its precursors are present in in small amounts in foods, it is not easy to attain vi-

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*Correspondence to: Sunil J. Wimalawansa, Cardiometabolic & Endocrine Institute, North Brunswick, N.J., USA; Email: suniljw@hotmail.com

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tamin D sufficiency exclusively by the diets[1]. Despite this, the vast majority of people for various reasons, are not receiving sufficient expose to sunlight for adequate synthesis of vitamin D *in vivo*. For them, the benefits of vitamin D can obtain by consuming appropriate oral doses of supplementary vitamin D.

For those who are receiving inadequate sun exposure, especially during the winter months and for those who live in northern and southern latitudes, and those who have condition that needs higher amounts of vitamin D or have enhance vitamin D catabolism, will be benefitted on taking vitamin D supplements. Especially for those who are unable to attain sufficient exposure of their skin surfaces to sunlight du to any reason could have higher risks to develop hypovitaminosis D and its consequences[2]. This is also applicable to those who are avoiding sunlight, for cultural or personal reasons, the excessive us of sunscreens or over clothing, the elderly, and those who confine predominantly to indoors, as those in tropical regions due to hot climate. Such people also will be benefitted from vitamin D supplementation[3].

5 How and who will benefit from food fortification programs?

To overcome not only vitamin D deficiency but also micronutrient deficiencies, it is necessary for each country (or ethnic group) to have guidelines and implement them, especially targeted, food fortification programs that are highly cost-effective. Such programs consist of providing one or more of the deficient nutrients and essential micronutrients, such as vitamin D, vitamin A, iron, iodine, or calcium, and targeting specific population groups or the entire country. Target groups can be ethnic or certain cultural groups; those with certain disorders, such as obesity, metabolic syndrome, cancer, or autoimmune disorders[4]; pregnant and lactating women; infants; or the elderly.

However, merely establishing supplementation guidelines or government recognition of the problem, as is currently happening in many countries, is clearly insufficient. For example, food fortification policies do not benefit the population or have the intended effect unless they are implemented. Parallel actions are needed to effect a change in behavior (*e.g.*, balanced diet and increasing physical activity and healthy behaviour) and raise the population's serum 25(OH)D concentrations to a predetermined beneficial level, at least above 30 ng/mL. This is also applicable to the other micronutrients mentioned.

Some individuals cannot rely on orally administered vitamin D (those with gastrointestinal absorption abnormalities) or even sun exposure (*e.g.*, those with disorders such as lupus, or who take medication that increases sensitivity to the sun's rays, or have insufficient generation of vitamin D in the skin) to achieve target vitamin D status. Thus, guidelines and recommendations must also encompass modes of safe sun exposure, food fortification strategies for communities, and supplementation guidelines for those who with special needs, as well as, when appropriate, the measuring of serum 25(OH)D concentration[5–8].

6 The need for vitamin supplements

For people living in the west and some affluent people living in other parts of the world consumed balanced diets and getting some exposure to sunlight; For them, it is a waste of material and money and unlikely needing vitamin or herbal supplementation. Whereas, those who truly need nutrient supplements to maintain their health, live in poor communities, and cannot afford to purchase nutrient supplements or not aware of the need will be benefitted from targeted food fortification programs.

The dose of oral vitamin D_3 supplements required to rectify the vitamin D deficiency is depend in part on associated diseases or the conditions (cancer and cardiovascular diseases), conditions to be prevented (*e.g.*, autoimmunity), ethnicity, darkness of the skin, general exposure to sunlight, the regular use of sunscreen, concomitant use of medications that enhance catabolism of vitamin D, malabsorption syndromes, and having comorbidities such as obesity or metabolic syndrome[9–13].

People who are not regularly receiving sun exposure or have exposure of less than 15 minutes a day and the elderly would benefit from regular supplementation with 2,000 IU/day. Others with higher risks, are going to need doses in excess of 2,000 IU, of between 4,000 and 6,000 IU/day or even more. Others having difficulty of fat absorption, such as those with gastrointestinal disorders, malabsorption syndrome may even need significantly higher daily doses of vitamin D.

