

Vitamin D's Potential Function in the Treatment of Patients Suffering From Chronic Pain

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ABSTRACT:

Chronic pain is extremely common in developed countries, and people who suffer from illnesses associated with chronic pain frequently have lower levels of vitamin D than those who do not. The use of vitamin D supplements as a potential alternative treatment for patients suffering from chronic pain has been the subject of research. The purpose of this study is to offer an overview of the scientific data and provide some recommendations regarding the use of vitamin D in clinical practise with patients who suffer from chronic pain.

Keywords: chronic pain, supplementation, treatment, vitamin D.

INTRODUCTION:

Based on the findings of a literature review that we conducted using the search terms chronic pain, musculoskeletal pain, vitamin D, vitamin D deficiency, treatment, supplementation, trials, and epidemiology, we investigated the subject of whether or not vitamin D has a role in chronic pain. Manual searches, including hand searching of major journals and references from recognised papers, were conducted in addition to searches conducted in the databases PubMed, Google Scholar, and Cochrane. This allowed for the identification of relevant articles. All of the searches were carried out all the way through the month of June 2020.

Chronic pain

According to one definition, chronic pain is "pain that persists beyond the typical time for tissue repair, which is approximately three months. [1] Chronic pain is extremely widespread due to the fact that a variety of different disorders, such as back pain, migraines, and osteoarthritis, often come under this overarching group. Estimates of prevalence from developed countries are somewhere around 20%, but these estimates range from 12–44% in the overall adult population. Women and older persons are most frequently affected by this condition.[2–5] Because the aetiology of chronic pain is so complicated, treating the

condition typically needs a combination of pharmacological and nonpharmacological methods. 6,7 In addition, it is of the utmost importance to develop effective treatments for the management or elimination of chronic pain, as chronic pain is the primary cause of disability⁸ and imposes significant financial burdens on society. [9–11]

The significance of vitamin D in one's diet

Vitamin D can be obtained by exposure to sunlight, food consumption, as well as nutritional supplements.^{P12]} Calcidiol, also known as 25-hydroxyvitamin D (25(OH)D), is produced by the liver and then distributed throughout the body via the bloodstream. Once there, it is converted into the hormone calcitriol, also known as 1,25-dihydroxyvitamin D (1,25(OH)₂D), by other tissues in the body as well as by the kidney. [13,14] It is critical to have adequate levels of vitamin D circulating in the bloodstream in order to absorb other essential vitamins and minerals, particularly calcium, which plays an important part in ensuring that bones and muscles remain in good health.[15] Vitamin D is of utmost significance to the body's physiological functioning since it plays a role in the reduction of inflammation, the regulation of cell growth, and the exertion of an influence on the immunological and neuromuscular systems.

Vitamin D levels that are insufficient or deficient have been linked to a wide variety of negative health outcomes, such as cardiovascular disease, hypertension/blood pressure, type-II diabetes, cancer (e.g. colorectal, breast, prostate), autoimmune diseases (e.g. multiple sclerosis), inflammation, mood disorders/depression, cognitive function, and Alzheimer's disease, as well as all-cause mortality,^{16–20}. Despite the fact that the results of observational studies are largely ^{19,20} According to research conducted in North America, Europe, and Australasia ^{21–22}, the high prevalence estimates of vitamin D deficiency range from 20–50%. This is consequently cause for great public health concern.

The prevalence of vitamin D deficiency among those who suffer from chronic pain

Evidence of the prevalence of vitamin D deficiency [serum 25(OH)D levels 50 nmol/l] in rheumatic and chronic pain populations mainly comes from smaller clinic-based studies. Estimates of the deficiency in the general population have come from large population studies.

