EFFECTS OF LOW STATUS OF VITAMIN D ON BONE MINERAL DENSITY AND OSSEOINTEGRATION

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Summary
Aim. To evaluate the effect of low vitamin D status on bone mineral density and implant osseointegration.
Material and methods. A systematic literature review was performed of observational studies in English identified in MEDLINE (PubMed), Cochrane Central Register of Controlled Trials (Cochrane Library), Springer Link, Science Direct and Google Scholar databases, published between 2011 and 2021. Studies had to be performed in vivo.
Results. 135 publications were found, out of which 4 observational studies were identified as relevant to the theme and underwent systematic review: 2 case reports, 1 cross-sectional study and 1 retrospective cohort study.
Conclusion. The published data is not sufficient to confirm a specific effects of low vitamin D status on bone mineral density and osseointegration. Although, the published results are promising more prospective randomized controlled clinical trials are required in order to confirm the presence of an association between low serum levels of vitamin D and an increase in the incidence of early implant failure.

Introduction
Vitamin D, like calcium, has long been regarded as a fundamental part of the prevention and treatment of osteoporosis [1].
The prevalence of low vitamin D status depends on the cutpoint used, however, many studies report that more than half of the population studied is “low”. Due to inadequate dietary intake combined with sun avoidance, low vitamin D status is extremely common. Inadequate vitamin D status may have multiple adverse health consequences, including skeletal fragility, muscle weakness, and potentially, a multitude of non-skeletal morbidities [2].
In recent years the percentage of patients with mineral imbalances, such as vitamin D deficiency, affecting the bones and teeth has been increasing [3].
There are studies that prove a direct link that osteoporosis is caused by an imbalance of vitamin D even to the number of people who were not previously at risk of osteoporosis [1,4].
The purpose of this study is to investigate any possible correlation between the imbalance of vitamin D and indirect effect of bone density, periodontal disease status and tooth loss.

Methods and material
A systematic literature search was performed according to PRISMA guidelines in search of clinical trials published between 2011 and 2021. Electronic and manual literature searches were conducted independently by all authors in several databases, including MEDLINE (PubMed), Cochrane Central Register of Controlled Trials (Cochrane Library), Springer Link, Science Direct and Google Scholar. Databases were searched using different combinations of the following key words: vitamin D, deficiency, osseointegration, mineral density.
The titles and abstracts first were analyzed, followed by the selection of complete articles for careful reviewing and analysis according to the eligibility criteria. All animal and in vitro studies were excluded. Publications that met inclusion criteria were drawn to the qualitative analysis study pool. From this, publications that met qualitative assessment criteria were selected into this literature review.
Research results

Vitamin D: production and mechanisms of action.

Vitamin D, or calciferol, is an inactive pro-hormone that follows a complex metabolic pathway and requires conversion to calcitriol (1,25-dihydroxyvitamin D) to exert a physiologic effect. Vitamin D comes from two major sources: exposure to sunlight and dietary intake. After exposure to sunlight, vitamin D3 (cholecalciferol) is synthesized in the skin from precursor compounds. Cholecalciferol and vitamin D2 (ergocalciferol) can also be ingested from supplements or diet. Regardless of the source, both cholecalciferol and ergocalciferol must undergo two enzymatic reactions to become physiologically active. The first occurs in the liver, where cholecalciferol and cholecalciferol are converted to calcidiol (25-hydroxyvitamin D; 25-OHD). Although not the active form, calcidiol is the major circulating form of vitamin D and is the compound measured in the laboratory when serum vitamin D levels are ordered. Calcidiol subsequently undergoes conversion in the kidneys to calcitriol, the biologically useful form of vitamin D [5].

Vitamin D is well known for its role in calcium homoeostasis and bone metabolism. Vitamin D increases the levels of calcium and phosphate in blood by stimulating intestinal absorption, bone resorption and renal reabsorption. It helps provide optimal conditions for bone mineralization and is important for the developments and maintenance of the mineralized skeleton. Vitamin D also activates phagocytosis involving monocytes and enhances monocytes differentiation. Moreover, Vitamin D has anti-inflammatory properties and has non-calcemic effects on the body [6].

The classical target tissues of Vitamin D are bone, intestine, and kidney. In bone vitamin D stimulates the activity of osteoclasts and increases the production of extracellular matrix proteins by osteoblasts. Vitamin D deficiency has also been linked to impaired fracture healing in the clinical practice, and vitamin D accumulates in the fracture callus in preclinical studies. Serum vitamin D is also reduced in patients suffering a fracture. Together, these results support the role of the steroid hormone in controlling bone regeneration. As osseointegration of dental implants also depends on bone regeneration, peri-implant bone formation was reduced in vitamin D deficient [7].

