

Iatrogenic risk of osteonecrosis of the jaw? Bone substitutes for dental implants: a warning from Japan

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ABSTRACT

Commercial bone substitutes that are widely used for bone augmentation for dental implants are predisposing factors in the development of osteonecrosis of the jaw (ONJ), overlooking this situation may lead to serious problems. Most of these materials are supplied as inorganic porous granules of calcium phosphate, which have characteristics that exceed the bone resorption ability of normal osteoclasts; therefore, they can be equally regarded as existing antiresorptive necrotic bony granules in the body, i.e., micro-ONJs. In addition, because dental implants directly contact the surrounding bone without the periodontium with immunoprotective functions, the mucosal penetration of the dental implant itself predisposes the underlying bone to the risk of infection, latent osteomyelitis, and ONJ. Therefore, the remaining porous granules surrounding the dental implant pose an additional iatrogenic risk, even though the tissue may appear superficially healthy. In an aging society, an individual who was systemically healthy at the time of implantation with bone augmentation could develop osteoporosis or cancer bone metastasis later in life. ONJ can occur more easily if an antiresorptive agent such as bisphosphonates or denosumab is administered without sufficiently recognizing an intraoral situation. If the latent risk is known in advance, the selection or use of medicines could be restricted. Such restrictions can result in other crucial issues that are beyond the discretion of the dentists; however, dentists have not been warned about such possibilities. The use of antiresorptive agents and bone substitutes for dental implants should be reconsidered to avoid numerous adverse events such as ONJ.

Keywords: osteonecrosis of the jaw, bone substitute, dental implant, bisphosphonates, denosumab

Abbreviations:

ONJ: osteonecrosis of the jaw

BP: bisphosphonate

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Osteonecrosis of the jaw (ONJ) is a serious adverse complication of antiresorptive therapy for osteoporosis and cancer bone metastasis and it poses challenges to the medical and dental societies.¹ Commercial bone substitutes² that are widely used for dental implants are predisposing factors in the development of ONJ; moreover, overlooking this situation as in the past³ may lead to serious problems.

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Antiresorptive agent-related osteonecrosis of the jaw

Antiresorptive therapy includes bisphosphonates (BPs) and denosumab that are used as bone antiresorptive agents; therefore, antiresorptive agent-related ONJ includes BP-related ONJ and denosumab-related ONJ. It is characterized as follows: exposed bone in the maxillofacial region that does not heal within 8 weeks after identification by a healthcare provider, exposure to antiresorptive agent, and no history of radiation therapy to the craniofacial region.¹ The mechanisms of action underlying antiresorptive agents include the reduction of osteoclast numbers and activity. Although these effects are appropriate for the bones of the trunk, it is excessive for the jawbone, reducing the metabolic capacity of this bone, which could induce ONJ. The necrotic bone is intraorally exposed, and the patient's quality of life is severely deteriorated. The prescribing medical physician and referred oral surgeon often conflict on medication; consequently, academic societies across countries have organized position papers and treatment guidelines.^{1,4,5} However, a more crucial issue may result from situations that are not anticipated by the guidelines.

In patients with BP-related ONJ, a history of intravenous BP administration is overwhelmingly more common than oral administration. However, the situation is different in Japan, where approximately half of the >4700 prescriptions for BP-related ONJ were oral and the other half were intravenous.⁵ This difference is attributable to the large number of patients with osteoporosis and the high proportion of oral BP prescriptions. Japan has the largest aging society; one of two women and one of four men are diagnosed with osteoporosis during their lifetime, and these patients are widely and regularly prescribed medication because of easy access to medical services and the patient-friendly national health insurance system. Additionally, one in two individuals experience a malignant tumor, and the number of patients with bone metastasis of breast, prostate, or lung cancer is on the rise. Therefore, Japan is the first country to have the highest proportion of patients requiring and receiving antiresorptive agents.

Bone substitutes for dental implants and micro-ONJs

Dental implants that function as artificial tooth roots in the jawbone are popular as prosthetic treatment modalities. During treatment planning, dentists often encounter patients with a low bone volume and implant installation requires bone augmentation. Although autogenous bone graft is known as the gold standard of implants, it is associated with morbidity; therefore, dentists prefer convenient commercial products made of allogeneous, xenogeneous, or alloplastic materials as bone substitutes.² Most of these materials are supplied as inorganic porous granules of calcium phosphate, which is the main component of bone. The applied granules should ideally be replaced with a new bone as soon as possible via the bone remodeling process. However, in practice, these granules remain in the body for at least several years, despite the mention of their rapid resorptive characteristics on product documents. Furthermore, many dentists prefer to use bone substitutes that resorb slowly, remaining in place for at least 10 years to avoid bone resorption because of peri-implantitis.

These materials have characteristics that exceed the bone resorption ability of normal osteoclasts; therefore, they can be equally regarded as existing antiresorptive necrotic bony granules in the body, i.e., micro-ONJs. In addition, because dental implants directly contact the surrounding bone without the periodontium that naturally lies between the tooth roots and bone with immunoprotective functions, the mucosal penetration of the dental implant itself predisposes the underlying bone to the risk of infection, latent osteomyelitis, and ONJ. Clinical cases supporting this etiology have been reported.⁶ Therefore, the remaining porous granules surrounding the dental implant pose an additional iatrogenic risk, even though the tissue may appear superficially healthy (Fig. 1).

Iatrogenic risk of osteonecrosis of the jaw

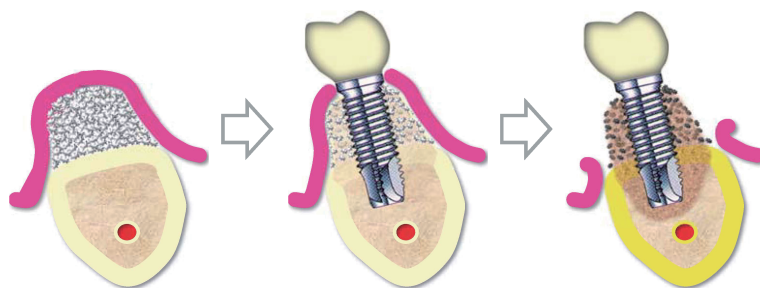


Fig. 1 Bone substitutes for dental implant and micro-ONJs

(Left) Bone augmentation using bone substitutes. (Middle) Dental implant in place. (Right) Development of ONJ. ONJ: osteonecrosis of the jaw.

Additional predisposing factors in the development of ONJ

In an aging society, an individual who was systemically healthy at the time of implantation with bone augmentation could develop osteoporosis or cancer bone metastasis later in life. ONJ can occur more easily if an antiresorptive agent is administered without sufficiently recognizing an intraoral situation. If the latent risk is known in advance, the selection or use of medicines could be restricted. Such restrictions can result in other crucial issues that are beyond the discretion of the dentists; however, dentists have not been warned about such possibilities. The use of antiresorptive agents and bone substitutes for dental implants should be reconsidered to avoid numerous adverse events such as ONJ.

CONFLICT OF INTEREST

The author has no conflict of interest directly relevant to the content of this article.

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