7 Specific serum 25(OH)D levels are required to overcome certain diseases

Different thresholds of serum 25(OH)D concentration are needed for different body tissues to reduce health risks or improve physiologic functions. For example, the musculoskeletal system can be maintained with serum 25(OH)D concentration of approximately 20 ng/mL[2, 14]; however, which is markedly inadequate for optimal functions of other body systems.

For example, prevention of cancer, cardiovascular disease, autoimmune disease, or bacterial infections, higher

serum 25(OH)D concentrations are needed. Thus, to prevent the mentioned diseases and to reduce their severities and complications, and reduce all-cause mortality, longer-term maintenance of serum 25(OH)D concentrations higher than 30 ng/mL are needed, preferably 40 to 60 ng/mL. Therefore, relying on a serum 25(OH)D concentration of 20 ng/mL as suggested by a few organizations only based on skeletal benefits, as the minimum necessary concentration for human health is a flawed concept.

As mentioned, serum 25(OH)D concentrations need to be kept between 40 and 60 ng/mL to achieve the pleiotropic benefits of vitamin D[2, 14]. Examples of such include, reducing multiple health risks and thus the incidence of disorders, such as obesity and diabetes[15], multiple sclerosis[16], autoimmune disorders[17], rheumatoid arthritis[18], osteoporosis[19, 20], and certain types of cancer[21, 22], as well as a reduction in all-cause mortality[23]. Having excess vitamin D is very rare occurrence, as discussed in the next section. For example, vitamin D deficiency [25(OH)D concentration, less than <20 ng/mL] increases insulin resistance and reduces insulin secretion from beta cells in the pancreas[24, 25].

8 Hypervitaminosis D and hypercalcemic syndromes

The most common cause of hypercalcemia in the persons with primary or tertiary hyperparathyroidism. Hypercalcemia caused by malignancy is the second most common cause and occurs secondary to inappropriate secretion of parathyroid hormone-related peptide (PTHrP)[26]. While the diagnosed and undiagnosed primary hyperparathyroidism is the commonest cause of hypercalcemia found in the community. However, in hospital-based patients, cancer-associated hypercalcemia is the most common[27]. All other causes of hypercalcemic conditions are rare, including the once due to excess vitamin D.

Rare causes of hypercalcemia include granulomatous disorders, milk-alkaline syndrome, and Williams' syndrome. Chronic hypercalcemia, irrespective of the cause, can lead to irreversible calcification of soft tissues, cardiac arrythmia, *etc.* If suspected of having overdoses of vitamin D related hypercalcemia, immediate and temporary stoppage of vitamin D and calcium supplements is necessary, together with implementation of supportive therapies such as maintenance of good hydration are generally sufficient[2, 28]. However, a very few patients might need temporary renal dialysis or plasma exchange to remove excess ionized calcium (Ca^{2+}) from the blood to prevent complications associated with high serum ionized calcium.

9 Diagnosis of hypervitaminosis D

It is noteworthy that the diagnosis of hypervitaminosis D should be made only when the serum 25(OH)D concentration exceeds 150 ng/mL (375 nmol/L) and is associated with raised blood Ca^{2+} and associated hypercalcemic clinical syndrome, including hypercalciuria and hyperphosphatemia, in the absence of hyperparathyroidism or cancer. The mere demonstration of an elevated serum 25(OH)D concentration is not equivalent with having hypervitaminosis D; it is essential to have cl the clinical syndrome associated with raised Ca^{2+}[1].

In a laboratory-based study, taking serum 25(OH)D concentrations of 64 ng/mL (160 nmol/L) as the cutoff point (which is grossly too low), a prevalence was less than 2% was reported[29]. In this study, only 15 subjects out of 25,567 (0.05%) had an elevated serum 25(OH)D level that was associated with hypercalcemia. More importantly, none of these patients had clinically significant hypercalcemia or hypercalcemic syndrome. Thus, in this real-world data series, of 25,567 subjects examined, none had clinically relevant hypervitaminosis D; it is that rare.

