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The Effect of Vitamin D Supplement as Analgesic in Low Back Pain Patients: A Literature Review

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ABSTRACT
Background: Low back pain (LBP) is a musculoskeletal disease characterized by severe pain in the lower back that originates in the spine's muscles, nerves, and other organs. Adults experience 50-80 percent of the symptoms, and it is the leading cause of disability when compared to other diseases. One of the risk factors for pain is vitamin D deficiency. Vitamin D aids in the maintenance of musculoskeletal health in patients with paraspinal muscle weakness and atrophy, such as those with LBP. Because of the controversy surrounding this topic, this research will specifically examine the effect of giving vitamin D as an analgesic in patients with low back pain. This is expected to serve as a model for the treatment of low back pain in Indonesia. **Purpose:** This research aims to specifically examine the effect of giving vitamin D as an analgesic to patients suffering from low back pain. **Method:** This research used the literature review method. Data were taken from articles published in Google Scholar, PubMed, and Science Direct in the last 10 years, which were then eliminated based on restriction criteria and PICO. **Results:** There were 988 articles found and then excluded based on the restriction criteria, yielding 15 articles to be reviewed. A review of 15 articles discovered several themes; vitamin D alone acted as an analgesic (9 articles), vitamin D combined with light physical exercise (4 articles), and the use of vitamin D did not show significant changes in pain (2 articles). **Conclusion:** By paying attention to the optimal dose and duration of administration, Vitamin D has the potential to aid in the healing process as an analgesic in patients suffering from low back pain. Vitamin D also has the potential to prevent disease or lessen its severity in people suffering from low back pain.

Keywords: *Low Back Pain, Musculoskeletal Pain, Vitamin D, Vitamin D Deficiency, Analgesic*

1. INTRODUCTION

Low back pain (LBP) is the most common musculoskeletal disease caused by work or excessive activity. It is estimated that at least 70% of people suffer from back pain, either chronic or sporadic (Gaya, 2015). About 50-80% of adults suffer from it, and it is the leading cause of disability when compared to other diseases (Fatoye et al., 2019). According to WHO (2013), LBP accounts for 33% of all persistent pain in developing countries (Harwanti et al., 2019). Research in Europe shows that most people with LBP have moderate to severe pain intensity despite receiving anti-pain medication. Vitamin D deficiency is one of the risk factors for pain, with a prevalence of 26% (Ardhini et al., 2015).

Research conducted by Zadro et al., 2017 on the relationship between vitamin D and low back pain found that treatment with vitamin D is easier to use because it is cheap, safe, and can improve symptoms, although vitamin D treatment is not effective overall in patients for a variety of reasons.

A number of studies have found that vitamin D has anatomical, hormonal, neurological, and immunological effects on pain manifestations, making it an important factor in the etiology and maintenance of pain states (Shipton & Shipton, 2015). Vitamin D therapy is a low-cost treatment with few side effects. Several other studies, however, have concluded that there is insufficient evidence to support the use of vitamin D to treat pain (Ardhini et al., 2015).

Since there is a controversy regarding this topic, this research focuses on the effect of vitamin D supplementation on the treatment of low back pain. As a result, more research is needed to establish the use of vitamin D supplements as an analgesic or pain reliever in patients suffering from low back pain.

2. METHOD

This research used a literature review design. Researchers conducted a systematic search of all English-language medical literature that met the inclusion criteria published between early 2011 and early 2021 in the Google Scholar, PubMed, and Science Direct databases. Keywords ("Vitamin D" OR "25-

hydroxy vitamin D" AND "backache" OR "Low Back Pain" OR "Postural Low Back Pain" OR "Low Backaches" OR "Recurrent Low Back Pain" OR "Mechanical Low Back Pain").

The collection of related literature was accomplished in stages, including searching for articles based on an outline topic, grouping articles based on relevance to the topic and the year of publication, sorting the explanatory structure, and comparing interconnected data.

