

Vitamin D and Pain

THE EMERGING CONNECTION

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Feeling pain is a natural response of the body to protect further damage to tissues and reduce injury and to allow healing to occur. Pain is an alarm system designed for self-preservation. However, when pain becomes chronic or abnormal, this complex and potentially life-saving function can be disabling, stressful, and incapacitating. Pain can turn into nature's curse, affecting sleep, work, education, social life, and everyday tasks.^{1,2}

Due to the complexity and prevalence of chronic pain, researchers are investigating causes and non-pharmacological treatments, with a pronounced scientific interest over the last decade on the effects of vitamin D deficiency and the use of supplementation.¹ This article explores the emerging relationship between vitamin D and chronic pain.

The burden of chronic pain

Chronic pain is the leading cause of disability and disease burden globally.¹ Abnormal or chronic pain can be specific to a body part or area, be widespread, or vague, and can be due to tissue injury, an underlying health condition, or have an unknown (idiopathic) cause. Regardless of the aetiology, when pain lasts beyond three months it is classified as chronic.³

Most cases are estimated to be idiopathic, with around 20% of chronic pain sufferers finding little to no benefit from currently available analgesics.^{1,3}

Recent emerging research shows that improving vitamin D status has analgesic effects and can reduce chronic pain.¹

Globally between 8% to 60% of people suffer from chronic pain, depending on the population.⁴ In Australia, almost 20% (1 in 5) of Australians aged 45 and over are reported as having chronic pain.²



KEY HIGHLIGHTS

- Pain that persists beyond 3 months is chronic pain
- Research supports the improvement of vitamin D status to reduce chronic pain, with deficiency thought to be associated with increased non-specific chronic pain
- Vitamin D receptors (VDRs) are present in numerous cell types across the body including those involved in pain signalling
- Vitamin D may influence pain sensitivity and provide analgesic effects during inflammation and after injury through the modulation of inflammatory cytokines and prostaglandins

Vitamin D deficiency and chronic pain link

Vitamin D deficiency is a global public health imperative. Even in sunny Australia, approximately 20% of adults (over 25 years), 32% of young adults (18-24 years) and 17% of adolescents (12-17 years) are deficient in vitamin D.⁵ Deficiency may also increase by more than 50% in women during winter and spring and for those living in southern Australian areas.⁶

Many researchers suggest that a deficiency in this neuroactive steroidal vitamin may be the reason for non-specific chronic pain.^{3,7} Although research is conflicting, there are strong correlations between vitamin D levels and musculoskeletal pain, such as lower back pain, with a significant association in diabetic peripheral neuropathy. Additionally, research shows an association between improved vitamin D status and reductions in chronic pain for participants with insufficient or deficient 25(OH)D serum (vitamin D) levels.¹



Table 1. Chronic Pain conditions that may benefit from vitamin D supplementation

The following chronic pain conditions had analgesic benefits when given vitamin D supplementation, or are associated with low vitamin D levels, according to clinical trials:

Back pain in those overweight/obese ¹
Carpal tunnel syndrome ⁸
Chronic widespread pain ⁴
Diabetic neuropathic pain ¹
Fibromyalgia ⁹
Growing pains ^{1,8}
Headache/migraine ¹⁰
Lower back pain ^{1,7}
Menstrual pain in dysmenorrhoea ¹
Musculoskeletal pain (specific and non-specific) ^{1,3}
Neuropathic pain ¹
Osteoarthritis ¹
Postherpetic neuralgia ⁷
Rheumatoid arthritis ⁷

Potential mechanisms of action

Pain is a highly complex process involving multiple systems of the body. The potential mechanisms by which vitamin D exerts an analgesic effect are not fully understood. However, it is known that its role extends beyond bone metabolism functions, with vitamin D receptors (VDRs) found in numerous cell types across the body including those involved in pain signalling:

- skin (pain signal transduction)
- neurons (signal conduction)
- spinal cord (transmission/modulation)
- brain (pain perception).¹

Through its interaction with VDRs, vitamin D appears to mediate gene expression for pain-genes and encode for proteins involved in pain signalling, including nerve growth factor (NGF), glial-derived neurotrophic factor (GDNF), epidermal growth factor receptor (EGFR) and opioid receptors.¹ By modulating inflammatory cytokines and prostaglandins, vitamin D may also influence pain sensitivity and provide analgesic effects during inflammation and after injury.^{1,12}