10 Hypervitaminosis D and vitamin D toxicity

Vitamin D toxicity is rare and occurs only after ingestion of large doses of vitamin D, such as in excess of 20,000 IU/day for prolonged periods, usually taken in error. It generally occurs with serum 25(OH)D concentrations that exceed 150 ng/mL[30] and usually caused by mistakenly ingesting high doses of vitamin D for a prolonged period. Therefore, hypervitaminosis D should not be diagnosed solely on the basis of an elevated 25(OH)D level.

In the unlikely (rare) event of vitamin D toxicity, a patient can present with clinical signs and symptoms of "hypercalcemia," such as nausea, dehydration, and constipation, and eye irritation, and symptoms of hypercalciuria, such as excessive thirst, polyuria, and chronic kidney stones. These patients should be handed as described above.

11 The reliability of some recently published, large vitamin D clinical studies is questionable

Despite large number clinical publications supporting multi-system benefits of having normal serum 25(OH)D

concentrations, recently reported handful of mostly industry-funded large randomized clinical studies on vitamin D failed to report beneficia effects following vitamin D supplementation[24, 31]. Despite these studies cost millions of dollars (United States taxpayers' funds delivered through the national institutes of health and industry-funded) and recruited thousands of participants, all had more than one major study designed faults[32] that diminish the value of their outcomes. In addition, faulty-study design related misleading clinical outcomes and interpretations published by these studies have caused significant confusion of the field of vitamin D, harming millions of people globally.

Irrespective of the size of the study (*i.e.*, number of study participants) or the amount of money spent in a clinical trial (immaterial of spending several millions), failure to adhere to basic scientific principles and statistical methodologies (*i.e.*, clinical study design errors) have introduced confusing and contradictory clinical outcomes results; these were made worse by biased and contradictory interpretations by study authors pursuing same data set[31]. Thus, it is not surprised that such studies publicized, erroneous results and misleading conclusions.

Unreliable clinical outcomes from these large randomized clinical studies with inherent study design errors are continuing to generalize, despite their unreliability[33]. Therefore, all physicians and the general public must be aware of such inaccurate and misleading conclusions based on faulty clinical studies and the pharmaceutical bias in such highly publicized studies.

"Prevention is the cure." Therefore, no sensible person should wait and delay, or not take preventative steps, such as a healthier lifestyle, adequate sleep, or a balanced diet to proactively mitigate diseases. Not taking such actions is unwise, waste of money, and adversely affects the health.

12 Discussion

Serum 25(OH)D concentrations of less than 20 ng/mL indicate hypovitaminosis D and are unphysiological and unhealthy. Serum levels of between 21 and 30 ng/mL indicate vitamin D insufficiency, which is inadequate to maintain a healthier life and likely to increase susceptibility to disease. The goal is to keep the population and individuals' serum 25(OH)D concentration more than 30 ng/mL, in a longer-term basis. It is advisable that each country or at least groups of countries to have ethnic and culturally specific, vitamin D guidelines that also encompass safe sun exposure, cost-effective food fortification strategies, and vitamin D supplementation recommendations, including for especially for those with special needs. The goal is to keep the population healthy and prevent diseases.

Conflicts of interest

The author declares no conflict of interests. He received no funding for this work or assistance in professional writing for this review.

References

[1] Wimalawansa SJ. Vitamin D: Everything You Need to Know. ISBN: 978-955-9098-94-2, Homagama, Sri Lanka: Karunaratne & Sons, 2012. https://doi.org/10.4038/sjdem.v2i2.4776

[2] Wimalawansa SJ. Non-musculoskeletal benefits of vitamin D. The Journal of Steroid Biochemistry and Molecular Biology, 2018, **175**: 60-81. https://doi.org/10.1016/j.jsbmb.2016.09.016

[3] Wahl DA, Cooper C, Ebeling PR, *et al*. A global representation of vitamin D status in healthy populations. Archives of Osteoporosis, 2012, **7**(1): 155-172. https://doi.org/10.1007/s11657-012-0093-0

[4] Moukayed M and Grant WB. The roles of UVB and vitamin D in reducing risk of cancer incidence and mortality: A review of the epidemiology, clinical trials, and mechanisms. Reviews in Endocrine and Metabolic Disorders, 2017, **18**(2): 167-182. https://doi.org/10.1007/s11154-017-9415-2