The variables in this research refer to research journals that meet the restriction criteria and PICO (patient, intervention, comparison, outcome) (Table 1) as a method of determining the journal's provisions.

PICO	Description
Patient	Samples with low back pain or musculoskeletal pain
Intervention	Vitamin D supplementation in experimental studies
Comparison	Samples without vitamin D administration in the treatment process or with placebo
Outcome	Analgesic process or healing process

Table 1. PICO

3. RESULTS AND DISCUSSION

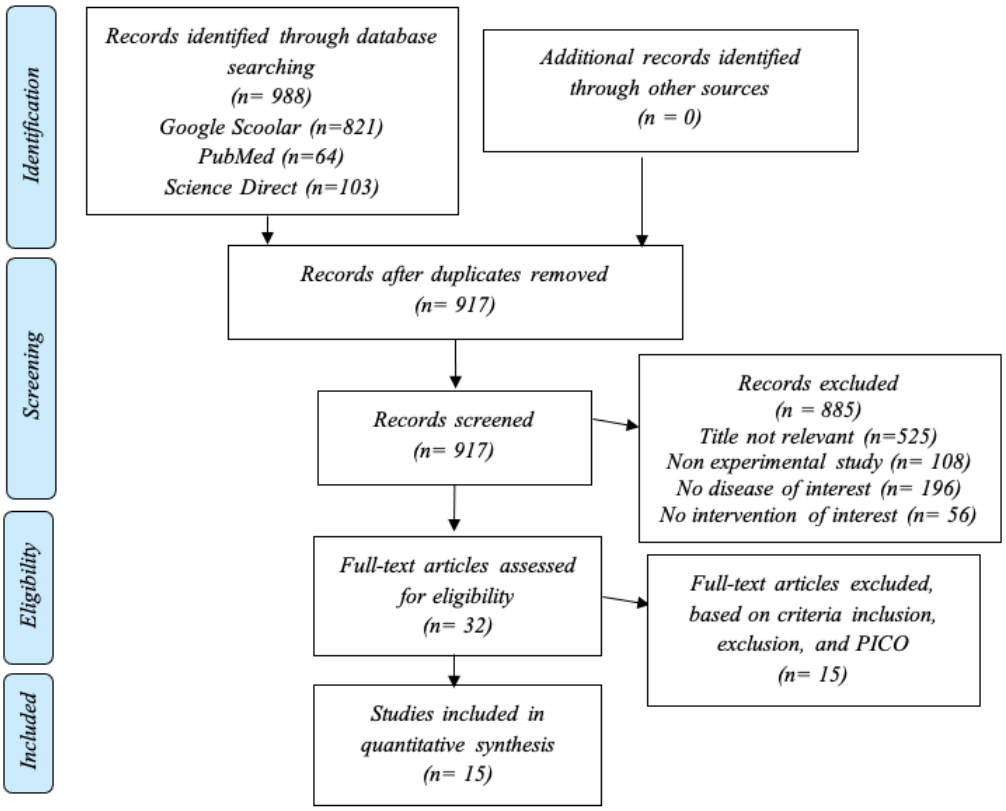

Figure 3.1 *Flowchart* of PRISMA Diagram

Table 2. Article's Characteristics

No	Author (Year)	Journal	Design	Country	Intervention (Number)	Comparison (Number)	Summary
1	(Gendelman et al., 2015)	British Medical Journal (BMJ)	Randomized double-blind placebo-Controlled Trial (RCT)	Israel	Vitamin D 4000 IU/day for 3 months (n=36)	Placebo (n=38)	The vitamin D group experienced a significant decrease in VAS scores at weeks 6 and 12 (overall p<0.001).
2	(Hanuman A et al., 2019)	International Journal of Orthopaedics Sciences	Interventional study	India	Vitamin D3 60,000 IU orally/week for 3 weeks (n=34)	Vitamin D3 60.000 IU orally/week for 2 months (n=15)	The association between 25 hydroxyvitamin D levels and presenting complaints was statistically significant (P-value < 0.05), 98% of subjects had shown improvement in symptoms with vitamin D supplementation.
3	(Soliman, 2018)	Journal of Medical Science And Clinical Research	Multicenter, Randomized placebo-Controlled Trial (RCT)	Cairo	Vitamin D injection 600,000 IU (one ampoule), injected 1-4x/2 months for 12 months (n=30)	Placebo: Platelet-rich plasma (PRP) mixed with buffered dextrose 15% or 25%, bone marrow aspirate was centrifuged mixed with buffered dextrose injected 1-3x / 2 months, (n=60)	Vitamin D has excellent results in the treatment of pain and musculoskeletal function after 12 months of pain evaluation using VAS.
4	(Englund et al., 2017)	Journal of Circumpolar Health	Randomized Controlled, Trial (RCT)	Stockholm, Sweden	Vitamin D 1,600 IU and 1,000 mg calcium/day for 3 months (n=21)	Placebo (n=4)	Immigrant women had significantly higher muscle strength and lower pain as measured by the VAS (p<0.05)
5	(Sandoughi et al., 2013)	International Journal of Rheumatic Diseases	Randomized double-blind Clinical Trial (RCT)	Zahedan, Iran	Vitamin D 50,000 IU weekly for 8 weeks (n=26)	Placebo (n=27)	The mean value of the VAS scores of the two groups decreased significantly from the beginning to the end of the study (P < 0.001). The mean change in chronic pain was 2.38 - 2.62, 95% confidence interval (CI) = 1.32-3.44 in the drug group and 3.33 - 3.67, 95% CI = 0.61 -2.55 in the placebo group.