Additionally, vitamin D may play a significant role in visceral pain. Short-chain fatty acids (SCFAs) and neurotransmitters produced by the gut microbiota are involved in pain signalling and inflammatory processes. Vitamin D may indirectly affect visceral pain through its action on gut microbiota modulation.¹

RESEARCH INSIGHT: Vitamin D and mindfulness have synergistic benefits on chronic pain

In a clinical trial published in 2021, researchers evaluated vitamin D supplementation and mindfulness separately and together to measure their effects on pain severity, pain-related disability, and quality of life (QoL) in diabetic neuropathy. They ran 12 mindfulness sessions, with a focus on relaxation skills, meditation, and emotional awareness. Vitamin D supplementation was dosed at 4000 IU daily for 12 weeks. This randomised study found that although independently vitamin D and mindfulness were similarly beneficial, the effects on pain and QoL were greatest with combined therapies.¹²

Vitamin D clinical prescribing for pain management

Clinical research shows vitamin D status has a potential role in patient case analysis for many debilitating conditions. However, research for chronic pain amelioration features varying dosages, making it difficult to ascertain a prescriptive protocol. One guide is that most studies involved a vitamin D3 treatment duration of 12 weeks. As there is no standardised vitamin D dose or duration, and research has shown decreases in pain correspond to increases in vitamin D levels, it is reasonable to suggest that serum 25(OH)D levels can be used as a guide for individual pain management.^{1,6,8}

Living with chronic pain every day can be devastating to a person's quality of life.^{1,2} Although the exact mechanisms are not fully understood, research supports the appropriateness of vitamin D testing, with adequate supplementation if serum levels are below optimal or in deficiency ranges.¹ This simple strategy may be a life-changing adjunct treatment protocol for those with chronic pain.

Table 1. Vitamin D testing and prescribing considerations for adults

VITAMIN D STATUS	THERAPEUTIC STRATEGY
All vitamin D dosing recommendations should be based on serum 25(OH)D (vitamin D) levels, while considering the individual's age, body weight, sun exposure, dietary habits and lifestyle ¹³	
Serum 25(OH)D deficiency levels reference	<50 nmol/L – requires immediate supplementation ^{13,14}
Serum 25(OH)D suboptimal levels	50 to 75 nmol/L ¹³
Optimal serum 25 (OH)D levels	75 to 125 nmol/L ¹³
High vitamin D supply	125 to 250 nmol/L; for levels >185 nmol/L cease supplementation and monitor serum 25(OH) D levels ¹³
Vitamin D dose to prevent deficiency	<ul style="list-style-type: none"> at least 600 IU–800 IU colecalciferol (vitamin D3) per day.⁶ Without adequate sun exposure and/or adequate dietary intake, this may increase to 1000 IU–2000 IU per day. Adults >75 years may require 2000 IU – 4000 IU per day¹³
Vitamin D dose for serum levels between 50 to 75 nmol/L	800 IU–2000 IU colecalciferol per day ¹⁵
Vitamin D dose for mild deficiency	25-50 nmol/L: 2000 IU–4000 IU colecalciferol per day ^{13,15,16}
Vitamin D dose for moderate to severe deficiency (<25/30 nmol/L)	3000 IU–5000 IU colecalciferol for at least 6-12 weeks (retest after 3 months) followed by 1000 IU–2000 IU for 6–12 weeks ^{6,16,17}
Maintenance of 75 nmol 25(OH)D	requires approximately 2000 IU–3000 IU vitamin D daily from all sources (food, UV light, supplements) ¹⁵

KEY DOSAGE CONSIDERATIONS

Each 1000 IU of colecalciferol can raise serum 25(OH)D levels by approximately 25 nmol/L over a few weeks¹⁶

Serum 25(OH)D levels take up to 2-5 months (3-5 if dosing monthly) to reach a steady state, so it is recommended to retest only after 3 months^{6,13}

Colecalciferol is the first-line treatment and preventative for vitamin D deficiency. In cases where vitamin D supplementation as colecalciferol does not improve serum 25 (OH)D levels, calcifediol may be recommended.¹³

SUMMARY

Chronic pain significantly impacts quality of life and global health. Research indicates a strong link between vitamin D deficiency and chronic pain, suggesting that supplementation could alleviate symptoms.

Clinical studies show potential benefits of vitamin D in managing various pain conditions. Optimal vitamin D levels are crucial for effective pain management, emphasizing personalized supplementation strategies.



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