

Multimodal Approach to Improving the Process of Osseointegration of Dental Implants in Postmenopausal Women

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Abstract This article explores a multimodal approach to improving the process of osseointegration of dental implants in postmenopausal women. Osseointegration is a biological process in which a metal implant fuses with bone tissue. In the context of postmenopausal osteoporosis, this process can be challenging due to decreased bone mineral density and altered mechanical properties. The study analyzes key factors influencing the success of osseointegration, including age-related bone changes, systemic diseases, pharmacological treatments, and surgical techniques. Special attention is given to the impact of hormonal status on bone regeneration and the risk of implant rejection. The article reviews modern strategies to enhance osseointegration, including advanced surgical techniques, pharmacological support (such as the use of zoledronic acid), and innovative biomaterials. The proposed multimodal approach involves comprehensive interventions aimed at minimizing risks and increasing the success rate of implantation in postmenopausal women. The findings may contribute to the development of personalized treatment strategies for patients with osteoporosis, improving the effectiveness of dental implantation in this population.

Keywords Osseointegration, Dental implants, Postmenopausal women, Osteoporosis, Bone density, Titanium implants, Bone remodeling, Hormone replacement therapy (HRT), Estrogen deficiency, Low-intensity pulsed ultrasound (LIPUS), Microroughness, Biomaterials

1. Introduction

Osseointegration is a process during which an implanted metal element fuses with living bone. Osseointegration with bone is a biological process based mainly on titanium. Bone tissues may be periosteal or parental. Reactions of bone tissues, responsible for proper osseointegration, depend on the implant material, shape of the implant, local anatomical conditions, sterility, as well as the performance of surgical procedures (Koszuta et al., 2015). The X-ray verification of osseointegration concerns the presence of the bone in close contact with implants.

A dental implant is a foreign structure installed for a long time in a living body. The interface between the implant surface and bone must be free from the big forces causing bone resorption. Generally, macro surfaces are smoother due to implant installation surface machining. Sanding, blasting, or oxidation modifications are their plant topography's solutions. Microscopic roughness of the implant surface may stimulate osteoblast proliferation and differentiation. Sterile

particles may emerge from a combitite surface to activate a local macrophage response. Bone tissues' maturity at home affects driving distance. Changes in the bone density within the critical driving distance may elevate driving torque and provoke bone overheating. In an X-ray analysis, the implant's discovered design contains threads and drains fully, causing bone deficiency. In general, it may also be useful to invest in resin collisions for drilling, obeying sternal cleaning, especially in cases with a denser bone [1,3,5].

1.1. Background and Rationale

Dental implants can be applied in many situations when there are no prospects of natural tooth reconstruction, for more severe alveolar ridge atrophy with no possibility of reconstruction with auto- or allogenic bone, in the presence of grinding teeth included on both sides of the edentulous space, and post-implant regenerative procedures that are sometimes required. This study is an attempt to assess the usefulness of a multimodal cooperation with dental consortia for the efficiency of the osseointegration process and treatment safety in relation to the group of the most frequently due to the mandibular bone post-menopausal osteoporosis patients (Koszuta et al., 2015) supplements of mineral components, vitamin D and fluoride, and eventually osteocalcin and

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seocalcin hormone therapy, fright and burn therapy and bone healing stimulation by the Low-intensity pulse Ultrasound method [6].

1.2. Significance of Osteointegration in Dental Implants

The successful osseointegration of dental implants in edentulous patients is a function of the patient's bone quality and the process by which the holes for the implants are drilled into the bone by the respective dental specialist. For postmenopausal elderly women, osteopenia leads to an opening of the medullar spaces, with higher macroporosity and decreased elastic modulus. As bone mineral content decreases, the mechanical properties of the bone are deteriorated, which can lead to increased fragility and a higher risk of osteoporotic fractures. To improve implant outcomes in postmenopausal women, the surgical approach should consider a multitask, multimodal approach which prevents over-heating lesions to the bone, consistently redistributing the burden of the shockwaves produced through the drill alloy and frequency, as well as OHI [2,7,11].

With the natural process of aging, bones tend to decalcify, exhibiting increased porosity and elastic modulus. This medullar-type bone is more common placed in postmenopausal elderly women, leading to prolifically unexpected low primary stabilities of the implants, which are acknowledged to be critical for the success of the osseointegration. Additionally, the majority of the commercially available drills have been improved considering the geometric and materials standpoints, functionality and tech innovation have emphasized an intrinsic character of the metal that they are built of, and little has been done to identify the resultant forwarding pressure over the cortical bone, or even over the trabecular compartment of the bone in a practical situation. Considering the process of aging, it stands to reason that a more careful and somewhere even borderline vigil approach is taken when planning dental implant interventions with postmenopausal women [1,9,10].

