

EVIDENCE BASED CASE REPORT

The Use of Vitamin D Supplement as a Treatment for Knee Osteoarthritis

**Azharuddin A,¹ Muhammad B. Z. Hutagalung,^{1*} Diaz Novera,²
Dadang Makmun²**

¹Department of Orthopedic and Traumatology, Faculty of Medicine, Syiah Kuala University-
dr. Zainoel Abidin Hospital, Banda Aceh, Indonesia

²Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia-
dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia

*Corresponding author: bayuzohari@gmail.com

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Abstract

Osteoarthritis is a chronic degenerative disease that causes functional disability with no disease-modifying treatment available. Management of osteoarthritis currently focuses on symptomatic relief or joint replacement. Recent studies have shown the involvement of vitamin D deficiency affecting the progression of knee osteoarthritis. However, the clinical use of vitamin D in the management of osteoarthritis remains unknown. The aim of the study is to investigate the efficacy of vitamin D supplement in management of knee osteoarthritis. Literature searching on Pubmed and ScienceDirect. The selection was made by title and abstract screening and applying inclusion and exclusion criteria. There were two randomized controlled trial studies selected for this report. Sanghi et al, reported that vitamin D supplement improves the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score in patients with osteoarthritis and vitamin D deficiency ($p < 0.02$). McAllindon et al, reported there is no improvement of knee pain in the general population ($p < 0.17$). There is no clinical significance of vitamin D supplementation in patients with osteoarthritis without proven vitamin D deficiency. However, the use of vitamin D as a therapy for vitamin D deficiency patients has proven to reduce the pain in osteoarthritis.

Keywords: vitamin D, supplementation, knee osteoarthritis.

Penggunaan Suplemen Vitamin D sebagai Tata Laksana Osteoarthritis Lutut

Abstrak

Osteoarthritis merupakan penyakit degeneratif kronik yang mengakibatkan kecacatan fungsional tanpa terapi modifikasi penyakit yang tersedia. Penatalaksanaan osteoarthritis saat ini fokus kepada pengurangan gejala klinis atau penggantian sendi. Penelitian terbaru menunjukkan keterlibatan defisiensi vitamin D yang memengaruhi terjadinya osteoarthritis, namun, penggunaan vitamin D dalam pengelolaan osteoarthritis lutut masih belum jelas. Tujuan penelitian ini adalah menilai efektivitas penggunaan suplemen vitamin D sebagai tatalaksana osteoarthritis lutut. Pencarian literature di Pubmed dan ScienceDirect. Pemilihan dilakukan dengan skrinig judul dan abstrak, menerapkan kriteria inklusi dan eksklusi. Dua studi percobaan acak terkontrol dipilih untuk laporan ini. Studi oleh Sanghi et al menunjukkan bahwa suplementasi vitamin D meningkatkan skor WOMAC pada pasien osteoarthritis dengan defisiensi vitamin D ($p < 0,02$). McAllindon et al melaporkan bahwa tidak ada perbaikan nyeri lutut pada populasi umum ($p < 0,17$). Tidak ada bukti klinis suplementasi vitamin D pada pasien osteoarthritis tanpa kekurangan vitamin D namun, penggunaan vitamin D sebagai terapi bagi pasien kekurangan vitamin D terbukti mengurangi rasa nyeri pada osteoarthritis.

Kata kunci: vitamin D, suplementasi, osteoarthritis lutut.