[5] Pludowski P, Holick MF, Grant WB, *et al*. Vitamin D supplementation guidelines. The Journal of Steroid Biochemistry and Molecular Biology, **2017**: S0960076017300316. https://doi.org/10.1016/j.jsbmb.2017.01.021

[6] Grant WB, Wimalawansa SJ, Holick MF, *et al*. Emphasizing the health benefits of vitamin D for those with neurodevelopmental disorders and intellectual disabilities. Nutrients, 2015, **7**(3): 1538-1564. https://doi.org/10.3390/nu7031538

[7] Wimalawansa SJ. Vitamin D adequacy and improvements of comorbidities in persons with intellectual developmental disabilities. Journal of Childhood & Developmental Disorders, 2016, **2**(3): 22-33. https://doi.org/10.4172/2472-1786.100030

[8] Haq A, Wimalawansa SJ, Pludowski P, *et al*. Clinical practice guidelines for vitamin D in the United Arab Emirates. The Journal of Steroid Biochemistry and Molecular Biology, 2018, **175**: 4-11. https://doi.org/10.1016/j.jsbmb.2016.09.021

[9] Mason C, Xiao L, Imayama I, *et al*. Vitamin D3 supplementation during weight loss: a double-blind randomized controlled trial. American Journal of Clinical Nutrition, 2014, **99**(5): 1015-1025. https://doi.org/10.3945/ajcn.113.073734

[10] Dhaliwal R, Mikhail M, Feuerman M, *et al*. The vitamin d dose response in obesity. Endocrine Practice, 2014, **20**(12): 1258-1264. https://doi.org/10.4158/EP13518.OR

[11] Knutsen KV, Madar AA, Lagerlov P, *et al*. Does vitamin D improve muscle strength in adults? A randomized, double-blind, placebo-controlled trial among ethnic minorities in Norway. The Journal of Clinical Endocrinology & Metabolism, 2014, **99**(1): 194-202.
https://doi.org/10.1210/jc.2013-2647

[12] Chaney A, Heckman MG, Diehl NN, *et al*. Effectiveness and Outcomes of Current Practice in Treating Vitamin D Deficiency in Patients Listed for Liver Transplantation. Endocrine Practice, 2015, **21**(aop): 1-26.
https://doi.org/10.4158/EP14416.OR

[13] Farahati J, Nagarajah J, Gilman E, *et al*. Ethnicity, Clothing Style, and Body Mass Index are Significant Predictors of Vitamin D Insufficiency in Germany. Endocrine Practice, 2015, **21**(2): 122-127.
https://doi.org/10.4158/EP14320.OR

[14] Nagarjunakonda S, Amalakanti S, Uppala V, *et al*. High Prevalence of Vitamin D Deficiency in Chronic Non-specific Musculoskeletal Pain. Musculoskeletal Care, 2017, **15**(2): 163-166.
https://doi.org/10.1002/msc.1154

[15] Gupta AK, Brashear MM and Johnson WD. Prediabetes and prehypertension in healthy adults are associated with low vitamin D levels. Diabetes Care, 2011, **34**(3): 658-660.
https://doi.org/10.2337/dc10-1829

[16] Munger KL, Zhang SM, O'Reilly E, *et al*. Vitamin D intake and incidence of multiple sclerosis. Neurology, 2004, **62**(1): 60-65.
https://doi.org/10.1212/01.WNL.0000101723.79681.38

[17] Ritterhouse LL, Crowe SR, Niewold TB, *et al*. Vitamin D deficiency is associated with an increased autoimmune response in healthy individuals and in patients with systemic lupus erythematosus. Annals of the Rheumatic Diseases, 2011, **70**(9): 1569-1574.
https://doi.org/10.1136/ard.2010.148494

[18] Merlino LA, Curtis J, Mikuls TR, *et al*. Vitamin D intake is inversely associated with rheumatoid arthritis: results from the Iowa Women's Health Study. Arthritis & Rheumatology, 2004, **50**(1): 72-77.
https://doi.org/10.1002/art.11434

[19] Feskanich D, Willett WC and Colditz GA. Calcium, vitamin D, milk consumption, and hip fractures: a prospective study among postmenopausal women. American Journal of Clinical Nutrition, 2003, **77**(2): 504-511.
https://doi.org/10.1093/ajcn/77.2.504

