Impact of bisphosphonate therapy on dental implant outcomes: a literature review of bone healing, stability, and peri-implant tissue health

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Abstract

Aim. **This literature review aims to evaluate the impact of bisphosphonate therapy on dental implant outcomes by analyzing clinical studies, including randomized controlled trials and multicentric studies, to guide clinicians in managing patients receiving bisphosphonates.**

Materials and Methods. **Studies published in the past 15 years were selected, focusing on human subjects who underwent implant therapy without contraindications. Data were gathered from scientific databases like Scopus, PubMed, and Google Scholar using the keywords "(bisphosphonate) AND (dental implant)." Only randomized controlled trials, clinical trials, and multicentric studies were included. Clinical outcomes such as bleeding on probing, probing depth, implant mobility, marginal bone loss, implant stability, and bone mineral density were assessed.**

Results. **Nine studies from an initial 312 were included. Bisphosphonate-coated implants showed slightly better marginal bone preservation and implant survival than uncoated implants, though the difference was not statistically significant. No cases of bisphosphonate-related osteonecrosis of the jaw were observed in most studies, though complications occurred in high-risk patients. Bisphosphonates appeared to have a less adverse effect on bone healing after implant osseointegration.**

How to Cite

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***Conclusions*. Bisphosphonates can benefit bone preservation around dental implants, but careful management is essential. Further research is needed to standardize treatment protocols for implant therapy in bisphosphonate-treated patients.**

Keywords: Bisphosphonates; dental implants; osteointegration; marginal bone loss; implant survival; bisphosphonate-related osteonecrosis (BRONJ); bone augmentation; implant stability.

Introduction

Implantology has become a widely accepted method for dental rehabilitation, addressing aesthetic and functional deficiencies caused by tooth loss. The practice primarily involves the insertion of titanium implants into the bone of the dental arch to achieve osseointegration (OI)—where the implant integrates effectively with the bone tissue. Successful OI ensures stability and long-term functionality comparable to natural teeth, offering a preferable alternative to removable prostheses, which can be uncomfortable and less aesthetically appealing (1–9).

The timeline for implant integration varies based on the anatomical site. Typically, OI takes about 4-6 months in the maxilla and 3-4 months in the mandibular bone. However, various factors can influence the healing process, potentially extending the required time for full integration. Despite these variables, global studies involving over 1.2 million implants report a success rate exceeding 98%, highlighting the reliability of dental implants (10–24). Notably, this success rate decreases significantly to around 85% among smokers, emphasizing the impact of lifestyle factors on OI outcomes.

Dental implantology is categorized under oral surgery, involving interventions on both hard and soft tissues of the maxillary bones (Figure 1). While generally safe, the procedure requires careful patient evaluation to identify contraindications that could compromise treatment outcomes. These contraindications may be local, such as poor bone quality, or systemic, including general health issues and pharmacological treatments (25–41).

A significant concern in implantology is the use of bisphosphonates (BF)—drugs commonly prescribed for conditions like osteoporosis, osteopenia, osteogenesis imperfecta, and bone metastases associated with malignancies. BF works by inhibiting bone remodeling and increasing bone density, which is beneficial for reducing fracture risk. However, due to their affinity for calcium, their long-term deposition in bone tissue poses risks for patients undergoing implant procedures (42–51).

Complications associated with BF therapy include osteonecrosis of the jaw (ONJ), characterized by oral mucosal ulceration, exposed bone, pain, swelling, inflammation, increased tooth mobility, and potential tooth loss. These adverse effects necessitate a comprehensive medical evaluation before implant surgery. Specifically, the duration of BF therapy and its administration route should be carefully reviewed, given the extended half-life of these medications and their potential to disrupt bone healing (52–58).

In summary, while dental implantology offers high success rates for most patients, those undergoing BF therapy require meticulous assessment to mitigate the risk of severe complications. Further research is necessary to establish standardized protocols for managing implantology patients on BF treatment (59–73).

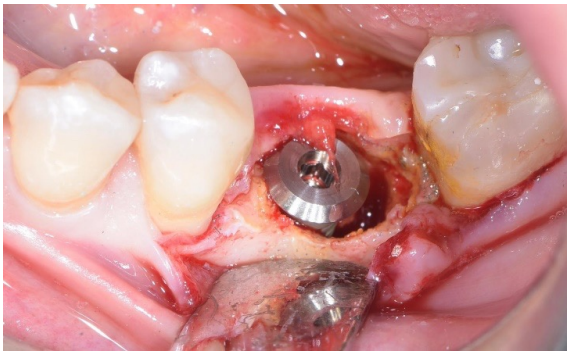

Figure 1. Dental Implant Placement - Surgical Stage

This literature review analyzes the impact of BF drugs on dental implant therapy by examining clinical and radiographic outcomes. It synthesizes findings from randomized controlled trials (RCTs), controlled trials, and multicentric studies, highlighting conflicting evidence. The aim is to clarify risks and guide clinicians in managing implant patients on BF therapy (74–93).

