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NUTRITIONAL MODULATION OF OSSEOINTEGRATION: A NARRATIVE REVIEW

Dentistry

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ABSTRACT

Osseointegration of dental implants is the key for implant success. Factors like implant biomaterials, their surface modification, type of prosthesis, grafting materials and operator skills contribute a major part for proper osseointegration. Additionally, immunity of host, and local factors such as bone quality and quantity, patient's nutritional status also plays a wholesome role in determining the success of the dental implant. Several studies confirmed that vitamins and minerals like calcium and Vitamin D have crucial role in the formation and maintenance of proper bone health around implant. However, other nutritional factors which include vitamin A,B,C,E,K and magnesium, phosphorus, fluoride and antioxidants like resveratrol are also a contributing factor for remodelling of bone tissue in the surgical site. It is always recommended to check for host's immune status and maintain the required level of vitamins and minerals in patients before undergoing dental implant treatment (DIT). This current review provides deeper insight about the significance of micro and macro nutrition in implant osseointegration.

KEYWORDS

Implants, Osseointegration, Nutrients, Vitamins, Minerals, Host immune status.

INTRODUCTION:

Dental implants have gradually superseded traditional tooth replacement modalities for rehabilitating partially or fully edentulous arches over time. Over the years, implant therapy has become a corner stone of restorative dentistry, offering a long-lasting, predictable and aesthetically favourable replacement option.

Successful osseointegration depends on a synergistic interplay between implant surface characteristics and host related factors. Implant surface characterisation encompasses topography, roughness, chemistry, surface energy charge and ion release properties, all of which influence protein adsorption, cellular behaviour and osseointegration.

The cellular and molecular physiology of osseointegration starts with a physiological integration of bone and implant, following the process of primary bone healing. Immediately after implant placement, the intercellular matrix proteins derived initially from the interstitial fluid, blood and from the cellular activity coat the implant surface. Via this protein layer, cell adhesion, migration, and differentiation are initiated, helping an interaction of the cells with the implant surface for several hours or days. These biological cues collectively influence and govern the process of osseointegration.

Although significant advancements have been made in enhancing implant surface characteristics, relatively less attention has been focused on the biological activity of the host bone which is also the crucial determinant of successful implant integration and long-term implant stability.

Historically, efforts to improve implant success have mostly concentrated on implant material, design, surface characteristics, surgical techniques, and mechanical loading. However, failures still occur despite high success rates and survival of implant therapy.

Implant failures can be categorized as "early dental implant failures" (EDIFs) or "late dental implant failures" (LDIFs) based on chronological criteria. EDIFs are caused by unsuccessful osseointegration, which indicates impaired bone healing. Factors leading to EDIFs include both local and systemic factors, such as inappropriate surgical and prosthetic protocols, operator experience, implant-related variables such as material, design, and surface characteristics. Systemic and patient-related factors including the host's bone volume and quality, immune response, history of radiotherapy, medication use, smoking and other parafunctional habits, as well as general health. These factors can significantly impair bone tissue repair mechanisms and bone metabolism processes ultimately compromising implant osseointegration. LDIFs are caused by loss of osseointegration, which is typically linked to infection (peri-implantitis), occlusal overloading, failure or fracture of the implant components.

Host defence and nutritional status are critical determinants of osseointegration as they promote bone formation and facilitate biological process necessary for implant integration and long-term survival. The host's nutritional status which includes a number of micronutrients like vitamin D, C, E, K, calcium, phosphorus, magnesium, resveratrol and zinc have been found to positively influence bone health.

Hence, specific dietary practices and nutritional balance before and after dental implant surgery may offer the best way to maximize healing in surgical site. Aim of this review is to summarize the available experimental and clinical evidence on the function of calcium, vitamin D, and other micronutrients in implant osseointegration.

Role of vitamins and minerals in osseointegration:

The ossification process surrounding the dental implant can be influenced by a variety of factors, such as hormones, nutrition, and supplements.

Vitamin D: One of the most important micronutrients for dental implant osseointegration is vitamin D. It is one of the eighteen components included in the European Register of Nutrition and Health that directly impact bone (one of the "standard" tissue targets) and teeth.

The vitamin D serum level plays a predominant role in bone metabolism since it stimulates the activity of osteoblasts and increases the production of extracellular matrix proteins. Vitamin-D also promotes the osteoblastic expression of osteopontin, osteocalcin as well as chondroitin sulfate glycosaminoglycans in extracellular matrix. By this mechanism an extracellular matrix will be laid down by these cells and an initial immature bone (bone callus) called the woven bone is formed.

Vitamin D has also been found to be essential for the maturation and proper functioning of bone cells for increasing osteoid mineralization that helps in stabilization of implant during healing phase. Beyond modulation of bone formation, vitamin D has an impact on the innate and adaptive immune response in the field of osteoimmunology and could therefore influence early implant healing. Bone necrosis during implant bed preparation or placement is considered as a reason for early implant failures. Vitamin D regulates the migration and differentiation of osteoclast precursor monocytes. These osteoclasts play a vital role in removal of bone debris in the implant site. Low vitamin D levels may lead to altered cytokine release by immune cells leading to dysregulation of osteoclast activation and differentiation. Such disturbances can compromise bone remodelling and negatively osseointegration.

