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Effect of Antiresorptive Drugs on Oral Implant Therapy: A Systemic Review

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Abstract

Clinicians who practice implant dentistry are still concerned about the life and longevity of dental implants in patients who have used anti-resorptive drugs. The alveolar bone must undergo significant remodelling to prepare the bone and surrounding tissues for surgery. Furthermore, throughout and after the dental implant's osseointegration phase, the bone around the implant fixture continuously remodels. Anti-resorptive drugs can hinder osseointegration and even cause medication-related osteonecrosis of the jaw (MRONJ). These drugs are used to decrease bone remodelling. Specifically, Bisphosphonates (BPs) can negatively impact osteoclasts and predispose other cells, such as osteoblasts, vascular cells, and fibroblasts, to death. This disturbance may lead to soft tissue toxicity and hinder angiogenesis. Increased BP release from inflammation surrounding dental implants may result in postponed implant failure. This article delves further into how anti-resorptive medications affect oral implant therapy.

Keywords: Implant, Dental, Antiresorptive Drugs, MRONJ.

Introduction

One popular and successful treatment for tooth loss is dental implant therapy, which enhances patients' quality of life about their oral health. [1] Dental implant therapy has been shown to have high success rates, particularly in people with normal bone metabolism. [2] Nonetheless, some individuals who have dental implants or are considering getting them also have age-related illnesses including osteoporosis. [3–5] The lifespan of implant-supported reconstructions in these individuals may be

impacted by some drugs that aim to balance bone metabolism, such as antiresorptive treatments for osteoporosis. [6]

Low bone mass and microarchitectural degradation of bone tissue are the hallmarks of osteoporosis, a systemic skeletal disease that increases bone fragility and fracture risk. [7] An estimated 200 million women worldwide are thought to be afflicted by this syndrome [8], which occurs at the same time as postmenopausal estrogen insufficiency. This condition is linked to bone resorption because of a major increase in osteoclastic activity. [9] Conversely, a major decline in osteoblastic activity is the cause of senile osteoporosis, which affects both men and women after the age of 70. [10]

Because osteoporosis increases the risk of fractures, primarily at the wrists, hips, and vertebrae (spine), it is a public health problem because it contributes significantly to disability and medical expenses. [11] In the United States alone, osteoporosis causes 1.5 million fractures annually, mostly in postmenopausal women. [12,13] Treatment for osteoporosis often focuses on lowering fracture risks through dietary and lifestyle changes, as well as reducing bone resorption using antiresorptive medications that may be taken orally or intravenously and have an appropriate risk-benefit ratio. [14]

By altering bone metabolism, antiresorptive medicines (ARDs) are a family of pharmaceuticals intended to prevent bone resorption. By preventing osteoclasts (OCLs) from differentiating and activating or encouraging their death, they mainly serve to lessen aberrant bone remodelling and excessive bone resorption. [14] Although their modes of action differ, ARDs typically preserve structural integrity and bone density. Bisphosphonates (BPs), a family of drugs that have been on the market for more than 30 years, are the most well-known ARDs. The nitrogen-containing BPs that are now administered, such as zoledronate, alendronate, risedronate, ibandronate, and pamidronate, have a strong affinity for hydroxyapatite and integrate into the bone matrix.

Inhibiting OCL progenitor development and disrupting OCL function are the main mechanisms by which they exhibit antiresorptive effects, which in turn reduce bone resorption and remodelling. [14] A novel class of "biological" ARDs has emerged more recently, utilising monoclonal antibodies to target different bone remodelling-related pathways. Denosumab, [15] a completely humanized antibody of RANKL (Receptor Activator of Nuclear Factor-κB Ligand), is the most often utilized. Denosumab, unlike BPs, does not attach to bone and instead interferes with OCL development by preventing RANKL from binding to RANK. This has an antiresorptive effect. Depending on its intended use (e.g., for osteoporosis or cancer), denosumab is given subcutaneously (sc) and at different intervals. [15]

Osteoporosis and skeletal tumours, particularly primary and metastatic bone cancers, are the conditions for which these medications are most frequently recommended. They are essential in restricting the spread of metastatic illness, avoiding pathological fractures, and minimizing discomfort. ARDs are also utilized to treat less prevalent disorders such as osteogenesis imperfecta and Paget's disease of the bone. ARDs are commonly used in oncology to treat patients with skeletal involvement from multiple myeloma and advanced cancers such as breast, lung, and prostate cancer. [16] Medication-related osteonecrosis of the jaw (MRONJ) is a major side effect of ARD therapy, even though ARDs significantly improve bone health.

The hallmark of this disorder is the necrosis of jawbone tissue, which frequently happens spontaneously or after

dental operations and can cause issues with implant therapy and oral health. Studies on both humans and animals indicate that MRONJ arises when antiresorptive drugs are used in conjunction with infection or inflammation. [17] This severe and enduring illness is characterized by patches of exposed necrotic bone in the jaw. By addressing these factors, this research sought to inform clinical decision-making and advance knowledge of dental implant outcomes in patients slated to undergo antiresorptive treatment.

