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Vitamin D concentration in patients with normal and impaired bone union

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Summary

Background: The aim of the study was to compare vitamin D concentration in patients treated due to delayed bone union and non-union (pseudoarthrosis) and patients with normal fracture healing.

Material/Methods: A retrospective case-control study was conducted. We enrolled 35 patients with inexplicable (standard and correct surgery, closed fracture, no comorbid metabolic diseases) fracture healing impairment, and 35 patients assigned by age and measurement season. Vitamin D (as 25OHD) concentration was measured in all patients.

Results: Vitamin D deficiency was reported in 86% of examined patients. No difference was shown between groups in deficiency prevalence.

Conclusions: Previous studies indicated decreased vitamin D concentration in patients with impaired fracture healing. However, these studies did not include control groups. No difference was demonstrated between patients with normal fracture healing and those with impaired bone union in terms of vitamin D deficiency prevalence.

key words: **vitamin D • deficiency • non-union • fracture healing**

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Background

Vitamin D deficiency is a prevalent condition in many populations [1–3]. Information concerning vitamin D supplementation in patients with impaired bone union is limited [4–7]. In previous studies control groups were not included or were improperly assigned [4–6]. Therefore, the interpretation of obtained results was difficult. Vitamin D concentration is influenced by many factors, for example skin colour, age and yearly variability in sunlight exposure. Decreased concentration can be observed especially in people of black race, elderly people or during winter months [8]. Because of that, appropriate patients selection and determination obtained in a similar season is required in order to compare the concentration between groups. A retrospective case-control study was conducted. The aim was to compare vitamin D concentration in patients with nonunion and properly assigned control group. The study hypothesis was there would be a difference in vitamin D concentration between these two groups.

Material and Methods

In this study, we enrolled patients treated in the clinic (located on 52 degree of northern latitude) due to delayed bone union or non-union (pseudoarthrosis), who fulfilled inclusion criteria. Inclusion criteria were: closed facture of a long bone diaphysis with surgical standard of care (femur, tibia and humerus – implantation of an intramedullary rod, humerus, radius and ulna – fixation using a plate). Patients were excluded from the study if they were treated using unconventional methods, had an open fracture, inflammatory complications, and had a comorbid disease or were taking drugs of known adverse effect on bone healing (diabetes, malnutrition, anaemia, hypothyroidism, long-term steroid therapy, anticonvulsants). The use of non-steroidal anti-inflammatory drugs was not assessed. The correctness of a fixation and fracture healing was assessed by three orthopaedic surgeons prior to study enrollment. Each patient in impaired bone union group, fulfilling inclusion criteria, had one patient with normal bone union assigned. Patients in control group were assigned to patients from impaired bone union group in respect of sex, age (with accuracy of 10 years) and time of determination (with accuracy of 1 month). Patients were not assigned with regard to fracture type, but all of them had long bone diaphysis fracture. Impaired bone healing group (N=35) was similar to normal bone union group (N=35) with respect to age (mean=40.32 SD=13.32 and mean=40.11 SD=12.85, respectively), sex (men 25/31) and smoking prevalence (40% and 37%). 25 cases of atrophic pseudoarthrosis and 10 cases of hypertrophic pseudoarthrosis were reported in the impaired union group.

After having obtained informed consent, 5 mL sample of venous blood was collected from each patient. Frozen serum was sent for LIAISON test (by DiaSorin, Saluggia, Italy). LIAISON test measures concentration of total 25(OH)D, which is the sum of D_2 and D_3 form [9]. Vitamin D deficiency was defined as its concentration below 30 ng/mL. Observation pairs were compared using Wilcoxon signed-rank test. The impact of vitamin D concentration on the success of fracture healing was assessed using McNemar non-parametric test. Stata software was used.

Results

Mean vitamin D concentration was 20.86 mg/mL (SD=8.46) in impaired union group (20.21 ng/mL, SD=8.31 in atrophic pseudoarthrosis subgroup) and 19,32 ng/mL (SD=12.76) in normal bone union group. No difference was reported between groups in Wilcoxon test for observation pairs ($p>0.1$). In both groups vitamin D deficiency was present in 86% of patients.

The impact of vitamin D concentration on the success of bone union was assessed using McNemar test (Table 1.) No relationship was shown.

Discussion

It was shown that vitamin D deficiency is present in 86% of patients treated in our clinic due to a failure of fracture healing. In other studies, conducted in Texas (30 degrees of northern latitude), vitamin D deficiency was reported in 57% of patients [4]. We think that the difference in deficiency prevalence is a result of latitude discrepancies. In another study examining the same problem, deficiency was demonstrated in all seven patients [5]. The lack of control groups in previous studies makes it impossible to see whether deficiencies noted by the authors are specific for healing failure or reflect the status of a population treated due to a fracture. The impact of yearly variability on vitamin D concentration has not been excluded in previous studies [7]. The interpretation of obtained results is hindered by these significant drawbacks.

The conducted study was designed to compare vitamin D concentration in patients with fracture healing failure and those with normal healing process in such a way that could

Table 1. Table cells represent number (and fraction) of pairs with similar or different concentration of vitamin D. In 71% of pairs both subjects were vitamin D deficient, whereas in 14% – patient from non-union group was vitamin D deficient and patient from union group represented normal vitamin D concentration. In 14% of pairs non-union patient had vitamin D above 30 ng/mL and union group patient was deficient. Vitamin D concentration did not influence bone union (McNemar's test, $p>0.1$).

35 pairs	Union group		Total
Non-union group	Vitamin D <30 ng/mL	Vitamin D >30 ng/mL	
Vitamin D <30 ng/mL	25 (71%)	5 (14%)	30 (86%)
Vitamin D >30 ng/mL	5 (14%)	0	5 (14%)
Total	**30 (86%)**	**5 (14%)**	**35 (100%)**

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exclude main factors affecting this vitamin concentration variability. No difference was shown between these two groups with respect to vitamin D concentration. The reduction of vitamin D concentration was not a risk factor or union failure. This observation casts doubt on earlier reports suggesting that reduction of vitamin D concentration may be a potential goal in bone union impairment treatment [4,5]. At the same time, it is advisable to compensate for this deficiency.

There are some significant limitations associated with this study. Due to retrospective data collection, the assessment of patient use of NSAIDs/COX2, which can affect healing ability, was limited. Moreover, a substantial prevalence of vitamin D deficiency was observed in both groups, which is probably the effect of Otwock's geographical location. Finally, the aim of the study was to compare vitamin D concentration between groups. For this reason, we have not measured other variables, the analysis of which could be useful: PTH concentration, calcium, bone turnover markers.

Conclusions

There is no difference in vitamin D deficiency prevalence between patients with normal and impaired bone union.

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