Introduction

Osteoarthritis (OA) is a condition in which the hyaline articular cartilage degrades accompanied by the presence of osteophyte in bone remodeling.¹ The most common clinical presentation of OA is a pain with loss of joint function.^{2,3} Though OA is not classified as a lethal disease, it increases the dependency of patients on healthcare system and services, accounting for AUD \$12 billion with 57% spent on knee and hip joint replacement.⁴

The major burden of OA lies with the pain experienced by the patient. The pain in OA is thought to be transmitted from articular nerve endings that innervates the joint capsule, subchondral bone, periosteum, ligaments and the menisci.^{2,5} Pain in early stages of OA came through the joint activity that eventually persistence without any joint movement.⁶ However, the exact etiology of pain in OA remains unknown.^{1,7}

To date, there is no cure for OA, and management of knee OA largely focused on symptomatic pain relief through both pharmacologic and non-pharmacologic therapy.⁸ There has been numerous attempt on vitamin and mineral supplementation as an alternative of anti-inflammatory agents to relieve the pain of OA.^{9,10}

Recent studies have shown that vitamin D deficiency has a positive association with the worsening of OA both clinically and structurally. It is thought that vitamin D deficiency alters the cartilage metabolism as the hypertrophic chondrocytes in OA redevelop vitamin D receptors altering the process of bone remodeling in OA.^{10,11} Current treatment regimens for OA recommended by American College of Rheumatology (ACR) is to use analgesics and arthroplasty as a symptomatic relief and functional improvement.⁸ To our knowledge, there is no available recommendation for the use of supplements in the management of OA despite the growing number of research in such direction. This evidence-based case report is aimed at evaluating whether the use of vitamin D supplementation has an effect in improving the symptoms of OA.

Case Illustration

Male patient 54 years old, came with the chief complaint of pain in the left knee that worsened since 3 years prior to hospital admission. At first, the patient felt fatigued on the left knee followed recently by pain. The sensation worsen when descending stairs compared to walking on a level plain and currently the pain persists even when walking on a level plain accompanied by swelling of the left knee. The patient

does not feel any joint stiffness in the morning. The patient had no previous history of trauma on the knee, however, the patient already had a hip replacement 5 years ago and was told that there was a rheumatic disease of the hip. The patient had received treatment of 1x20mg of piroxicam combined with 1x20mg of omeprazole previously, but the regiment was changed into 2x1000mg of paracetamol daily as the patient complaint of epigastric pain. The patient felt the current drug regiment is inadequate as he felt that the knee pain worsened. There was no history of diabetes mellitus, hypertension, and dyslipidemia in this patient. On family history, the patient's mother had received knee replacement therapy. The patient is a high school teacher without any history of smoking and alcohol consumption.

On physical examination, vital signs within normal limit. Examination on the knees, look: no sign of inflammation and deformity. Feel: there was no warmth or tenderness found on both knees, crepitus was found on both knees. Move: active and passive range of motion within normal limit. Other physical examinations were unremarkable.

Recent laboratory result showed that the creatinine level was 0.90, ureum 15, uric acid 7.0, triglycerides 98, total cholesterol 197, HDL 54 and LDL 134. The plain radiographs of the knee showed subluxation of left femoropatellar joint to the lateral side, intact bone structure, osteophyte formation in medial and lateral condylar notch of the femur bone of the right tibia and at the patellar base of both knees. There radiographs also showed reduced compartment of the medial of the right tibiofemoral compartment, left medial and lateral femorotibial compartment, and the left femoropatellar compartment. This findings is correlated with OA of the knee. The patient was diagnosed with bilateral knee OA of Kellgren-Lawrence grade III with subluxation of the left femoropatellar joint to the lateral.

Methods

Formulation of Research

Is the use of Vitamin D supplement can reduce the symptoms of OA and prevent the disease progression?

Evidence Research Strategy

The literature search was performed on 12-14 January 2015 from two databases namely PubMed and ScienceDirect (Table 1 and Figure 1). The keyword used in this article is "Vitamin D" and "Osteoarthritis". A further refinery was done using Bolleen and MESH combination.