In a population of rheumatology outpatients in Switzerland, researchers discovered that hypovitaminosis D had a prevalence of 86%.²⁸ Estimates range from as high as 93% among those who suffer from persistent, nonspecific pain ²⁹ to as low as 26% in a group of chronic pain patients who are receiving treatment at a pain clinic. ³⁰ Deficiency among Musculoskeletal (MSK) conditions associated with chronic pain was as follows: inflammatory joint diseases/connective tissue diseases, 69%; soft tissue rheumatism, 77%; osteoarthritis, 62%; nonspecific musculoskeletal back pain, 75%; and osteoporosis, 71%. Among consecutive new patients in a rheumatology clinic, the prevalence of vitamin D

deficiency was 70% [serum 25(OH)D 21 An analysis of 25(OH)D levels in rheumatology outpatients revealed that the levels of 25(OH)D in rheumatology patients were lower when compared with osteoporotic/osteopenia patients, with the overall lowest values finding in patients suffering from inflammatory arthritis and fibromyalgia/chronic pain. [12]

There is a direct relationship between vitamin D deficiency and persistent discomfort. A lack of vitamin D has also been connected to people experiencing chronic discomfort. The results of a cross-sectional study indicate that men with chronic widespread pain (CWP) and 'other pain' had a greater likelihood of having lower levels of 25(OH)D when compared with those who did not experience pain. This was the case even after age and lifestyle factors were taken into account. [13] In the Concord Health and Ageing in Men Project, the researchers adjusted for a number of confounding factors, but the relationships that had been seen between lower serum 25D concentrations and chronic pain did not persist. [14] Only among women in the British birth cohort of 1958 was a cross-sectional link between vitamin D and CWP identified. This association persisted even after the models were adjusted for all possible factors. [15] In a primary care setting in Sweden, a case-control research did not uncover any evidence to support the hypothesis of a relationship between vitamin D levels and chronic low back pain. 36 In Brazil, there was found to be no statistically significant difference in the mean levels of serum 25(OH)D between patients diagnosed with fibromyalgia and age- and gender-matched healthy controls. 17

Men who had low levels of 25(OH)D (15.6 ng/ml) had approximately two times greater odds of getting CWP than those who had levels 36.3 ng/ml. However, this link did not stay significant after accounting for body mass index (BMI) or depression levels.

fundamental mechanisms that underlie the connection between vitamin D and persistent discomfort

A lack of vitamin D in the body may be a factor that exacerbates a condition known as chronic pain. According to the findings of certain studies, vitamin D may play an essential part in a number of cellular processes that are thought to provide protection against the onset and modulation of chronic pain. Vitamin D has been shown to, among other things, act as a neuroactive steroid, interfere with the production and function of neurotrophins, influence the activity of prostaglandins, effect inflammatory pathways, and inhibit nitric oxide synthase and T-helper cells. These are only some of the findings. [19, 20] There is not yet a conclusive knowledge of how vitamin D or vitamin D supplementation precisely operates to prevent or relieve chronic pain, despite the growing volume of research that has been conducted on the topic.

The use of vitamin D supplementation as a therapy for persistent pain

Recent systematic reviews and meta-analyses have compiled information from clinical studies that used vitamin D as a therapeutic intervention for the treatment of chronic pain. A

Cochrane review published in 2015 identified ten papers that met their criteria of being double-blind trials of using vitamin D supplementation as a treatment for chronic painful illnesses. These studies evaluated the effectiveness of vitamin D supplementation with active comparators or placebo. 21 The included studies were found to have poor methodological quality, and they were also found to be heterogeneous, meaning that they varied in terms of painful chronic conditions, the amount of vitamin D that was administered, and the outcome measures that were evaluated. 21 There is a moderate level of evidence that vitamin D supplementation was not helpful for treating chronic nonspecific musculoskeletal pain patients 22, and there is inconclusive evidence of a definitive positive effect of vitamin D on chronic pain states. These findings have also been reached by the findings of other systematic reviews. [13]

The current standard of care regarding 25(OH) D levels and the therapy and maintenance doses of vitamin D in patients with chronic pain

Guidelines for vitamin D levels as well as the treatment and maintenance doses of dietary vitamin D supplements have not been defined particularly for a population of people who have chronic pain. The standard of care should therefore be based on the guidelines that have been developed for people who are healthy as well as those who are at risk for vitamin D deficiency.

