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Is vitamin D insufficiency or deficiency related to the development of osteochondritis dissecans?

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Abstract
Purpose The aetiology of osteochondritis dissecans is still unclear. The aim of this prospective pilot study was to analyse whether vitamin D insufficiency, or deficiency, might be a contributing etiological factor in the development of an OCD lesion.
Methods The serum level of vitamin D3 in 23 consecutive patients (12 male and 11 female) suffering from a stage III, or stages III and IV, OCD lesion (mostly stage III) admitted for surgery was measured.
Results The patients' mean age was 31.3 years and most of them already exhibited closed epiphyseal plates. In the majority of patients (18/23), a distinct vitamin D3 deficiency was found, two patients were vitamin D3-insufficient and, in three patients, the vitamin D3 level reached the lowest normal value.
Conclusion These first data show that a vitamin D3 deficiency rather than an insufficiency may be involved in the development of OCD lesions. Probably, with a vitamin D3 substitution, the development of an advanced OCD stage could be avoided. Further analyses, including morphological analyses regarding a possible osteomalacia, and examination of the PTH and other determinants of the bone metabolism, should be undertaken to either confirm or refute these data.
Level of evidence IV.

Keywords Osteochondritis dissecans · Aetiology · Vitamin D · Deficiency · Insufficiency

Introduction

Osteochondritis dissecans (OCD) is a common disease of the joints and belongs to the group of osteonecroses [3, 10, 14, 31, 50]. The knee and ankle joint in the lower extremity and the elbow joint in the upper extremity are most frequently involved [14, 47]. The peak incidence of OCD is seen in patients aged between 10 and 25 years and, although quite common, little is known about its aetiology [14, 47].

The pathophysiological pathway of OCD is, however, well defined [3, 10, 14, 28, 42, 47]; depending on which staging system has been chosen, three or four stages can be differentiated [14]. Stage I OCD starts in the subchondral bone with a circumscribed area of osteonecrosis and it is thought that bone marrow oedema are the initial changes in this area [4, 29]. Around the necrotic area, the surrounding bone develops a sclerotic wall (stage II) which separates healthy and diseased bone [3, 10, 14]. Partial loosening of the overlying cartilage determines the third stage; it can be damaged either by separating from the healthy cartilage surrounding it, which results in the development of a loose body, or by chondromalacia of the cartilage of the loose body. The final stage is characterised by one or several loose bodies which separate from the surrounding healthy joint surface leaving an osteochondral crater [3, 10, 16].

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However, the aetiology of OCD lesions still remains a mystery. Previously discussed etiological aspects include hereditary [38, 47–49], endogenous [7, 14, 47], vascular [20, 47], mechanical [2, 6, 10, 15, 17, 18, 30] and infectious [14, 32, 47] factors. There has been no precise proof yet for any of these theories.

For several authors [5, 8, 17, 18, 30, 37, 40], mechanical reasons are among the most common causes of OCD lesions. However, it has been suggested that, besides these obvious mechanical factors, there must be something else contributing to the lesions. Under the hypothesis that a vitamin D3 insufficiency or deficiency might be this missing etiological co-factor, in a first pilot study, the vitamin D3 level in all patients admitted consecutively to surgery for an OCD lesion had been measured to see whether a vitamin D3 insufficiency or a deficiency was detectable.

Material and methods

In a prospective pilot study, the vitamin D3 (25-Monohydroxycholecalciferol) level in a consecutive group of patients admitted to our department for surgical therapy of an OCD lesion was measured. Using the classification described by Bruns 1996 [14] which resembles the ICRS-classification, most of the patients were suffering from an OCD lesion of at least stage III. Owing to the fact that the patients' blood was analysed using varying units of measurement in different laboratories used by their general practioner, which resulted in different ranges of the normal values, it was decided to regard the individual values as being a percentage of the lowest normal value of each particular laboratory. Vitamin D3 insufficiency was defined according to Priemel et al. [43] and von Domarus et al. [51] as values between 20 and 30 ng/mL (50–75 nmol/L) = 66.7–100 %, vitamin D3 deficiency as <20 ng/mL (<50 nmol/L) = <66.7 %.

All patients agreed to the analysis of the vitamin D3 values. The local ethical committee of the Agaplesion Diakonieklinikum consented orally to the analyses since, in Germany, an official statement for such an analysis, which is included in a routine blood analysis, does not need a written approval.