ARDs and their effect

A significant percentage of adults (roughly 15% of those over 50) have osteoporosis and have had or are currently undergoing treatment with ARDs, primarily BPs and denosumab; these medications are also used to treat other conditions, such as primary or metastatic bone cancers. Oral, Subcutaneous (SC), and Intravenous (IV) are the three routes of administration that have historically been used to categorize ARDs. However, it is now understood that dosage, not the exact method of administration, is crucial; as a result, ARDs at low and high doses can now be provided by all three ways. Low doses are mostly used to treat osteoporosis, whereas large doses are used to treat individuals with cancer that has spread to their bones.

Examining potential adverse effects of ARD consumption about several facets of implant therapy, such as fixture installation, bone augmentation procedures, and late biological problems, is pertinent in this context. It is well known that OCL-mediated bone resorption is crucial for maintaining peri-implant bone homeostasis and for different phases of the morphogenesis of dental implant osseointegration. For instance, in the first few weeks after implantation, there is a lot of bone resorption at the thread pitches where the implant is in contact with the bone to achieve primary anchorage, or at the points of pressure. OCL also removes bone fragments from the hard tissue wound around the implant. [18,19]

Additionally, OCLs are essential for maintaining peri-implant bone homeostasis under functional loads (such as bone microcrack repair) and mediate marginal peri-implant bone modelling at later stages of healing to create the marginal hard tissue seal around the implant. [20,21]

It is reasonable to assume that ARDs may compromise aspects of implant therapy because they interfere with bone remodelling, primarily with OCL function, through a variety of mechanisms. For instance, more implants may fail to integrate, or there may be a greater peri-implant marginal bone loss during modelling or functional loading, or those patients may be more susceptible to peri-implant infections. According to the National Health Service (NHS) [22], due to the increased recognized risk of bone necrosis, individuals using intravenous bisphosphonates are often not good candidates for implant therapy. However, those using oral bisphosphates for a brief period are less likely to develop bone necrosis.

The risk of MRONJ and the treatment of patients who start antiresorptive medication therapy after implant implantation and complete osseointegration are two areas that are yet unknown. [23] The majority of MRONJ instances, according to studies, occur in the mandible, especially in the posterior section, highlighting the increased risk of implant placement in this region. [24] Considering these findings, implants in the posterior mandible require cautious planning, with continuous monitoring and frequent follow-ups being essential for detecting problems early.

In terms of implant failure, osseo-integrated implants have a significant failure rate when antiresorptive treatment is started. Furthermore, research indicates that MRONJ often appears during the first three years of antiresorptive medication usage, underscoring the vital need of careful observation during this time. According to another research, MRONJ is more commonly linked to oral antiresorptive treatment than intravenous bisphosphonates. This casts doubt on the widely held notion that using intravenous bisphosphonates is a strict no-go for placing dental implants, indicating that, in some carefully controlled circumstances, implant therapy may still be a viable choice for these individuals. [23,24]

The development of MRONJ may be influenced by peri-implantitis, which emphasizes the significance of preserving ideal periodontal health and putting in place routine monitoring procedures, especially during the first three years after antiresorptive therapy is started. A high probability of successful healing at necrotic areas has been shown for effective management options for MRONJ, such as excision, sequestrectomy, antibiotic medication, and chlorhexidine treatment.

These results highlight the necessity of comprehensive patient evaluation, proactive monitoring, and well-planned treatment strategies to reduce risks and maximize implant results, particularly for patients receiving antiresorptive medication or those with a family history of osteoporosis.

The available data indicates that low-dose oral bisphosphonate therapy for osteoporosis does not substantially impair implant success because, when compared to those who were not exposed to bisphosphonates, these patients do not show increased rates of implant failure or implant-related complications, such as problems with bone grafting, peri-implant marginal bone loss, MRONJ, or peri-implantitis. Nevertheless, there is still a significant dearth of information about the possible impacts of high-dose bisphosphonates or other widely used antiresorptive drugs, including denosumab, on the results of implant therapy.[24]

Conclusion

MRONJ risk should be enhanced in patients with comorbidities, those taking long-term oral bisphosphonate medication, and those receiving large doses of antiresorptive therapy for the management of malignancy. In these situations, the placement and removal of implants as well as the implants themselves might act as precursors to the development of MRONJ. To enable early identification and action, prolonged follow-up periods are advised in light of these hazards. Furthermore, educating patients about MRONJ and its localized effects surrounding dental implants should be a key part of the informed consent process for those who are thinking about getting implant therapy while receiving antiresorptive medication. By educating patients and putting preventative measures in place, medical professionals may improve patient safety and foster implant dentistry's long-term success.

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