Calcium, Phosphorus and Magnesium:
Calcium plays a major role in mineralization of bone, around dental implants and provides skeletal strength, which is a well-regulated Multistep process. Calcium promotes biphasic formation and deposition of HA (hydroxyapatite) crystals with the help of calcium binding acidic phospholipids, calcium binding protein and phosphohydrolase like alkaline phosphatase enzymes in the extracellular matrix. Vitamin D regulates calcium homeostasis, by controlling intestinal calcium absorption, renal calcium reabsorption, and bone remodelling. While calcium provides the strength and volume of the implant bone, Phosphorous provides the structural integrity and density needed to secure a load bearing implant. Magnesium converts dietary vitamin D into its active form which is necessary for the body to absorb and utilize calcium. Also, magnesium stabilises immediate implants and enhances radiodensity of the bone around implants Magnesium has also been shown to inhibit bacterial growth and reduce biofilm formation, promoting soft tissue integrity around implants.

Vitamin C: Vitamin C and Calcium primarily influence collagen and callus development in implant bone interface. Vitamin C supplementation can lower the PTH levels in circulating blood, thereby it inhibits bone resorption to maintain serum calcium levels. In an osteoporosis state, vitamin C can increase the expression of the osteoblast-specific genes BMP-2, SMAD1/5/8, RUNX2, osteocalcin, and COL-1, furthermore, through the Wnt/β-catenin signalling pathway, vitamin C has been shown to promote osteoblastogenesis and suppress osteoclastogenesis. Additionally, tissue integrity and healing around dental implants may be impacted by vitamin C. Collagen biosynthesis, a component of the connective tissue of the gingiva, peri-implant mucosa, and alveolar bone, also depends on the level of vitamin C in tissue matrix. [11]

Vitamin E: One of the vitamin E family, α-tocotrienol, has an impact on bone biology, particularly on osteoclast differentiation and bone loss, by significantly suppressing the production of RANKL - a crucial component of osteoclast differentiation and the expression of c-Fos in osteoclast precursors. Additionally, α-tocotrienol significantly reduce the mature osteoclasts ability to resorb bone through the calcium-phosphate apatite-coated OAAS (OsteoAssay) plate. Also, it inhibits osteoclastogenesis by decreasing the expression of receptor activator of nuclear factor kappa B (NF-κB) ligand (RANKL) in osteoclasts.

Vitamin K (MK-7 -vitamin K2): One of the most prevalent non-collagenous proteins in bone is osteocalcin. Osteocalcin is produced by osteoblasts and secreted into the extracellular matrix of the bone, where it attaches itself to hydroxyapatite crystals. Binding of osteocalcin to hydroxyapatite is dependent on the carboxylation of three Glu residues by vitamin K2. And, vitamin K may also influence the transcription of genes necessary for the production of osteoblastic markers and collagen assembly, in addition to γ-carboxylation of osteocalcin.

Vitamin A: Retinoic acid (RA), a molecule generated from vitamin A, is implicated in the up-regulation of osteogenic genes, which increases the osteogenic differentiation of several cell types, including mesenchymal stem cells, osteoblasts, preadipocytes.

Vitamin B: Vitamin B6 acts as a substrate of alkaline phosphatase in bone formation and play a role in the coupling between osteoblasts and osteoclasts where calcification depends on periosteal glucose 6 phosphate dehydrogenase (G6PD) activity, which is induced by putrescine, a compound derived from a B6 dependent enzyme, ornithine decarboxylase. Physiologically, B12 is linked to the action of enzyme methionine synthase, which is involved in the metabolism of homocysteine. Studies suspect that B12 deficiency may cause, hyper homocysteinemia which in turn stimulates osteoclastogenesis leading to bone repair.[7]

Resveratrol: Resveratrol is an antioxidant which activates the PI3K/Akt, SIRT1, AMPK, and GATA-1 pathways to promote osteoblastogenesis. It also decreases inflammation by activating the Hippo/YAP pathway and mitigates oxidative stress and inflammation by activating the NRF2 pathway and by decreasing the ROS/HIF1α and Nox4/NF-κB pathways. It inhibits osteoclastogenesis by suppressing the MAPK and TRAF6/TAK1 pathways. Furthermore, resveratrol promotes autophagy through AMPK/JNK1 activation, which improves osteocyte activity and contributes to bone homeostasis.

Fluoride: Fluoride can act on osteoblasts and osteoclasts, in the trabecular bone resulting in increase in volume and trabecular thickness. At local concentrations such as those that occur following fluoride modification of dental implants, there is enhanced osteoblastic differentiation and interfacial bone formation concomitant with increased expression of osteogenic markers at the implant site.