6	(K. Dzik et al., 2017)	European Journal of	Randomized Controlled	Germany	Supplementation (SUP) Vitamin D	Placebo (n=24)	Vitamin D supplementation increases serum levels.

		Applied Physiology	Trial (RCT)		3200 IU/day for 5 weeks (n=14)		
7	(Ghai et al., 2017)	Pain Physician Journal	An Open-Label, Single-Arm Clinical Trial	Chandigarh, India	Oral vitamin D3 60,000 IU/week for 8 weeks, oral vitamin D 60,000 IU/day for 6 months (maintenance phase) (n=68)	-	Serum vitamin-D levels increased significantly post-supplementation (P< 0.01). Significant reduction in post-supplementation pain score (P ≤ 0.001). A significant improvement in functional disability was also observed after supplementation (P ≤ 0.001).
8	(Hansen, 2014)	Journal of Medicine with Industrial Specialization	Randomized parallel double-blinded placebo-Controlled Trial (RCT)	Aalborg, Denmark	Vitamin D3 50 g (2000 IU)/day for 12 weeks (n=5)	Placebo (n=5)	The main results showed a significant difference for maximal muscle strength (MVC) (P = 0.01) and Timed Up and Go (TUG) (P = 0.05) due to the anti-inflammatory effect of vitamin D3.
9	(Brady et al., 2019)	Journal of Steroid Biochemistry & Molecular Biology	Randomized, double-blind, placebo-Controlled Trial (RCT)	Melbourne, Australia	Vitamin D 100,000 IU + 4,000 IU/day for 16 weeks (n=26)	Placebo (n=23)	In those with more severe baseline vitamin D deficiency (25(OH)D< 30nmol/L), there was a significant reduction in back pain disability scores in the vitamin group compared with placebo after adjustment for the relevant covariates. (p<0.05)
10	(Elwan & Moneer, 2020)	Al-Azhar Assiut Medical Journal	Randomized Controlled Trial (RCT)	Cairo, Egypt	Oral Vitamin D3 50,000 IU/week + Walking Exercise Program for 8 weeks (n=55)	Placebo: Oral vitamin D3 50,000 IU/week for 8 weeks (n=55)	Of all patients, only 49 patients reported pain relief in low back pain (LBP) after oral vitamin D therapy, and 51 patients reported pain relief in LBP after oral vitamin D and WEP therapy, so the combination of both (correction of vitamin D3 and WEP) was more beneficial in improving chronic LBP (P<0.05).
11	(Aoki et al., 2018)	Journal of Orthopedic Science	A randomized trial with a parallel-group design (RCT)	Japan	Vitamin D 25 mcg (1000 IU)/day, (n=64) Vitamin D 25 mcg (1000 IU)/day, + Exercise for 24 weeks (n=64)	Placebo (n=20)	The increase in lower extremity muscle mass tends to be higher in the Exercise + Vitamin D group compared to other groups (p = 0.002 in Exercise, p = 0.005 in vitamin D, p<0.001 in Exercise + Vitamin D)
12	(Ali et al., 2021)	The journal Frontiers in Nutrition	Quasi-Experimental Clinical Trial	Dhaka, Bangladesh	Vitamin D3 40,000 IU/week for 8 weeks +	Placebo (n=67)	The combined intervention of vitamin D and physiotherapy showed significantly better results in reducing pain-related