It is advised that serum 25(OH)D be used as the biomarker to evaluate vitamin D exposure.[14] Vitamin D deficiency is indicated in healthy people by levels of 25(OH)D concentration that are below 30 nmol/l (less than 12 ng/ml), whereas vitamin D insufficiency is indicated by levels of 25(OH)D concentration that range from 30 to 50 nmol/l (12 to 20 ng/ml). Concentrations of serum 25(OH)D that are greater than 50 nmol/l (>20 ng/ml) are regarded as adequate amounts of vitamin D; on the other hand, concentrations that are greater than >125 nmol/l (50 ng/ml) may be thought to be detrimental. [14]

Some experts recommend more conservative cutoff points for individuals who are at risk for vitamin D deficiency. These individuals include people who have malabsorption syndromes (such as inflammatory bowel disease or Crohn's disease), are taking certain medications (such as anticonvulsant medications or steroids), older adults who have a history of falls or fractures, and obese adults with a BMI of more than 30 kg/m².

15 25(OH) D concentrations of 52.5–72.5 nmol/l (21–29 ng/ml) indicate insufficiency, whereas 25(OH) D concentrations of >75 nmol/l (>30 ng/ml) indicate sufficient vitamin D levels. For these individuals, levels of 25(OH)D concentration 50 nmol/l (20 ng/ml) may be considered to indicate vitamin D deficiency. 15

Individuals at risk for vitamin D deficiency are recommended to take at least 1500–2000 IU/d of supplemental vitamin D in order to raise the 25(OH)D serum concentration above 30 ng/ml. The recommended dietary intakes of vitamin D are 600 IU/d for adults aged 19–70

years and 800 IU/d for adults aged 70+ years. 15 The Scientific Advisory Committee on Nutrition is in the process of reevaluating these recommended intakes for the United Kingdom at this time. It is suggested that those at risk for vitamin D deficiency who are obese or using drugs (such as anticonvulsants or steroids) consume at least two to three times the amount of vitamin D that is recommended for their age group, with an acceptable upper consumption level of 10,000 IU per day. [15]

Recommendations for the practical application of vitamin D supplementation in the management of vitamin D deficiency in patients with chronic pain

People who suffer from chronic pain may have an increased risk of vitamin D insufficiency, particularly if they are obese, likely to have restricted sun exposure, inactive for long periods of time, consume diets low in vitamin D-rich foods, or have malabsorption concerns. Anticonvulsants and steroids, both of which are often used to treat chronic pain and rheumatic disorders (such as fibromyalgia), can lower the body's levels of vitamin D. 15, 21 In addition, having a concurrent condition that affects the liver or the kidneys can make it more difficult for the body to metabolise vitamin D. 15,21 There is no evidence that vitamin D supplementation is an effective treatment for chronic pain; however, there are no contraindications for the use of vitamin D supplementation among patients who suffer from chronic pain. This is because vitamin D is associated with a low risk of harm to one's health in general, is generally well accepted, and is relatively inexpensive.[21,22]When an individual's levels of vitamin D are either insufficient or deficient according to additional risk factors (such as the medications they are currently taking, their level of obesity, or their amount of time spent in the sun), an appropriate vitamin D supplement should be advised.

CONCLUSION:

In conclusion, there is no question that vitamin D performs a very important physiological function in the human body. Although links between insufficient and deficient levels of vitamin D and poorer health outcomes have been proven, the connection between vitamin D and chronic pain is not as well recognised. [Citation needed] [Citation needed] In point of fact, there is no single mechanism that can definitively explain how vitamin D affects the development of chronic pain. The prevalence of vitamin D insufficiency in people suffering from chronic pain suggests that supplementation may give a wide range of positive health effects. Vitamin D supplementation, on the other hand, cannot be considered an effective independent treatment for chronic pain at this time because there is not yet enough evidence to support such a claim.

REFERENCES:

1. International Association for the Study of Pain, Subcommittee on Taxonomy. Classification of chronic pain. In: Merskey H and Bogduk N (eds) Descriptions of Chronic Pain syndromes and definitions of pain terms, 1986, pp. S1–S226.