Other trace minerals like zinc, copper and manganese acts a critical cofactor for enzymes that synthesize and crosslink the collagen matrix which serves as the foundational scaffolding of bone.[7] Further zinc stimulates bone formation and helps maintain bone mass. Copper promotes vital blood vessel growth(angiogenesis)and Manganese regulates bone remodelling and protects cells from oxidative damage.

DISCUSSION:
Several micronutrients are hypothesized to have an influence on skeletal system, particularly on jaw bone and alveolar bone and on dental implant osseointegration. According to recent national surveys, Indian nutritional status is characterised by double burden of malnutrition-the coexistence of undernutrition and overnutrition within the population. Dietary patterns often provide sufficient calories but may lack adequate protein quality and essential micronutrients. Vitamin D deficiency is the most prevalent affecting approximately 60 -90% of the population followed by iron, vitamin B12, Folate, zinc, calcium and vitamin A. Very few elements (i.e., vitamin D, magnesium, resveratrol, and vitamin C) were the matter of previous investigations on their role in dental implant osseointegration.

Fretwurst et al confirmed successful Implant osseointegration after vitamin D supplementation in patients with vitamin D deficiency and EDIF.

Schulze-Spate et al investigated the effects of calcium (600 mg) and vitamin D3 (5,000 IU) on the production of new bone after sinus lift surgery in a randomized, controlled, double-blind study. Calcium and vitamin D3 administration shown to have positive effects on bone growth when histology was performed 6–8 months after surgery.

Kwiatek et al, observed significantly higher bone density in patients who took vitamin D supplements after 12 weeks, suggesting that vitamin D has a positive effect on bone quality. They also proposed that having the right amount of vitamin D on the day of implant placement and treating vitamin D deficiency after surgery can increase the bone level at the implant site during osseointegration as assessed radiologically. Thus, maintaining bone density and promoting the healing process in bone regions impacted by dental implant treatments are depends on maintaining adequate levels of vitamin D, especially those with systemic diseases like osteoporotic condition, diabetes mellitus etc.

Recent studies by Mangano et al have shown that vitamin D deficiency has been linked up to 300% increase in early dental implant failure and is potentially associated with a number of other dental-related complications. Hence, he proposed, that vitamin D treatment should be continued until the necessary levels are reached before implant surgery, particularly in patients with severe deficiencies.

Wagner et al., evaluated the influence of osteoporosis on the marginal peri-implant bone level. Osteoporosis was shown to have a significant negative influence on the marginal bone loss (MBL) at the mesial and the distal implant aspect. Vitamin D positively and significantly affected the MBL, showing beneficial effects on the peri-implant bone formation.

Wu et al, combined the effect of insulin and vitamin D3 on implant osseointegration in diabetic mellitus rats. This study led to an improvement of bone volume per total volume, percentage of osseointegration, mean trabecular thickness, mean trabecular number, connective density, maximal push-out force, and ultimate shear strength, BIC, and bone area ratio (BA). These indexes showed values comparable to those of healthy control rats.

Del Barrio et al, found that magnesium intake reduction of 90% in diet of rats led to a statistically lower removal torque of the implants compared to rats fed with the recommended magnesium content, while no difference was demonstrated between the group with a 75% magnesium reduction and the control group.

In order to assess the impact of resveratrol consumption on titanium implant osseointegration, Casarin et al. in 2014 carried out an animal investigation. They concluded that resveratrol consumption improved biomechanical retention of the implants because rats given resveratrol had noticeably higher average counter-torque values during implant removal.

Li et al. in his study reported that vitamin C administration enhanced postoperative wound healing after dental implant surgery. They explored the effects of vitamin C supplementation in wound healing, following placement of dental implants with or without bone grafts and patients with chronic periodontitis. Patients received implants with guided bone regeneration (GBR) or with Bio-Oss collagen grafts and received vitamin C supplements, 14 days post-surgery, showed significantly improved wound healing compared with patients receiving the same surgical therapy but without vitamin C supplements.

Major nutrients involved in skeletal health include calcium, phosphorus, vitamin D, magnesium, and potassium, but other micronutrients and trace elements such as boron, selenium, iron, zinc, and copper also impact bone metabolism. Information on the influence of such “minor” elements from studies on osseointegration is still lacking. Data for many micronutrients and dosing regimens for dietary supplements that improve dental implant osseointegration are not defined according to available findings.

CONCLUSION:

Just as implant surface characteristics influence osseointegration, the host's nutritional status represents a modifiable biological factor that warrants assessment and optimization prior to implant therapy to promote predictable implant success. Assessment of patient's nutritional status, including serum vitamin and micronutrient levels, should be considered during pre-implant evaluation, particularly in individuals with risk factors such as advanced age, osteoporosis, mal-nutrition, chronic systemic diseases, smoking or a history of wound healing. Identification and correction of nutritional deficiencies before implant placement may help optimize healing outcomes and enhance implant success.

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