Material and methods

This literature review explores BF therapy's impact on dental implant outcomes. Studies published in the past 15 years were prioritized to ensure relevance and avoid outdated or less safe pharmacological data. The analysis included research on human subjects who had completed implant-prosthetic therapy without absolute contraindications to implant treatment (94–107).

Research data was collected from established scientific databases widely recognized in the academic community, including Scopus, Web of Science, Google Scholar, PubMed, and MDPI. The search strategy used the keywords "bisphosphonate" AND "dental implant" to identify pertinent studies. Filters were applied to focus on recent clinical studies, such as RCTs, controlled trials, and multicentric studies, to capture a range of clinical experiences (108–124).

The initial screening involved reviewing titles and abstracts to exclude studies not meeting the inclusion criteria. Full texts of relevant studies were then analyzed to assess implant therapy's clinical and radiographic outcomes in patients undergoing BF treatment. Independent evaluations by multiple reviewers minimized bias and ensured a comprehensive interpretation of the findings (125–143).

This review synthesizes the available evidence to clarify conflicting data in the literature and provide practical insights for clinicians managing patients on BF therapy.

Data items

The outcomes assessed in the studies include clinical indicators like bleeding on probing, probing depth, and implant mobility. Thread Exposure, Marginal Bone Loss (MBL), and implant stability quotient reflect implant and bone health. Bone mineral density is used to

evaluate bone structure, while Implant Survival (IS) rates measure long-term success. Soft tissue health is also considered when assessing surrounding tissue conditions (144–151).

Risk of bias

Evaluating the reliability of studies on BF therapy's impact on dental implants is essential for drawing accurate conclusions. Potential biases, especially in randomized clinical trials, can affect study validity, so minimizing them is crucial for more precise clinical guidance. Citation analysis was used to assess the relevance and impact of the included studies (152–160). Despite some limitations in study design and sample size, the low risk of bias observed strengthens the overall reliability of the findings. Data were analyzed collectively to compare outcomes and identify patterns, considering methodological differences, patient characteristics, and treatment protocols. This approach provides a clearer understanding of the risks and benefits of implant therapy in BF-treated patients (161–170).

Results

This literature review examines the impact of BF on dental implants, focusing on nine selected studies from an initial pool of 312 articles. To ensure relevant results, only RCTs, multicentric studies, and clinical trials were included. Key exclusion criteria involved studies unrelated to dental implants or BF (171–185).

Several studies compared BF-coated implants with uncoated implants. Abtahi et al. found no significant difference in implant stability between the groups, but BF-coated implants had less MBL (0.20 mm vs. 0.70 mm after five years). Zuffetti et al. reported improved IS and less bone loss in the BF-treated group (186–202). Mozzati et al. found no cases of bisphosphonate-related jaw osteonecrosis (BRONJ) after 24 months. However, implant failures due to mobility were observed, especially in patients with risk factors like diabetes and smoking. López-Cedrún et al. highlighted complications in BRONJ patients related to implants, requiring surgical interventions (203–216).

Griffiths assessed bone mass density around implants in patients on BF and found less bone loss when alendronate was given after OI. Abtahi et al. observed better OI and marginal bone preservation with BF-coated implants. Shabestari et al. reported no significant differences in clinical parameters between patients on BF during or after implant surgery, indicating BF does not negatively affect implant success when adequately managed (217–235).

BF-coated implants show better marginal bone preservation than uncoated implants, with slower bone resorption. However, the difference was insignificant in long-term data ($p = 0.1483$). More randomized clinical trials and multicentric studies are needed to confirm the long-term effects of BF and establish more straightforward guidelines for implant therapy in patients undergoing BF treatment (236–257).

Discussion

Several studies have explored the impact of BF therapy on dental implant success, revealing a range of clinical outcomes. Abtahi et al. (2011) found no significant differences between BF-coated dental implants and uncoated implants during early healing, although uncoated implants showed more MBL (258–265). In a follow-up study, Abtahi et al. (2014) demonstrated that BF-coated implants may help preserve peri-implant marginal bone over five years. Tallarico et al. (2015) suggested that BF therapy did not significantly affect IS or prosthetic rehabilitation, provided treatment timing and minimally invasive surgical techniques were followed. Similarly, Zuffetti et al. (2016) showed that the topical administration of BF drugs improved IS and the pre-and post-loading phases (266–279).

The safety of dental implant placement in BF-treated patients was supported by Mozzati et al. (2017), who reported no cases of BRONJ following implant surgery. This highlights that such procedures can be safely performed, provided proper healing techniques are used. However, López-Cedrún et al. (2018) demonstrated that BRONJ lesions can still develop in patients with dental implants, with lesions appearing in both early and late phases of implant or prosthetic rehabilitation. Griffiths (2019) emphasized that BF may suppress healing if administered before or at the time of implant surgery, but after six months, their effects on bone healing may be more positive (280–295).