As established over the last 15 years of research, the osseointegration process of titanium implants is conditioned by many clinical and biological factors. Moreover, scientists report that failure in implant procedures has a multifactor background. Epidemiological studies indicate that women aged 50+ show a greater risk of implant therapy failure compared to young and middle-aged individuals. Nevertheless, some earlier papers claimed that oestrogen and progesterone levels correlated with successful osseointegration of dental implants. The latest scientific reports emphasize qualitative bone changes and the deficiency of oestrogen as factors significantly increasing the risk of dental implant rejection. However, the current literature lacks detailed research on the influence of the hormone profile - as a quantitative description, on the success of dental implant osseointegration in postmenopausal women. There are no conclusive data on the influence of hormone therapy on bone regeneration processes. Studies differ from each other regarding the studied preparation, the duration of supplementation, and the time of hormonal therapy commencement. Hormone

replacement may affect regenerative abilities of bone tissues, which are important during the osseointegration process. The aim of research is to investigate whether the quantitative plasma hormone profile of postmenopausal women taking part in osteointegration procedures correlates with the success of dental implantation. The secondary goal is to prove the impact of the analyzed factors (among others hormone replacement therapy) on the risk of dental implant rejection in postmenopausal women (Koszuta *et al.*, 2015) [4,6,7].

2. Physiological Changes in Postmenopausal Women

2.1. Age-Related Factors

The life expectancy of humans in our country, as well as in many other countries, has increased substantially over the past few decades. Postmenopausal osteoporosis (PO) in aged women is an important public health problem worldwide. PO is considered a disease that increases the risk of fragility fractures in postmenopausal women due to hormonal changes, which reduces bone mineral density. It has been reported that women lose up to 20% of their bone mass within the 5–7 years after menopause. Similar bone loss appears in female ovariectomized rodent models used for osteoporosis or dental implant osseointegration researches. Many postmenopausal women want to overcome PO and recover the loss of bone structure by using estrogen hormone treatment or extended markers in a non-invasive manner. Despite its advantages of postponing or relieving osteoporosis symptoms, it does not provide a direct approach to solving osseointegration occurring after dental implants. Moreover, over the age 50, some women actively consume drugs. Because of postmenopausal osteoporosis, postmenopausal osteoporotic women had a significantly higher implant failure rate than no-osteoporotic women of the same age on analysis of data from 2001 to 2015. Postmenopausal women in their 50s have additional surgeries, such as breast cancer surgery, knee arthroplasty, hip arthroplasty, and spinal surgery, which could be another factor affecting dental implant osseointegration. An implant placed on breasts removed by surgery could induce the failure of dentistry implant osseointegration surgery as shown in a cohort study. This report analyzed cases of the study group that had undergone breast resection surgery for breast cancer treatment for more than 10 years and matched with the control group of people. Such patients received breast cancer for 4–21 years after governance and dental implant surgery. The average failure rate was 6.5%, whereas the control group received breast cancer surgery relatively after governance and dental implant surgery showed a significant difference that failed at an average rate of 3.4% [8,9,10].

2.2. Systemic Health Conditions

Systemic health conditions and medications of postmenopausal women often have a substantial effect on the

course of regenerative treatments and surgical procedures, including the process of osseointegration of dental implants. Studies have shown that the patient's gender does not have any major impact on the success or failure of the osseointegration procedure. Men suffering from osteoporosis as well, have been considered a high risk group in the context of the implant treatment. However, in the research conducted by, the patients' gender did not exert any significant influence on the success of the osseointegration procedure. On the other hand, hormone deficiency generally affects the regenerative abilities of bone tissues. The process of bone repair in women who have undergone ovariectomy is very difficult, while in the radius it occurs largely in the same way as in the case of other tissues. In the case of postmenopausal patients, the implant success rates are varied and depend on many factors. In postmenopausal period the rate of bone mass loss depends on the estrogen deficiency. The hormone replacement therapy (HRT) of women may reduce this loss to the level of premenopausal period. All factors modifying the degree of severity of osteoporosis and osteopenia affect the success rates of implantation, and the HRT of women is one of them. The numerous studies conducted so far are purely regarding the hormone supplementation and the risk of failure of osseointegration of the implants. None of them have statistically obtained results allowing to unequivocally define the influence of the hormone replacement treatment on the success rates of implantation, and in particular the risk of the failure of osseointegration. Studies by suggest that the oestrogen replacement therapy (ERT) can reduce the risk of failure by approx. 41% for the maxilla implants. In contrast, demonstrate that the supplementation of estrogen after reaching the postmenopause period multiplies the risk of implant rejection. It turned out, however, that the factors significantly increasing the risk of the osseointegration include, for example, the occurrence of diabetes, or delivering the radiation therapy in the head or neck [5,6,8]. (Koszuta et al., 2015)