					physiotherapy (n=76)		outcomes ($p < 0.001$).
13	(Hashemi Sangatrashani et al., 2020)	Journal of Inflammatory Diseases	Randomized Controlled Trial (RCT)	Iran	Vitamin D 50,000 IU/week, Vitamin D 50,000 IU/week + Exercise for 8 weeks (n=36)	Control group: Oral paraffin/week (n=12)	The effect of the combined intervention on decreasing AST and ALP enzyme activity was higher than that of the other two groups (overall: P<0.001).
14	(Cuellar et al., 2019)	Journal of Cachexia, Sarcopenia, and Muscle	Randomized, placebo-Controlled, and double-blind clinicalTrial (RCT)	Australia	Vitamin D3 capsules 50,000 IU (1.25 mg)/month for 24 months (n=129)	Placebo (n=132)	There were no statistically significant differences in changes in muscle thickness or CSA between the vitamin D and placebo groups, and all effect sizes were small and not clinically significant. (all P < 0.05).
15	(Schlögl et al., 2019)	Journal of the American Medical Directors Association	Single-center, double-blind Randomized placebo-Controlled, Trial (RCT)	Waid, Switzerland	Vitamin D3 60,000 IU once/month for 12 months (n=84)	Control group: Vitamin D3 24,000 IU once/month (n=116)	There were no changes in the high-dose group. Among seniors who were vitamin D deficient at baseline (n = 116), chronic pain did not differ by treatment group over time (P = .33)

Where, VAS = Visual Analogue Scale, AST = Aspartate Aminotransferase, ALP = Alkaline Phosphatase, ALP = Alkaline Fosfatase WPE = Walking Program Exercise, MVC = Maximal Muscle Strength, PPT = Pressure Pain Thresh-old, CLBP = Chronic Low Back Pain, CSA = Cross-Sectional Area

Table 3. Respondent Demographic Information

No	Author (Year)	Population (number)	Sex (number)		Age (Year)
			Men	Women	
1	(Gendelman et al., 2015)	74	14	60	26.78 ± 57.3 (P) and 28.78 ± 56.8 (VD)
2	(Hashemi Sangatrashani et al., 2020)	48	48	0	36.60 ± 5.44 (exercise) 35.50 ± 6.79 (VD) 39.30 ± 3.69 (Combined) 34.58 ± 5.50 (Control)
3	(Schlögl et al., 2019)	200	66	134	78.0 ± 5.3
4	(Hanuman A et al., 2019)	49	12	37	39.02 ± 12.8
5	(Soliman, 2018)	270	Not reported	Not reported	67,4 ± 12,4
6	(Englund et al., 2017)	25	25	0	32.0 ± 4.7
7	(Sandoughi et al., 2013)	53	13	40	33.19 ± 6.51 (intervention) and 33.29 ± 6.65 (placebo)
8	(Elwan & Moneer, 2020)	110	15	95	28.8 ± 8.1
9	(Dzik et al., 2017)	38	19	19	48.2 ± 9.9
10	(Aoki et al., 2018)	148	Not reported	Not reported	68.8 ± 5.25
11	(Ghai et al., 2017)	68	37	31	44 ± 12.0
12	(Ali et al., 2021)	143	52	91	38 ± 26.6
13	(Hansen, 2014)	10	Not reported	Not reported	72,8 ± 5,5
14	(Cuellar et al., 2019)	265	113	152	63.7 ± 7.4 (VD) and 63.0 ± 7.3 (placebo)
15	(Brady et al., 2019)	49	31	18	31.8 ± 8.9