Abtahi et al. (2012) further explored the potential of BF-coated implants in enhancing OI, finding that a fibrinogen coating with BF improved OI in human bone, indicating potential applications in orthopedic and dental rehabilitation. In a multicentric study, Shabestari et al. (2020) found no correlation between BF therapy and ONJ during dental implant surgery. However, their study had a limited patient pool and incomplete follow-up data (296–312).

BF are potent molecules widely used to treat various osteolytic conditions, including osteoporosis and bone metastases. Despite their therapeutic benefits, BF is known to be associated with ONJ, particularly following dental procedures. This condition is a rare but severe complication, predominantly observed in patients receiving intravenous BF. However, cases are increasingly being reported in patients treated with oral BF for osteoporosis or Paget's disease (Figure 2). The first reported cases of BRONJ date back to 2003, and its onset can be subtle, with symptoms ranging from gum inflammation to tooth loss and non-healing extractions (313–325).

Managing patients with BF-induced ONJ requires a multidisciplinary approach, including preventive strategies such as maintaining oral hygiene, scheduling regular dental visits, and considering alternative therapies for osteoporosis, especially for patients with risk factors for BRONJ. In cases where dental surgery is unavoidable, minimizing tissue trauma and adopting less invasive techniques is crucial (326–336). Guidelines recommend completing dental extractions or other procedures before initiating BF therapy to allow for adequate healing time. However, dental extractions and invasive periodontal procedures should be avoided in cases where BF has already been started, with endodontic therapies being preferred (337–341).

Despite these risks, the literature highlights that dental implants can still be successfully placed in BF-

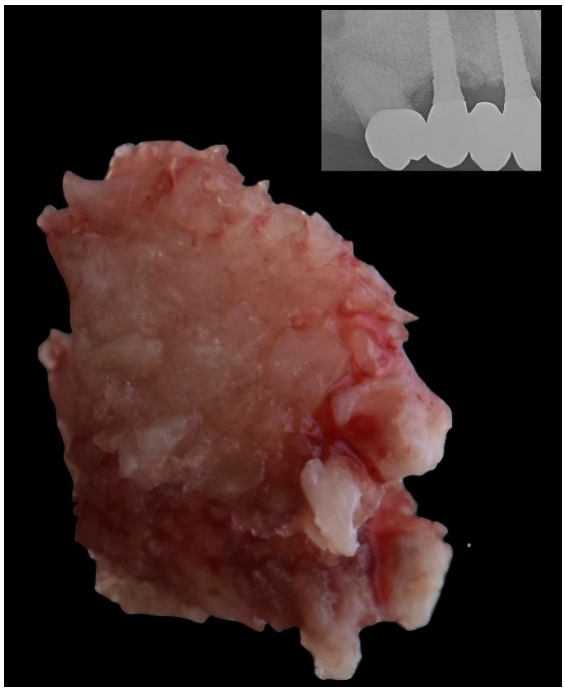

Figure 2. Bisphosphonate-Related Osteonecrosis

treated patients, provided careful patient selection and treatment planning are followed. Mozzati et al. (2017) and Shabestari et al. (2020) emphasize the importance of a detailed medical history to assess the patient's risk factors, such as the type and duration of BF therapy, along with other conditions like diabetes and smoking. These factors play a significant role in determining the risk of implant failure and BRONJ (342–345).

Furthermore, specific BF molecules, such as risedronate, carry a higher risk of BRONJ in patients undergoing dental implant surgery. Other risk factors identified in the literature include smoking, diabetes, and the use of corticosteroids, all of which contribute to an increased likelihood of developing complications. Zuffetti et al. (2016) and Griffiths (2019) suggest that a thorough evaluation of the patient's medical background and the timing of BF therapy is essential for minimizing risks associated with dental implants (346–350).

In conclusion, while BF poses certain risks, especially concerning ONJ, many studies indicate that dental implants can be safely placed in patients undergoing BF therapy with appropriate precautions. Success lies in carefully selecting patients, managing their treatment protocols, and using minimally invasive surgical techniques. Regular follow-up and close collaboration between dental and medical professionals are crucial to ensure the optimal management of BF-treated patients undergoing dental implant surgery. However, due to the variety of protocols and outcomes across studies, further research is needed to standardize treatment approaches and clarify the long-term effects of BF on implant success and bone healing (351–358).

Conclusions

This study clarifies the effects of BF on bone during and after implant-prosthetic rehabilitation. The data suggest that MBL around implants, like teeth, progresses at about 0.1 mm per year. However, implants coated with BF show a slightly reduced bone loss compared to uncoated implants (359–362,363–366). The study indicates that implant surgery is safe and predictable with appropriate pharmacological prophylaxis. No statistically significant differences in bone loss were found between BF-associated implants and non-associated ones. Further randomized, multicentric trials are needed to address unresolved concerns and improve patient outcomes.

Abbreviations

BF	Bisphosphonates
BRONJ	Bisphosphonate-Related Osteonecrosis of the Jaw
IS	Implant Survival
MBL	Marginal Bone Loss
OI	Osseointegration
ONJ	Osteonecrosis of the Jaw
RCT	Randomized Controlled Trial

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