

# Prevention and treatment of osteonecrosis of the jaw

Coha Bozena\*, Holik Hrvoje, Knezevic-Pravecek Marijana

Department for Internal Medicine, General Hospital "Dr. Josip Benčević", Slavonski Brod, Croatia;

\*Corresponding Author: [bozena.coha@sb.t-com.hr](mailto:bozena.coha@sb.t-com.hr)

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## ABSTRACT

**Purpose:** to update recommendations for the prevention and treatment of osteonecrosis of the jaw in patients on bisphosphonate therapy. **Osteonecrosis of the jaw is a rare and serious complication of bisphosphonate therapy. Also, it is one of the important and growing clinical public health issues, because bisphosphonates are now more commonly used than before. Bisphosphonates are primarily used in the treatment of cancer-related conditions such as bone metastases, hypercalcemia, lytic skeletal lesions. More recently, bisphosphonate has been approved for the management of osteoporosis. The etiology and pathogenesis remain unknown, however, two important risk factors have been identified, i.e. the potency and length of bisphosphonate use, and recent dental intervention. Recommendations:** prior to the introduction of bisphosphonate therapy, all patients should undergo complete dental examination, any active oral cavity infection should be treated and the potential sites of new infection removed. **During bisphosphonate therapy, patients should strictly comply with oral hygiene and avoid any invasive procedure of the oral cavity.**

**Keywords:** Bisphosphonates; Osteonecrosis; Jaw

## 1. INTRODUCTION

Osteonecrosis of the jaw is a rare and serious complication of bisphosphonate therapy, first described in the literature in 2003. A patient currently or previously treated with bisphosphonates, having a bone protruding in the maxillofacial region persisting for more than eight weeks, without a history of radiotherapy, can be considered as having osteonecrosis of the jaw associated with bisphosphonates [1]. Bisphosphonates are primarily used in the treatment cancer-related conditions such as bone metastases, hypercalcemia, lytic skeletal lesions, but more

recently use to treat varied of other skeletal conditions, such as heritable skeletal disorders in children, multiple forms of osteoporosis (juvenile, postmenopausal or involutional, glucocorticoid-induced, transplant-induced, immobility-induced, and androgen-deprivation-related) [2]. According to literature data, the expected risk of jaw osteonecrosis in patients suffering from malignant diseases treated with bisphosphonates ranges from 1% to 11%, depending on the type, dosage and duration of bisphosphonate therapy, and on dental or oral procedure [2-5]. In patients with multiple myeloma, the prevalence of jaw osteonecrosis has been estimated to 7% - 10% [2]. The etiology and pathophysiology of jaw osteonecrosis remain obscure; however, two important risk factors have been identified, *i.e.* the potency and length of bisphosphonate exposure, and recent dental or oral surgery. Some 70% of patients developing osteonecrosis of the jaw had a recent dental or oral surgical procedure in their history, whereas spontaneous occurrence of jaw osteonecrosis was recorded in 30% of patients [4]. The length of bisphosphonate therapy is strongly associated with the occurrence of jaw osteonecrosis. The patients developing jaw osteonecrosis received 35 bisphosphonate infusions on an average, in comparison with 15 infusions in those without jaw osteonecrosis. The prevalence of jaw osteonecrosis was significantly greater after the use of zoledronic acid than after pamidronate [4,6]. In their study, Bamias *et al.* found the expected risk to be 1% in the first year and 21% in the third year of treatment with zoledronic acid, whereas for pamidronate it was 0% in the first two years and 7% after four years of treatment [6]. The disease more frequently involved the mandible than the maxilla (63% vs 38%). Several groups and organizations (American Society of Clinical Oncology (ASCO), Mayo Clinic, and American Association of Oral and Maxillofacial Surgeons (AAOMS)) published guidelines for the prevention and treatment of bisphosphonate-related osteonecrosis of the jaw, and they all agree that prevention is the best approach in the management of this rare and severe complication [1-3]. In 2009, AAOMS published their guidelines for the pre-

vention and management of bisphosphonate-related osteonecrosis of the jaw [1].

