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Review Article

Association of vitamin D and knee osteoarthritis – A review

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ABSTRACT

Osteoarthritis (OA) is a progressively degenerating joint disease primarily affecting the weight-bearing joints of the body. The precise etiopathogenesis and mechanism of progression of osteoarthritis still remain elusive. However, many known risk factors such as vitamin D deficiency, obesity, genetics, and trauma, etc. have been studied and hypothesized to play a significant role in its occurrence and progression. Studies into the effects of low vitamin D levels on pain and joint function to date have yielded equivocal results. Due to the apparent conflicting effects of vitamin D in knee OA, further research is required to fully elucidate its role in the development and progression of the disease.

1. Introduction

Osteoarthritis (OA) is a chronic progressive and degenerative joint disease which commonly affects weight bearing synovial joints. It is characterized by gradual degradation and subsequent loss of articular cartilage, abnormal subchondral bone growth, and remodeling, and, in early stages also causes inflammation of the synovium. The complexity of OA has hindered attempts to understand its etiology and pathogenesis which still remains equivocal.[1] There are, however, a range of risk factors which are known to associate with OA including age, gender, obesity, previous joint trauma, and genetics.[2]

Historically, it was assumed that only cartilage contributed to the progression of OA, but all tissues within the joint structure are now known to be involved. In osteoarthritic knees, the most common location of OA, the subchondral tibial and femoral bones play central roles in the pathology of joint degeneration.[3]

Vitamin D has recently found focus due to its widespread effects on the musculoskeletal system. Also, the prevalence of vitamin D deficiency has consistently been on the rise.[4] These two factors have led to an increased focus on the effect of vitamin D deficiency on the incidence and progression of OA, especially in the weight bearing joints like hip and knee.

2. Role of vitamin D deficiency in OA

Vitamin D (25-dihydroxy-cholecalciferol) is a steroidal hormone that has diverse biological functions in target tissues.[5] The primary functions of vitamin D are calcium homeostasis

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and regulation of bone metabolism; however, the full extent of vitamin D's biological action remains to be determined with a broad range of effects on different cell and tissue types being reported. Vitamin D deficiency results in hypocalcemia, and hypophosphatemia and also causes an increase in PTH secretion.[5] Hypovitaminosis D, generally (though not universally) defined as circulating serum 25(OH)D3 levels of <20 ng/ml and frequently found to coexist with OA, particularly in the elderly patients.[6] Acting via the vitamin D receptor (VDR), vitamin D regulates circulating calcium and phosphate homeostasis through altering kidney reabsorption and intestinal absorption.[7] Low vitamin D leads to vascular smooth muscle proliferation, endothelial cell dysfunction and increased inflammation.[8]

In the etiopathogenesis of OA, vitamin D has recently gained focus. The receptors of vitamin D have been found in chondrocytes.[9] Vitamin D acts through controlling the matrix metalloproteinase and prostaglandin E2 secretion.[8] Vitamin D has also been shown to affect the production of proteoglycans which are necessary for maintaining cartilage health.[10] The bone remodeling is also inhibited by vitamin D, and hence it plays a major role in the metabolism of the subchondral bone.[11,12]

2.1. *Vitamin D deficiency and prevalence of radiographic knee OA*

Vitamin D deficiency has long being speculated to be a profound risk factor for the occurrence and progression of knee OA, but its objective evidence till date remains bleak. However, several major studies, both cross sectional and longitudinal, have since been done which has enhanced our understanding its actual underlying pathophysiology (Tables 1 and 2).

Muraki et al. conducted a cross-sectional study consisting of 787 participants, with a baseline age of 65.6 ± 2.7, and baseline vitamin D levels of 42.5 ng/ml. OA assessment was done using Kellegren and Lawrence Grading.[13] The results showed that there was no significant association between a polymorphism of VDR with radiological knee OA. However, a low tertile level vitamin D was associated with knee pain than with a high tertile. Hence, the study concluded that vitamin D deficiency was showed more significant association with knee pain rather than radiographic knee OA.

In a cohort study conducted by Ding et al., there were 880 participants with male, the female ratio of 50:50. The mean age was 61 years and baseline vitamin D levels were52.8 ng/ml.[14] It was found that there was a significant association of vitamin D deficiency with knee cartilage loss as evidenced by JSN (joint space narrowing). However, it showed no direct correlation with radiographic knee OA as assessed by osteophytes on plain radiograph. Consequently, the study concluded that vitamin D and sun exposure was helpful in reducing knee cartilage loss.

2.2. *Vitamin D deficiency and incidence of radiographic knee OA*

There have also been longitudinal studies where patients with vitamin D deficiency were followed in a prospective manner to assess the incidence of radiographic knee OA.

A prospective cohort study conducted by Berginik et al. included 1248 participants with an average age of 66.2 and a male to female ratio of 58:42. Their mean vitamin D levels were 26.4 ng/ml.[15] Radiographic assessment was done using Kellgren and Lawrence Grading. The results showed that a low tertile level vitamin D showed significant association to JSN and radiographic progression of knee OA. Hence the study

Table 1 – Cross sectional and cohort studies studying the association of vitamin D with knee osteoarthritis.

Author and year of study	Type of study	Number of participants (*n*)	Age (years)	Male: female	Mean vitamin D levels in ng/ml	Outcome	Clinical conclusion
Malas et al. (2013),[17] UK	Cross sectional study	80	20–45	0:100	20	Patients with vitamin D level (<10 ng/ml) showed a thinner distal femur cartilage when compared to patients with vitamin D level (>10 ng/ml)	Vitamin D deficiency is clinically responsible for thinning of distal femoral cartilage
Ding et al. (2009),[14] Australia	Cohort study	880	61	50:50 (440/440)	52.8	Vitamin D and sunlight exposure showed no concise correlation to knee ROA	Vitamin D deficiency showed more correlation to knee cartilage loss than radiographic knee OA
Muraki et al. (2011),[13] Japan	Cross sectional study	787	65.6 ± 2.7	49:51 (388/399)	42.5	Low levels of vitamin D were associated with knee pain, however polymorphism of vitamin D receptor showed no association with radiological OA	Vitamin D deficiency was more correspondent to knee pain than radiographic OA. Also, vitamin D receptor polymorphism and knee OA showed no association.
Bergink et al. (2009),[15] Netherlands	Cohort Study	1248	66.2 (6.7)	58:42 (728/520)	26.4 (10.8)	JSN and radiographic OA had significant association to a low vitamin D level	Patients with low vitamin D intake showed increased of radiographic knee OA

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