DENTAL APPROACH IN THE TREATMENT OF ONCOLOGY PATIENTS ON BISPHOSPHONATE THERAPY

Anela Hardaga - Muzurović[1]*, Sadeta Šečić[2]

[1] Oral surgery clinic, Faculty of Dentistry with Dental Clinical Center, University of Sarajevo, Bosnia and Herzegovina

[2] Department of Oral Surgery with Dental Implantology, Faculty of Dentistry with Dental Clinical Center, University of Sarajevo, Bosnia and Herzegovina

*Corresponding author

dr. Anela Hardaga- Muzurović,
Oral surgery specialist,
Faculty of Dentistry
with Dental Clinical Center,
University of Sarajevo,
Bosnia and Herzegovina,
Department of Oral Surgery,
Bolnicka 4A, 71 000 Sarajevo,
Bosnia and Herzegovina,
Phone: +387(33)214 294,
e-mail: dranelahm@gmail.com

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ABSTRACT

Oncology patients belong to a high- risk group in dentistry and require a meticulous and planned treatment approach. The role of dentists in treating oncology patients includes understanding therapeutic methods for malignant diseases and their oral side effects, as well as adopting an appropriate treatment approach. Dentists are responsible for preventing potential oral complications, educating patients about them, rehabilitating the oral cavity before initiating oncology therapy, assessing the risk of dental interventions during therapy, and providing long-term monitoring due to increased risk of complications.

This paper focuses on preparing oncology patients undergoing bisphosphonate therapy for oral surgical interventions and highlights the importance of preventive dental check-ups to reduce the risk of severe complication, particularly bisphosphonate-induced osteonecrosis of the jaws.

Keywords: oncology patients, multidisciplinary approach, bisphosphonates, osteonecrosis, prevention.

Introduction

The treatment of oncology patients is a complex process requiring the expertise of multiple healthcare professionals, including doctors of dental medicine. During oncology therapy, acute and chronic oral complications frequently arise, compromising the patient's quality of life and potentially causing interruptions in primary therapy due to their aggressive progression [1]. This underlines the importance of involving doctors of dental medicine before, during, and after oncology therapy [2]. The increasing number of oncology patients receiving bisphosphonates therapy who visit dental clinics highlights the growing awareness of oral complications associated with these drugs [1, 3].

Bisphosphonates are part of the antiresorptive group of drugs and are highly significant in treating patients with bone metastases [4]. These synthetic analogs of inorganic pyrophosphate have a high affinity for calcium. They are strong inhibitors of osteoclastic activity and tend to accumulate in the mineralized bone matrix, where they may remain for years [4]. Because of these characteristics, bisphosphonates are used to prevent complications in oncology patients such as pathological fractures and bone pain caused by bone metastases [4].

Bisphosphonates are medications used to treat and prevent osteoporosis, Paget's disease, bone metastases from cancers such as lung, breast and prostate, multiple myeloma, and malignant hypercalcemia [4]. They main characteristic is that they deposit on bone surfaces within minute or hours of administration [5]. In oncology therapy, intravenous bisphosphonates (e.g., pamidronate and zolendronic acid) are used to treat primary bone lesions or bone metastases [5]. Intravenous bisphosphonates are significantly more potent, achieving 50% bioavailability after administration [6]. A protentional complication of bisphosphonate therapy in the oral cavity is osteonecrosis of the jaws, known as bisphosphonate-induced osteonecrosis of the jaw (BIONJ) [7]. The jaws are particularly susceptible due to their high vascularization and daily remodeling from oral activities [6]. Bisphosphonates inhibit osteoclast differentiation and induce apoptosis, impending the bone healing process [6]. These drugs also have an extended elimination half- life, ranging from one to ten years. Studies show that intravenous bisphosphonate therapy increases the risk of osteonecrosis sevenfold compared to oral therapy, with longer treatments and higher doses further elevating the risk [8, 9]. Bisphosphonate –related osteonecrosis of the jaw fallowing tooth extraction is often an irreversible condition that significantly affects the quality of life in oncology patients [10].

Aim

This paper aims to emphasize the importance of preventive dental check-ups for oncology patients before initiating bisphosphonate therapy and highlight the risk of severe complications, specifically bisphosphonate-induced osteonecrosis of the jaws, in patients undergoing invasive dental procedures such as tooth extractions.