## 2. RECOMMENDATIONS FOR PREVENTION

1) Prior to the introduction of bisphosphonate therapy (if compatible with the patient's condition), the patient should undergo thorough dental examination; extraction of teeth that cannot be saved; elective dentoalveolar surgical procedures should be completed, waiting for bone healing and mucous membrane epithelialization; and the patient should be informed on the importance of strict oral hygiene and possible mucosal trauma, in particular along the lingual region, occurrence of pain, edema or bone protrusion [1-5].

2) Asymptomatic patient on bisphosphonate therapy: strict oral hygiene; avoiding any procedure that may result in bone lesion; a tooth than cannot be cured may be treated by crown removal and endodontic therapy of the remaining roots; avoiding implants; and annual dental examination [1,3,4].

3) Asymptomatic patient on bisphosphonate therapy: elective dentoalveolar surgical procedures may not be contraindicated in this patient category, but they should be informed on the risk of osteonecrosis of the jaw [1,2]. The individuals taking oral bisphosphonates for less than three years and are free from other clinical risk factors need not postpone the scheduled operative procedures in the oral and maxillofacial region[1]. If compatible with the patient condition, in those taking corticosteroids along with bisphosphonates therapy interruption for at

least three months prior to the procedure should be considered, and it should not reintroduced until complete wound and bone healing [1]. In patients taking oral bisphosphonates for more than three years, therapy should be discontinued at least three months prior to the procedure and resumed upon complete bone healing [1].

## 3. RECOMMENDATIONS FOR TREATMENT

The aim of treatment in patients diagnosed with osteonecrosis of the jaw is to alleviate pain, control the infection, and reduce progression or development of bone necrosis. Surgical treatment is less efficient than in osteomyelitis or bone osteoradionecrosis, therefore it should be delayed if possible [1,2]. Surgical treatment is reserved for patients in the third stage of disease and those with bone sequestration [1]. Elective surgical procedures should be avoided [1].

Specific treatment depends on clinical stage. According to AAOMS, there are four stages of the disease, presented in **Table 1**. [1]. Discontinuation or reintroduction of bisphosphonate therapy i.v. depends on the assessment of the risk and benefit for the patient, which should be done by a hemato-oncologist and oral/maxillofacial surgeon together [1]. Short-term therapy interruption is of no use, however, if the patient's condition allows it, then long-term therapy discontinuation may prove useful to stabilize osteonecrosis of the jaw, reduce the risk of new sites of bone necrosis and alleviate disease symptoms. In patients with osteonecrosis of the jaw, discontinuation of oral bisphosphonate therapy is associated

**Table 1.** American Association of Oral and Maxillofacial Surgeons: treatment of bisphosphonate-related osteonecrosis of the jaw according to four stages.

Stage	Treatment
<b>Stage 0</b> Nonspecific clinical signs and symptoms No signs of bone necrosis	Analgetics and antibiotics
<b>Stage 1</b> Bone necrosis in asymptomatic patient and without signs of infection	Antibiotic solutions for mouth wash Clinical follow up every three months Patient education, revision of indication for bisphosphonates
<b>Stage 2</b> Protruding and necrotic bone with signs of infection (pain, redness, with or without purulent discharge)	Symptomatic therapy with oral antibiotics Antibacterial solutions for mouth wash Analgesics Superficial debridement
<b>Stage 3</b> Protruding and necrotic bone associated with pain, infection, and one or more of the following findings: bone necrosis extending beyond alveolar bone (e.g., lower edge of mandibular ramus, maxillary sinus and zygomatic part of the maxilla resulting in bone fracture, extraoral fistulas, oral-antral/oral-nasal fistulas, osteolysis expanding to the lower edge of the mandible or sinus bed	Antibacterial solutions for mouth wash Antibiotic therapy Analgesics Cleaning and resection

with gradual improvement of clinical status. A 6- to 12-month interruption may lead to spontaneous sequestration or healing following surgical intervention [1].

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