[20] Meier C, Woitge HW, Witte K, *et al*. Supplementation with oral vitamin D3 and calcium during winter prevents seasonal bone loss: a randomized controlled open-label prospective trial. Journal of Bone and Mineral Research, 2004, **19**(8): 1221-1230.
https://doi.org/10.1359/JBMR.040511

[21] McCullough ML, Robertson AS, Rodriguez C, et al. Calcium, vitamin D, dairy products, and risk of colorectal cancer in the Cancer Prevention Study II Nutrition Cohort (United States). Cancer Causes Control, 2003, **14**(1): 1-12.
https://doi.org/10.1023/A:1022591007673

[22] Tretli S, Schwartz GG, Torjesen PA, *et al*. Serum levels of 25-hydroxyvitamin D and survival in Norwegian patients with cancer of breast, colon, lung, and lymphoma: a population-based study. Cancer Causes Control, 2012, **23**(2): 363-370.
https://doi.org/10.1007/s10552-011-9885-6

[23] Garland CF, Kim JJ, Mohr SB, et al. Meta-analysis of all-cause mortality according to serum 25-hydroxyvitamin D. American Journal of Public Health, 2014, **104**(8): e43-50.
https://doi.org/10.2105/AJPH.2014.302034

[24] Grober U and Holick MF. Diabetes prevention: Vitamin D supplementation may not provide any protection if there is no evidence of deficiency! Nutrients, 2019, **11**(11): 2651.
https://doi.org/10.3390/nu11112651

[25] Wimalawansa SJ. Associations of vitamin D with insulin resistance, obesity, type 2 diabetes, and metabolic syndrome. The Journal of Steroid Biochemistry and Molecular Biology, 2018, **175**: 177-189.
https://doi.org/10.1016/j.jsbmb.2016.09.017

[26] Wimalawansa SJ. Significance of plasma PTH-rp in patients with hypercalcemia of malignancy treated with bisphosphonate. Cancer, 1994, **73**(8): 2223-2230.
https://doi.org/10.1002/1097-0142(19940415)73:8⟨2223::AID-CNCR2820730831⟩3.0.CO;2-C

[27] Cooper C, Li H and Wimalawansa SJ. Cancer-associated hypercalcemia and parathyroid hormone-related peptide: a new peptide with diverse roles. Reg. Peptide Letters, 1997, **7**: 39-42.

[28] Wimalawansa SJ, Razzaque DMS and Al-Daghri NM. Calcium and Vitamin D in Human Health: Hype or Real? The Journal of Steroid Biochemistry and Molecular Biology, 2017, **180**: 4-14.
https://doi.org/10.1016/j.jsbmb.2017.12.009

[29] Perez-Barrios C, Hernandez-Alvarez E, Blanco-Navarro I, *et al*. Prevalence of hypercalcemia related to hypervitaminosis D in clinical practice. Clinical Nutrition, 2016, **35**(6): 1354-1358.
https://doi.org/10.1016/j.clnu.2016.02.017

[30] Jones G. Pharmacokinetics of vitamin D toxicity. American Journal of Clinical Nutrition, 2008, **88**(2): 582-586.
https://doi.org/10.1093/ajcn/88.2.582S

[31] Scragg R, Waayer D, Stewart A, *et al*. The Vitamin D Assessment (ViDA) Study: design of a randomized controlled trial of vitamin D supplementation for the prevention of cardiovascular disease, acute respiratory infection, falls and non-vertebral fractures. Journal of Steroid Biochemistry & Molecular Biology, 2016, **164**: 318-325.
https://doi.org/10.1016/j.jsbmb.2015.09.010

[32] Manson JAE, Cook NR, Lee IM, *et al*. Vitamin D Supplements and Prevention of Cancer and Cardiovascular Disease. New England Journal of Medicine, 2019, **380**(1): 33-44.
https://doi.org/10.1056/NEJMoa1809944

[33] Wimalawansa SJ. IOM recommendations vs. vitamin D guidelines applicable to the rest of the world[C]//5th International Conference on Vitamin D. **2017**: 9.