Results

Between March 2011 and July 2013, the levels of vitamin D3 in blood taken from 23 patients (12 male and 11 female) suffering from an OCD lesion (at least stage III) at the femoral condyles, talar domes or capitulum humeri were measured. The patients' mean age was 31.3 years (range 10.8–70, median 27.3). In 15 patients, the lesion was located in the talus, in seven patients in the knee condyles and, in one patient, in the capitulum humeri. The epiphyseal plate was "closed" in 17 patients and "open" in six patients; two patients had a stage II lesion, 20 a stage III and one a stage IV. The gender distribution was 11 females and 12 males.

Regarding the above-mentioned definition of vitamin D3 insufficiency or deficiency, 18 out of 23 exhibited a deficiency and three out of 23 an insufficiency. In two patients (one male, one female), the minimum value of the normal range was detected. The mean value for vitamin D3 was 41.9 % (31.4 ng/mL; range 13.3–100 %/4–30 ng/mL). The overall minimum was found in one female and one male, with a vitamin D3 level of 13.3 % (4 ng/mL) in the female and 19.7 % (5.9 ng/mL) in the male. The individual data (age, gender, stage of the epiphyseal plate, stage of the OCD lesions, etc.) are listed in Table 1. For all patients, it was the initial surgery for the OCD lesion at the side involved. Seventeen patients were suffering from a lesion in the talar dome, most of them being located on the medial talar rim. Two patients had two lesions, one in the knee joint and one in the ankle joint.

Discussion

The main most recent finding was that almost all patients suffering from an advanced OCD lesion exhibited a

Table 1 Summary of the patients data

Analysed patients	23
Location of OCD	
Talus	15
Knee	7
Capitulum humeri	1
Stage of the lesion	
Stage II	2
Stage III	20
Stage IV	1
Epiphyseal plate	
Open	6
Closed	17
Gender	
Female	11
Male	12
Age	
Min–max (years)	10.8–70
Median	27.3
Value vitamin D3 (converted to ng/mL)	
Min–max	4–30
Median	13.2
Vitamin D3 deficient	18
Vitamin D3 insufficient	3
Vitamin D3 normal	2

vitamin D3 deficiency. A minor number showed a vitamin D3 insufficiency and only two had a normal vitamin D3 value near to the lowest normal value. To our knowledge, this is the first scientific analysis of the vitamin D3 levels in patients suffering from an advanced OCD lesion. Most of the patients exhibited a distinct deficiency of this, for bone metabolism, very important vitamin. So far, only a single case has been published describing an adolescent male patient with clinically manifest rickets and a recent onset of knee pain caused by bilateral OCD in the knee joints [44]. A systemic analysis of the levels of vitamin D3 in OCD patients is still not available, although O'Loughlin et al. [41] mentioned their suspicion that a low vitamin D level might be involved in the development of OCD lesions; the probable connection has already been referred to on the internet [54]. Today, vitamin D3 insufficiency and deficiency are discussed as a main factor or co-factor connected with overall mortality [36] and several diseases such as cancer [1, 24, 27, 51, 52], diabetes [27] and diseases of the cardiovascular [27] and autoimmune systems [27] and also with poor physical performance [11, 12, 21, 53].

A high rate of vitamin D3 insufficiency or deficiency has been found in musculoskeletal diseases, especially in those of the metabolism [45, 46] as well as in trauma and orthopaedic cases [35], and reported by several authors from all over the world.

Recently, Bogunovic et al. [13] reported that among 723 patients, who were scheduled for orthopaedic surgery, overall 43 % of the patients had insufficient levels of vitamin D, 40 % had deficient levels. The highest rates of vitamin D levels were seen in trauma cases and sports injuries. The rates of abnormal (insufficient or deficient) vitamin D3 levels were 66 and 52 %, respectively. Patients between the age of fifty-one and seventy were 35 % less likely to have low vitamin D levels than those aged between eighteen and fifty years ($p = 0.018$). Furthermore, the authors reported that the prevalence of low vitamin D3 levels was significantly higher in men than in women ($p = 0.006$). In addition, individuals with dark skin were 5.5 times more likely to have low vitamin D levels than those with lighter skin ($p < 0.001$) [13]. Among sixty-eight women with osteoarthritis who were about to undergo a total hip arthroplasty, a vitamin D3 deficiency was found in 22 % [25]. Recently, it has been shown that a slipped capital femoral epiphysis is associated with vitamin D3 deficiency [34] and a high rate of vitamin D3 insufficiency, in groups of trauma patients who had fractured a bone during the winter or summer months and were about to undergo surgery [9].