Table 1. Search Strategy

Database	Search Strategy	Hits
Pubmed	(Vitamin D) AND Osteoarthritis	250
ScienceDirect	(Vitamin D) AND Osteoarthritis	356

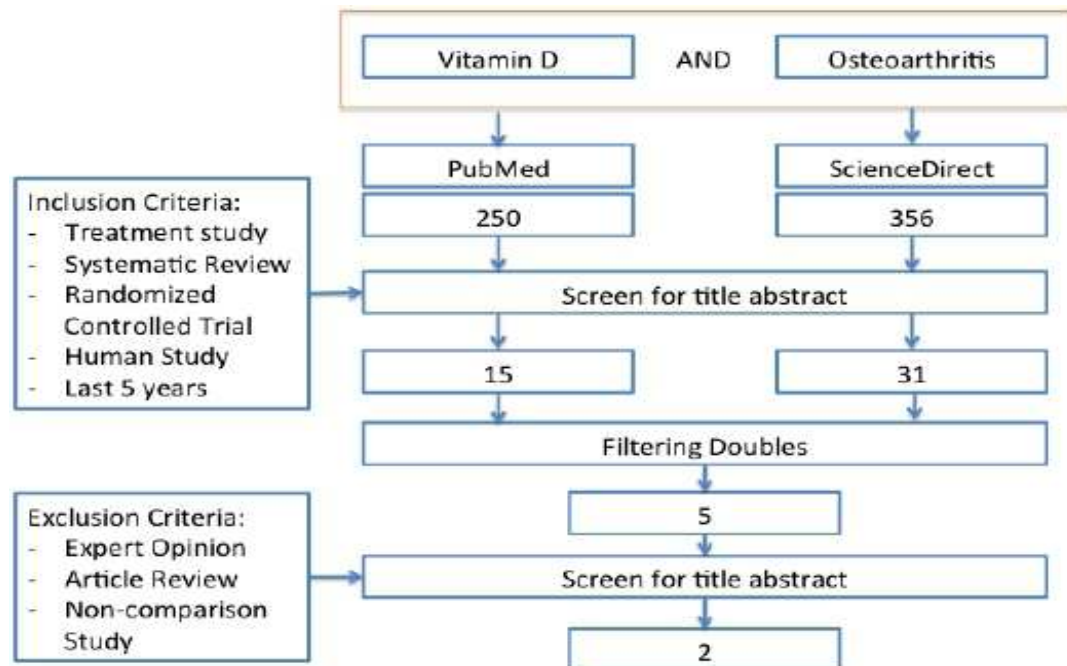


Figure 1. Flowchart of Selecting Articles in The EBCR

Results

After searching for the article as above, the results were filtered using inclusion criteria as shown in the Figure 1. From the filtration using inclusion and exclusion criteria, there were 2 available articles that are used in this report, which were:^{12,13}

1. Sanghi D, Mishara A, Sharma AC, Singh A, Natu SM, Agarwal S, Srivastava RN. Does Vitamin D Improve Osteoarthritis of the Knee: A Randomized Controlled Pilot Trial. *Clinical Orthopaedics and Related Research*. 2013;471:3556-62. The severity of the subjects are varies based on Kellgren-Lawrence grade. The subjects divided into Grade 2: 19 subjects (8 men, 11 women), Grade 3: 48 subjects (14 men, 34 women), grade 4: 36 subjects (10 men, 26 women).
2. McAllindon T, LaValley M, Schneider E, Nuite M, Ji YL, Price LL, Lo G, Dawson-Hughes

B. Effect of Vitamin D Supplementation on Progression of Knee Pain and Cartilage Volume Loss in Patients with Symptomatic Osteoarthritis. A Randomized Controlled Trial. *JAMA*. 2013;309(2):155-62. The severity of the subjects are varies based on Kellgren-Lawrence grade. The subjects divided into Grade 2: 73 subjects, Grade 3: 42 subjects and grade 4: 31 subjects.

Appraise the Studies

In appraising the scientific evidence of 2 articles, we use the guidance of QUORUM (The Quality of Reporting Meta-analysis) combine with GRADE (Grading of Recommendation Assessment Development and Evaluation) Working Group. In general, both guidance focus on three aspects abbreviated as VIA (Validity, Importance, Applicability). The following are the critical appraisal for each of those aspects (Table 2).