In total, the initial search strategies generated 135 articles. After the first evaluation duplicates were identified and excluded. After screening 10 potential articles were selected for full article review and 6 were excluded because they lacked at least one of the required inclusion criteria. Finally, 4 observational studies fulfilled all inclusion criteria and underwent systematic review: 2 case reports, 1 cross-sectional study and 1 retrospective cohort study.

Kim H. et al investigated cross-sectional data from 5045 Koreans aged ≥ 50 years with severe periodontal disease parameters associated with vitamin D serum levels which were classified as reflecting severe deficiency, deficiency, insufficiency, or sufficiency. Overall severe deficiency, deficiency, insufficiency, or sufficiency were 6.5%, 67.9%, 22.4%, 3.2% respectively. This population based cross-sectional study indicates that low serum vitamin D is significantly associated with tooth loss and severe periodontitis in Korean aged 50 years and older [6].

Diachkova E. et al presented case report about the experience of six years of treatment with dental implants in a patient with a secondary loss of tooth and mineral imbalance (osteopenia) due to vitamin D deficiency in collaboration with endocrinologist. The bone system was monitored through regular blood test, skeletal bone densitometry and x-ray of maxillofacial region and special medication was prescribed in this pathology. This management plan allowed dental implants to be maintained in a good condition for 7 years. Summarizing all data presented in the article and following authors recommendations patients with partial secondary loss of teeth must be recommended to get blood test performed for key signs of mineral imbalance before dental implantation. If bone mineral metabolism disorder is detected patient should consult endocrinologist for further investigation and if necessary special therapy with vitamin D should be prescribed [3].

In two case reports presented by Fretwurst T. et al an association between vitamin D deficiency and early dental implant failure was highlighted. Article illustrates two case reports where both patients received dental implants from different manufactures in molar region in the mandible together with bone grafting which within 15 days after implant placement were removed. Vitamin D serum level were measured and both patients showed deficiency (serum vitamin D level < 20 μg/l). After vitamin D supplementation implant placement was successful in both patients [8].

According to Mangano F et al study severe deficiency of vitamin D in the blood might be related to an increase in the incident of early implant failure. A retrospective evaluation of 1625 implants placed in 822 patients were considered the main target in this study. 27 early failures were recorded of which vitamin D levels were taken from blood tests. Statistical analysis reported 9 early failures in patients with serum level of vitamin D less than 30 μg/l, 16 early failures in patients with levels between 10-30 μg/l, and 2 early failures with less than 10 μg/l. Therefore, the continuous treatment of patients with low vitamin D serum levels was not performed the study does not prove affective link between low serum levels of vitamin D and increased risk of early implant
failure. However, it should be considered that all 27 early implant failures were detected with low vitamin D levels [9].

Currently, the number of people with mineral balance disturbances is increasing. This hormone has a crucial function in skeletal mineralization, bone remodeling, but also plays an important role in immunity and inflammatory response, increasing anti-inflammatory cytokines and decreasing pro-inflammatory ones [10]. Bone remodeling, a balance between bone formation and bone resorption, is defective in vitamin D deficiency. Whereas the initial osseointductive event is independent of vitamin D but the other factors that may intensify and modulate the cellular processes are dependent on the vitamin D.

Relatively small number of experimental studies has attempted the effects of vitamin D on the osseointegration process. Most of these studies are preclinical and would appear to indicate the positive effect of vitamin D on osseointegration, but it is not yet entirely clear wether supplementation would promote the healing of bone tissue clinically. This is probably due to the fact that there are many factors which can determine the success or failure.

**Conclusion**

More and more scientists are paying attention to the need for an integrated approach for treating patients with vitamin D deficiency, by adding endocrinologist to the medical team and working closely with them. Therefore, randomized clinical trials are needed to confirm the presence of an association between low serum levels of vitamin D and an increase in the incidence of early implant failure.

**References**


**VITAMINO D TRŪKUMO ORGANIZME POVEIKIS KAULŲ MINERALINIAM TANKUI IR OSTEOINTEGRACIJAI**

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Raktažodžiai: vitaminas D, trūkumas, osteointegracija, mineralų tankis.

Santrauka

Tikslas. Įvertinti vitamino D trūkumo organizme įtaką kaulų mineraliam tankiui ir implantų osteointegracijai.


Rezultatai. Rastos 135 publikacijos, iš kurių 4 stebėjimo tyrimai nustatytų susiję su tema ir sistemingai peržiūrėti: 2 atvejų atsakymai, 1 retrospektyvus kohortinis tyrimas, 1 skerspjūvio tyrimas ir 1 retrospektyvus kohortinis tyrimas.


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