Among 1,119 orthopaedic patients in Germany, 84 % had insufficient levels of vitamin D3 and 60 % were even vitamin D3-deficient. Only 15 % were in the target range of 30–60 ng/mL, the prevalence of low vitamin D levels being greater during the winter and those months with fewer hours of sunshine. Vitamin D levels did not vary according to age, sex or disease. Individuals with obesity, hypertension and/or osteoporosis were more likely to have low levels of vitamin D as compared to their healthy counterparts [35].

Previously, in 2006, Erkal et al. [22] had reported a high prevalence of vitamin D deficiency, secondary hyperparathyroidism and generalised bone pain in Turkish immigrants in Germany. In comparison to non-immigrants, similar results were found by Hintzpeter et al. [26] in German children and adolescents with an immigrant background. However, vitamin D3 insufficiency and deficiency is a global problem [13, 23, 33, 39]; even in Australia with its many hours of sunshine, the overall incidence in children $\leq$15 years of age is 4.9/100,000/year.

The majority (98 %) had a dark or intermediate skin colour and 18 % of the girls were partially or completely veiled. Most of the children were born in Africa (252; 63 %), 75 % were refugees [39].

Apart from clinically manifest rickets in children and adolescents, or osteomalacia in adults with other orthopaedic diseases, little is known about the probable connection to a vitamin D hypovitaminosis.

Since the measurement of vitamin D3 levels is critical and is only one out of at least three criteria (the other two are detection of bone mineralisation defects and the serum PTH level) for determining vitamin D insufficiency or deficiency [13, 19, 43, 51], Priemel et al. [43] analysed the vitamin D3 levels with regard to the presence or absence of mineralisation defects (increased osteoid indices and osteomalacia) in iliac crest-bone biopsies from 675 individuals. They found a high rate of these defects with an increased osteoid content. In 36.15 % of the patients, a ratio osteoid surface versus bone surface of more than 20 % was found. Thus, based on an estimated threshold of 2 % for the osteoid volume versus bone volume ratio, the authors observed manifest mineralisation defects in 25.63 % of the patients in all ages and in both sexes equally. Furthermore, they stated that no minimum vitamin D3 level could be defined where such a mineralisation defect was seen. Vice verse the authors did not find a pathological accumulation of osteoid in any patient with a circulating vitamin D3 level above 75 or 30 ng/mL. Regarding this hypothesis, a very recently published paper by Busse et al. [19], which analyses the effect of vitamin D deficiency on bone in apparently healthy people, exhibited that, in those who were deficient ($N = 15$), they had found the expected thicker unmineralised osteoid layer. However, the authors also unexpectedly discovered that the bone underneath the osteoid layer was more heavily mineralised than the same bone from persons non-deficient in vitamin D3. Furthermore, the bone of a vitamin D-deficient person exhibited a substantial reduction in its ability to deflect and bridge cracks, leading to more cracks across osteons, this being characteristic for aged bone.

Regarding the influence of vitamin D3 deficiency on the initiation and/or progression of an OCD lesion, more extended studies are necessary to reinforce the first results discussed in this paper and to analyse how vitamin D3 levels are affected by age, gender, skin colour, nutritional behaviour and ethnicity of patients. It is also necessary to analyse in which part of the development and/or progression of the lesion the deficiency is most noticeable. Furthermore, specimens taken from OCD lesions during a surgical repair procedure should be analysed regarding the bone density parameter and, probably, compared with PTH-serum levels and the bone density properties of bone biopsies from the iliac crest.

Conclusion

In a consecutive series of patients, it was analysed in a pilot study whether advanced OCD lesions can be etiologically connected with a lack of vitamin D3. First data on vitamin D3 levels point to a clear vitamin D3 deficiency (18/23) in almost all OCD patients analysed; in only a small number of patients (3/23) were a vitamin D3 insufficiency observed. Only two patients reached the minimum value of the normal range.

In the opinion of the authors, an insufficiency or deficiency of vitamin D3 might be a possible factor, or at least an important co-factor, in the initiation of an OCD lesion or either of these might contribute to the progression of the disease. It may be the suspected co-factor which, together with mechanical stresses in the involved joint, is responsible for the development of an OCD lesion. Regarding the great complexity of the vitamin D metabolism, further studies are necessary to confirm or refute our results.

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Conflict of interest The authors declare that they have no conflict of interest.

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