Dental approach to oncology patients prior to initiating bisphosphonate therapy

Before starting bisphosphonate therapy, the dentist's role involves comprehensive oral cavity rehabilitation including: removal of hard dental deposits, treatment of carious lesions, endodontic procedures, tooth extractions, and replacement of inadequate restorative fillings [11]. Dental rehabilitation should begin as early as possible to allow sufficient time for wound healing, ideally two to three weeks before bisphosphonate therapy is initiated. Considering the typically short timeframe between diagnosis and start of bisphosphonate therapy, dentist must prioritize addressing acute and advanced urgent conditions [11, 12].

As a rule, all surgical procedures should be completed at least 15 days before starting bisphosphonate therapy. The risk of jaw osteonecrosis is significantly reduced if tooth extraction are performed 21 or more days prior to therapy initiation [12].

In addition to treating pathological conditions, certain preventive measures are crucial to minimize the prevalence of oral complications. These measures include: adjusting existing dentures, removing overhanging restorations, sharp edges on teeth, and fillings, plaque removal, and enhanced oral hygiene practices ([2].

Since the oral mucosa is highly susceptible to damage, it is necessary to eliminate potential sources of local trauma that could lead to the development of osteonecrosis [12, 13, 25].

Dental approach during bisphosphonate therapy

Routine dental procedures are postponed until the completion of bisphosphonate therapy unless there is an urgent need [3]. During bisphosphonate therapy, oral surgical interventions should be avoided due to the high risk of bisphosphonate-related osteonecrosis of the jaw (BRONJ). However, if a surgical procedure is essential, it must be preceded by a consultation with the patient's oncologist [2, 3].

An individualized treatment plan is required for each oncology patient. In collaboration with the oncologist, the oral surgeon determines the type, dosage, and duration of antibiotic therapy [2].

Current guidelines do not specify an exact number of days for starting antibiotics prophylaxis before a tooth extraction. Recommendations range from one to seven days pre-procedure [8].

Similarly, post-extraction antibiotic therapy durations vary between five and seventeen days. Most experts agree that antibiotics should be continued until the wound heals. It is important to note that patients treated with bisphosphonate remain at risk of osteonecrosis even after the therapy has ended [8].

Dental approach for patients with clinical signs of Bisphosphonate- related osteonecrosis of the jaw (BRONJ)

Bisphosphonate- related osteonecrosis of the jaw (BRONJ) is characterized by exposed bone in the maxillofacial region that persist over time. According to the 2014 guidelines from American Association of Oral and Maxillofacial Surgeons (AAOMS), BRONJ is classified into the fallowing stages [14]:

1. At-risk patients - Patients who are currently or have previously been treated with oral or intravenous bisphosphonate but exhibit no clinical signs of exposed necrotic bone. These patients require careful monitoring and enhanced oral hygiene, even though they do not yet have a disease stage [14, 15].
2. Stage 0 (initial stage) - Patients with a history of bisphosphonate therapy who do not have clinically exposed bone but present nonspecific symptoms [14]. These symptoms may include: increased tooth mobility unrelated to periodontal disease, formation of fistulas not associated with endodontic pathology, radiographic findings such as bone resorption, sinus wall thickening, irregular trabecular patterns, or persistent lamina dura [16, 17]. Treatment in this stage involves conservative measures, including local antiseptics and analgesics [15].
3. Stage 1 – Clinically evident necrotic bone is exposed or can be probed through a fistula, but there are no signs of infection. Patients are asymptomatic [16, 17] (Image 1). Treatment includes local antiseptics, quarterly check-ups, and consultations with oncologists about the possibility of discontinuing bisphosphonate therapy ("drug holiday") [15].
4. Stage 2 – In this stage, exposed necrotic bone is accompanied by infection [16, 17]. Clinical signs include erythema, pain, and, in some cases, purulent discharge [16, 17] (Image 2.). Treatment involves systematic and local antibiotics, pain management with analgesics, and superficial debridement to reduce infection and tissue irritation [15].
5. Stage 3 – This stage includes exposed necrotic bone that extends beyond the alveolar ridge, causing complications such as: pathological fractures, extraoral fistulas, oroantral or oronasal communications, or osteolysis of the mandibular or sinus floor [16, 17] (Image 3). Treatment involves surgical debridement or radical surgical intervention [15].