2. Blyth FM, March LM, Brnabic AJM, et al. Chronic pain in Australia: a prevalence study. *Pain* 2001; 89: 127–134.
3. McBeth J and Jones K. Epidemiology of chronic musculoskeletal pain. *Best Pract Res Clin Rheumatol* 2007; 21: 403–425.
4. Breivik H, Collett B, Ventafridda V, et al. Survey of chronic pain in Europe: prevalence, impact on daily live, and treatment. *Eur J Pain* 2006; 10: 287–333.
5. Fayaz A, Croft P, Langford RM, et al. Prevalence of chronic pain in the UK: a systematic review and meta-analysis of population studies. *BMJ Open* 2016; 6: e010364.
6. Cunningham NR and Kashikar-Zuck S. Nonpharmacological treatment of pain in rheumatic diseases and other musculoskeletal pain conditions. *Curr Rheumatol Rep* 2013; 15: 1–8.
7. Uhl RL, Roberts TT, Papaliadis DN, et al. Management of chronic musculoskeletal pain. *J Am Acad Orthop Surg* 2014; 22: 101–110.
8. Vos T, Flaxman AD, Naqhav M, et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012; 380: 2163–2196.
9. Van Hecke O, Torrance N and Smith BH. Chronic pain epidemiology - where do lifestyle factors fit in? *Br J Pain* 2013; 7: 209–217.
10. Smith BH and Torrance N. Management of chronic pain in primary care. *Curr Opin Support Palliat Care* 2011; 5: 137–142.
11. Rasu RS, Vouthy K, Crawl AN, et al. Cost of Pain medication to treat adult patients with nonmalignant chronic pain in the United States. *J Manag Care Pharm* 2014; 20: 921–928.
12. Pearce SH and Cheetham TD. Diagnosis and management of vitamin D deficiency. *BMJ* 2010; 340: b5664.
13. Holick MF. Vitamin D deficiency. *N Engl J Med* 2007; 357: 266–281.
14. IOM: Institute of Medicine, Food and Nutrition Board. Dietary reference intakes for calcium and vitamin D. Washington, DC: National Academy Press, 2010.
15. Holick MF, Binkley NC, Bischoff-Ferrari HA, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab* 2011; 96: 1911–1930.

16. Gagnon C, Lu ZX, Magliano DJ, et al. Serum 25-hydroxyvitamin D, calcium intake, and risk of type 2 diabetes after 5 years: results from a national, population-based prospective study (the Australian Diabetes, Obesity and Lifestyle study). *Diabetes Care* 2011; 34: 1133–1138.
17. Ju SY, Lee YJ and Jeong SN. Serum 25-hydroxyvitamin D levels and the risk of depression: a systematic review and metaanalysis. *J Nutr Health Aging* 2013; 17: 447–455.
18. Annweiler C, Dursun E, Feron F, et al. Vitamin D and cognition in older adults: updated international recommendations. *J Intl Med* 2014; 277: 45–57.
19. Newberry SJ, Chung M, Shekelle PG, et al. Vitamin D and calcium: a systematic review of health outcomes (update). Evidence Report/Technology Assessment No. 217. (Prepared by the Southern California Evidence-based Practice Center under Contract No. 290–2012–00006-I). AHRQ Publication No. 14-E004-EF. Rockville, MD: Agency for Healthcare Research and Quality, 2014.
20. Autier P, Boniol M, Pizot C, et al. Vitamin D status and ill health: a systematic review. *Lancet Diabetes Endocrinol* 2014; 2: 76–89.
21. Looker A, Dawson-Hughes B, Calvo M, et al. Serum 25-hydroxyvitamin D status of adolescents and adults in two seasonal subpopulations from NHANES III. *Bone* 2002; 30: 771–777.
22. Rockell J, Skeaff C, Williams S, et al. Serum 25-hydroxyvitamin D concentrations of New Zealanders aged 15 years and older. *Osteoporos Int* 2006; 17: 1382–1389.