Note: VD = Vitamin D

It has been demonstrated that a lack of vitamin D can cause nerve fiber hypersensitivity, resulting in increased pain or tenderness. Optimizing vitamin D levels in patients with musculoskeletal disorders improves pain perception. Studies on the potential of vitamin D for analgesic regimens in patients with musculoskeletal pain have yielded relevant evidence. Patients with low back pain who received vitamin D treatment had lower TNF-α and PGE2 levels than those who did not receive vitamin D treatment. Prostaglandins can mediate neuropathic pain in the spinal cord by depolarizing neurons via PGE2. Vitamin D treatment resulted in a significant decrease in Visual Analogue Scale (VAS) scores in patients (Gendelman et al., 2015).

Vitamin D plays a key role in the etiology and development of various chronic pain conditions and their associated comorbidities by exerting anatomical, hormonal, neurological, and immunological influences on pain expression. Vitamin D can suppress tumor necrosis factor-alpha (TNF-α), macrophage colony-stimulating factor (M-CSF), and inducible nitric oxide synthase in astrocytes and microglia. TNF-α is conclusively involved in both peripheral and central levels of pain sensitization. M-CSF is a cytokine that stimulates the proliferation, differentiation, and survival of monocytes and macrophages. Macrophages can release many inflammatory mediators, including proinflammatory cytokines, particularly TNF- and interleukin-1 beta (IL-1β), nerve growth factor (NGF), nitric oxide (NO), and prostanoids. Evidence has shown that vitamin D in chronic low back pain patients experiences a healing process or decreases pain (Ghai et al., 2017).

According to the above-mentioned articles, the use of vitamin D supplementation did not always produce uniform results, due to a variety of other influencing factors such as previous analgesic therapy, duration of treatment, vitamin D dose, ranges of subjects, the timing of administration, and others.

Vitamin D plays a role in nociception and impaired neuromuscular function in chronic pain patients. In one study of patients with spinal stenosis with an average age of 41.9 years, vitamin D deficiency was associated with more severe pain, and vitamin D supplementation was linked with the resolution of pain. Furthermore, in two previous studies in patients with LBP or failed back surgery, an increase in serum vitamin 25-OHD in patients with vitamin D deficiency was related to improvement in back pain, even after a long median period of 2.6 years (Heidari et al., 2014).

Several studies have found a connection between low vitamin D levels and a higher incidence of chronic pain in various patient populations, including rheumatology patients, women with low back pain during pregnancy, patients with non-specific musculoskeletal pain, and patients with spinal stenosis (Papori et al., 2017).

4. CONCLUSION

Based on the findings of the research or a systematic review of 15 articles, it can be concluded that Vitamin D has an effect on the healing process as an analgesic in patients with low back pain, particularly in patients with Vitamin D deficiency, by paying attention to the optimal dose and duration of vitamin D administration, which is associated with pain treatment success.

From this systematic review, it is hoped that this research can serve as the foundation for further research.

AUTHORS' CONTRIBUTION

The authors are responsible for all significant parts of the text, as well as for thoroughly reviewing the entire article.

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