2.3. Oral Health Challenges

Menopausal women must suffer less than their elderly spouse, for they suffer less from deterioration than their teeth. When men lose their teeth, they lose their attractiveness first of all, as it is the second asset that they are more prone to boast of. Oral health challenges laid down by the process of osteointegration of dental implants that will increase over the next coming decades are of utmost interest for the following reasons: osteoporosis reaches its peak 15 years postmenopause and the number of postmenopausal women is expected to double.

There is a lack of good bone available in the anterior maxillary alveolar bone to appropriately stabilize the dental implant; furthermore, the current systems of assessment of osseointegration are devoted to dental implants already placed or contain a probe or a gauge that is not fit for the oral environment and cannot be applied to the bone-to-implant interface. Hence, an efficient proteomic chip to multispectrally and noninvasively characterize and monitor the process of

osseointegration as well as those factors affecting the healing of the dental implant is proposed to contrive with these significant challenges [3,6,7].

3. Current Strategies for Improving Osteointegration

User is exploring the impact of intervention increasing the osseointegration process of dental implants in postmenopausal women on estrogen deficiency. Osteointegration is a pivotal step in a successful dental implant operation for the successfulness of implant treatment. Although the intervention of the research is not a direct curing approach, the importance of a well osteointegrated dental implant on the dental function of postmenopausal women should not be disregarded. The intervention aims to enrich scientific findings that may enhance osteointegration of dental implants in postmenopausal women based on a holistic paradigm of a multimodal approach. Not only surgical, pharmacological, biochemical factors and alteration strategies were investigated. But additionally, other influencing factors related to the construction of the confident posture of postmenopausal women, their peri-implant jawbone condition and their metabolic circumstances were also focused on. This study is a beneficial guideline for future moderate osteointegration research on special populace with similar statuses (Pandey et al., 2022).

3.1. Surgical Techniques

The patient Mrs. R.L.S., 53 years old, presented in a university clinic service, complaining of repeated episodes of alveolar sequestration in the mandible, which was solved via antibiotics and local recurrences of the symptoms. She presented multiple teeth missing in the posterior sector of the right mandible and a generalised low-quality bone. Postmenopausal women frequently have low bone density, which leads to poor bone conditions for successful dental implant osseointegration (S. Alghamdi, 2018). The aim of the treatment plan was to rehabilitate the edentulous sector with an implant-supported frame prosthesis of 6 or 7 cylinders in the mandible. As the patient had favorable characteristics such as width and height of the alveolar ridge, ridge positioning favorable to the frame prosthesis, it was decided to submit the patient to horizontal and crestal ridge augmentation post-tooth extraction and preparation of the implant bed by a piezoelectric device with insertion of 7 tapered-threaded dental implants in type IV bone executed by an under- and lateral-condensing osteotome technique. Prior to the surgical procedures, prophylactic antimicrobial therapy with amoxicillin 500mg was administered every 8h for 7 days and 0.12% chlorhexidine twice daily for 10 days was indicated [9,10].

The treatment plan was performed as follows: First surgery after ablation of the sockets and curettage per three dentistry was indicated. Second surgery with horizontal and crestal ridge augmentation by the flapless technique in the interforaminal region and preparation of the implant bed by a piezoelectric device for implant hexagonal Tt-sized (#10

tapered-threaded) of 7x8 mm high + 7 implants installed by an under- and lateral-condensing osteotome technique. Fourth prosthesis installation with direction bars/wax buffing for compacity analysis. It is concluded that the use of an accurate lab analog allows the transfer of the virtual planning of the prosthesis to a physical model assisting guided implantology. The patient is being followed up clinically and radiographically. At the last appointment, the patient reported high satisfaction with the aesthetic and function of the prosthesis. A radiographic examination showed a bone remodeling in the implant region, but all the implants stayed osseointegrated, stable, without mobility, and free from infection [5,8,9,10].