Table 2. Critical Appraisal

	Sanghi et al ¹²	McAllindon et al ¹³
Subject	103 patients (52 Experiment and 51 Control)	125 patients (65 Experiment and 60 Control)
Validity		
Randomization	Yes	Yes
Intention to treat	Yes	Yes
Blind	Yes	Yes
Equal treatment	Yes	Yes
Similar Characteristics	Yes	Yes
Importance		
95% CI of group difference of WOMAC pain	-1.70 (-2.28, 1.12)	-0.87 (-2.12, 0.38)
95% CI of group difference of WOMAC function	-2.05 (-2.92, -1.19)	-3.11 (-6.52, 0.30)
Applicability		
Similar domain	Yes	Yes
Similar therapy	Yes	Yes
Similar outcome	Yes	Yes
Feasibility	Yes	Yes
Side effect	-	-
Level of Evidence	1B	1B

Discussion

OA is one of the most frequent causes of pain, loss of function, and disability in the elderly. Knee OA is common in patients in India and currently there is no strong evidence that vitamin D deficiency plays an important role in the development of knee. However, it is not known OA whether correcting

vitamin D deficiency will influence the progress of the disease.¹⁴ Several mechanisms such as alterations in mechanical properties of bones, increasing bone resorption by raising PTH level, increasing bone turn over, or direct effect of vitamin D metabolites on articular chondrocytes was postulated to explain the contribution of vitamin D deficiency in the progression of OA (Figure 2).^{15,16}

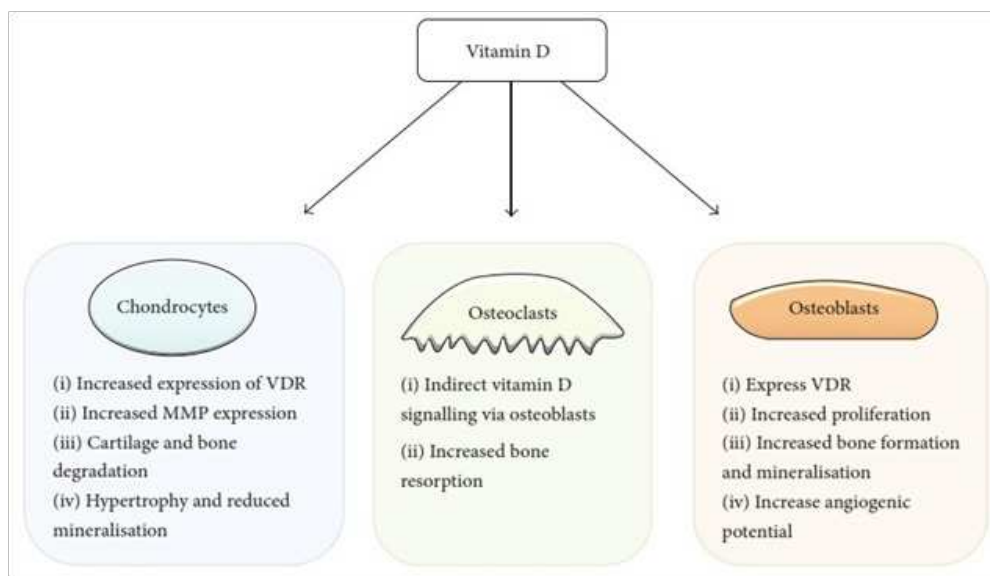


Figure 2. The Effects of Vitamin D on Several Different Cell Types in OA including Chondrocytes, Osteoclasts, and Osteoblasts. VDR: Vitamin D Receptor; MMP: Matrix Metalloproteinase.¹⁶

In progressive OA, bone metabolism and bone turnover are increased similar to patients with osteoporosis. Vitamin D status influences the incidence and progression of knee OA. Sunlight exposure and serum 25-OHD Low serum 25-OHD increases osteoblastic activity and bone turnover. Raising serum 25-OHD to sufficient levels of supplemental vitamin D will decrease the rate of bone turn-over, suppress the PTH level, increase BMD and even decrease fracture risk in the elderly population.¹⁷

Sanghi et al,¹² discussed the effect of vitamin D on OA, specifically on improving the (WOMAC) score and assessing whether there is a change in the patient's biochemical markers. The study involves 107 patients in India with knee OA and vitamin D insufficiency. The primary outcome measures were pain and functional WOMAC with the secondary outcome measure were biochemical markers. The patients were followed for one year. The results show that after 1 year, there is a decrease of knee pain measured both by visual analogue scale (VAS) by -0.26 (95% CI, -2.82 to -1.43) and WOMAC by -0.55 (95% CI, -0.07, 1.02). Both shows significant differences in group comparison as the p-values were 0.02 and <0.01 respectively. It was also seen that the group receiving Vitamin D supplements had the significant improvement on knee function measured by WOMAC by -1.36 (95% CI -1.87,-0.85) compared to the placebo group that had a mean of 0.69 (95% CI -0.03, 1.41). As for the secondary outcomes, Sanghi et al¹² had assessed there were several changes in the serum biomarkers in patients receiving vitamin D supplements compared to the placebo.

Study by McAllindon et al,¹³ also discussed the effect of Vitamin D on OA using WOMAC as the measurement tool for the clinical outcome. However, McAllindon et al¹³ also investigated the structural changes as the alternative outcome. The population in the study comprises of 146 people in the United States, divided equally into 73 people each in both the experimental and control group. The study was conducted for two years, where it was found that there was no significant difference over the decrease of knee pain and function measured by WOMAC, -0.87 (95% CI -2.12, 0.38) for WOMAC pain and -3.11(95% CI - 6.52, 0.30). Similar results were also seen for the changes of the knee structures measured by magnetic resonance imaging (MRI).

The study by Sanghi et al¹² concluded that daily supplementation of 6000 IU vitamin D is beneficial for the treatment of OA only in patients with the

comorbid of vitamin D deficiency. However, it is also needed to be considered that worsening of knee's pain in the placebo group might confound the significant difference between the two group. On the other hand, McAllindon et al¹³ carried out a trial with the lower dose of vitamin D supplementation at 2000IU for a longer period of time. The approach was taking into consideration the population of the study that many of them were not vitamin D deficient. McAllindon et al¹³ also did not find that vitamin D supplementation results in neither pain reduction nor knee structural changes in their population.

Based on the two studies, the use of vitamin D supplementation in OA still remains questionable. While Sanghi et al¹² showed that it is beneficial in patients with vitamin D deficiency, there are questions remained due to the confounding knee pain progression observed in their study's control group. However, McAllindon et al¹³ had contributed solid evidence that 2000 IU of vitamin D supplementation has no effect on knee structural changes observed on MRI. It can be concluded from the two studies that vitamin D supplementation has no effect on patients with OA without vitamin D deficiency.

In this case the patient had received therapy that goes in accordance with the current guideline that is by the use of analgetic complemented with physical therapy. The patient felt uncomfortable with the side effect of epigastric pain due to prolonged use of NSAIDs and the current regiment deemed insufficient as a symptomatic relief. Since the patient's vitamin D profile remains unknown, there is no evidence to start a vitamin D supplement in this patient. Shall the patient is known to have a vitamin D deficiency in the future, the use of vitamin D is directed to be a primary therapeutic management rather than as an adjuvant therapy.

Conclusion

While there are evidence that vitamin D deficiency has a role in disease progression of OA, at the moment there is still no strong evidence that shows vitamin D supplementation has significant clinical beneficence in patients with OA. Therefore, until further evidence is available, we conclude that vitamin D supplement has no effect in reducing pain and preventing disease progression on patients with OA.

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