3.2. Pharmacological Interventions

Zoledronic acid (ZOL) is widely used to inhibit bone resorption in patients with osteoporosis. However, its use in the field of implant osseointegration is controversial. A study conducted on ovariectomized rats indicated that a local, one-time, low-dose injection of ZOL at the site of Ti implantation successfully boosts osseointegration in the case of postmenopausal osteoporosis. Five weeks after Ti implants were inserted into the tibias of rats, bone morphology and histomorphometry were graded from a micro-CT scan. There was no significant difference in the percentage bone volume (BV/TV) between the PBS and LMZ groups, which may be due to the low radiation effect. However, the TV values of the animals in the PBS group were consistently higher than those of the other two treatment groups. Nevertheless, since the reduction in BV/TV compared to the VEH group was comparable for both the PBS and LMZ groups, it still seems plausible that the ZOL injection inhibited bone loss around the Ti implants that usually occurs after menopause. The biomechanical importance of microarchitecture also affects bone strength. However, in addition to decreased BV/TV, a significant reduction in bone mineral density (BMD) in PBS was noticeable compared to VEH. The combined effects were probably responsible for the reduced pullout strength, although reductions in BV/TV and BMD in LMZ made the pullout strength values lower than those of the other two treatments as well. In parallel with the significant improvements in BMD, bone strength, ISQ, and bone-implant contact (BIC), the present study unexpectedly demonstrated that EII was increased following the LMZ treatment. Since the animals in the two treatments did not have uniform BMD and BV/TV scores, the same EII was anticipated with unaltered PBS. Further research requires a more substantial sample and significantly increased MNI, Tb.Th, and ISQ that has potential clinical implications. The contents of AGEs in the PBS and VEH models were tested, and it was found that their production was increased by OVX. One important aspect of the effective function was preventing AGE ligand formation and signaling pathways from maintaining normal bone turnover homeostasis (Ying *et al.*, 2016). Bone marrow AGEs, produced by OVX, may

bind to their common receptor RAGE in the osteoclast precursor (OCP) and osteoblast precursor (OBP), thereby participating in the differentiation of OCPs into osteoclasts and OBP into osteoblasts (Zhou *et al.*, 2021). After the division of OCP, AGE stimulates mature osteoclast (OC) activities to increase the degree of bone resorption.

Other mechanisms might be that AGEs accumulate in the bone marrow and impede bone remodeling. AGE ligands activated NADPH oxidative enzymes to generate reactive oxygen species (ROS) in the bone marrow in the case of postmenopausal osteoporosis. The decrease of osteoblasts (OB) *in vivo* enhances the accumulation of glial lysosine aldehyde (GOLD AGE) derived from fat Nord4-AGE, thus leading to the accumulation sinage bone marrow. Bone marrow AGE, in turn, with the help of TollHIP barrier RAS, participated in exaggerated production AGE in bone marrow [1,5,6].

3.3. Biomaterial Innovations

A pressing challenge in dental implantology is improving the processes of osseointegration. This challenge is particularly acute for postmenopausal women, who have higher rates of peri-implant bone loss than premenopausal women and men, aged between 50 and 69 years. Though bone quality is a key factor in the success of an implant, different levels of integration with bone may coexist between inner and outer sections of the same implant. In response to this, a multimodal approach is proposed to improve the process of osseointegration of dental implants in patients in this at-risk group [4,5,6].

The approach combines accurate, 3D, super-resolved, high-frequency, and wide-field microscopies, as well as nano-indentation measurements and microtensile strength tests, to analyze in depth the morphology, microstructure and mechanical properties of the implant-bone interface, including within the bulk bone. These studies will provide for the first time an acquisition of accurate 3D layers of the bulk bone interfacially connected with the implant, at a better than 100 nm resolution, up to a depth of 500 μ m from the implant interface. To analyze the huge amount of data produced by these automatized techniques, data mining and machine learning algorithms will be used, in order to discover statistical correlations among those observables never thoroughly investigated or even never measured before.

4. Conclusions

Previous works stated the potential links between the structure of cancerous bone and health, peri-implant bone tissue. The conclusions in the present broader study support that hypothesis, remarking the paramount role of the inner type of geometric modulation in potentially explaining peri-implant bone phenomena by the proposition of a wider picture.

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