Discussion and conclusion

Many studies underline that medicines from a group of antiresorptive drugs can cause osteonecrosis changes in jaw bones [23]. Risk factors such as the use of the potent intravenous bisphosphonates and a medical history of invasive dental procedures, or radiation therapy have been

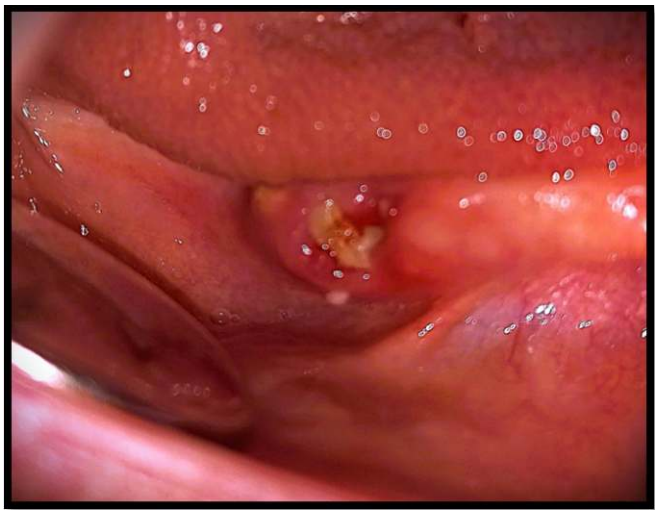

Figure 1. STAGE 1 : Clinically visible exposed bone in the mandible of an oncology patient receiving intravenous bisphosphonate therapy, which occurred after a tooth extraction. (A case presentation from personal casuistry)

identified [24]. The size of the affected area can be variable, and range from a nonhealing extraction site to exposure and necrosis of large sections of jawbone. The area of exposed bone is typically surrounded by inflamed erythematous soft tissue. Purulent discharge at the site of exposed bone will be present when these sites become secondarily infected [26].

Bisphosphonate –induced osteonecrosis of the jaws (BIONJ) was first described in 2001 in the book *"Oral and Maxillofacial Pathology: A Rational for Diagnosis and Treatment" by Marx and Stern.* The authors observed necrotic bone surfaces in the jaws of multiple myeloma patients treated with bisphosphonate and named this condition as "Drug-induced avascular bone osteonecrosis" due to the observed atrophy of nutritive blood vessels in the affected bone areas [18].

In 2003, Marx published the first scientific study on this topic, describing cases of exposed necrotic

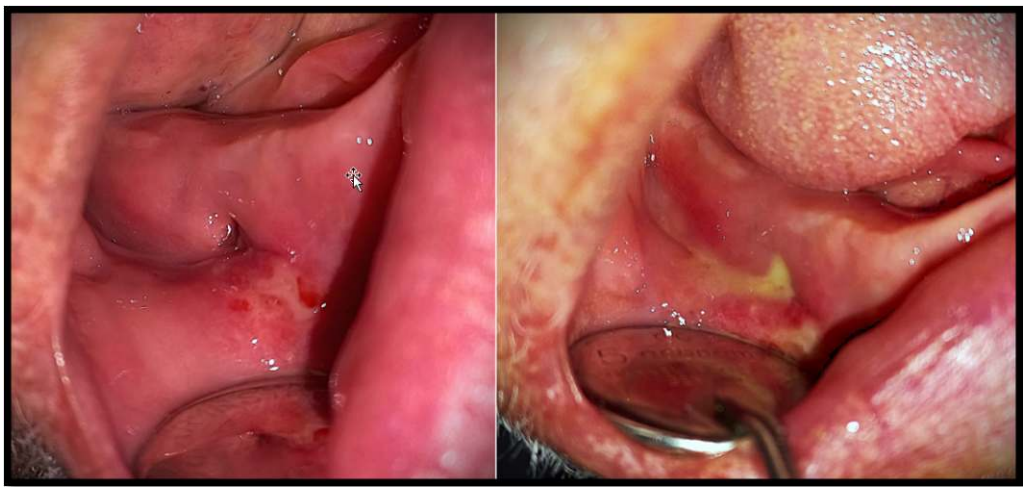

Figure 2. STAGE 2: Development of a bone-derived fistula with purulent exudate in an oncology patient receiving intravenous bisphosphonate therapy, as a complication following tooth extraction. (A case presentation from personal casuistry)

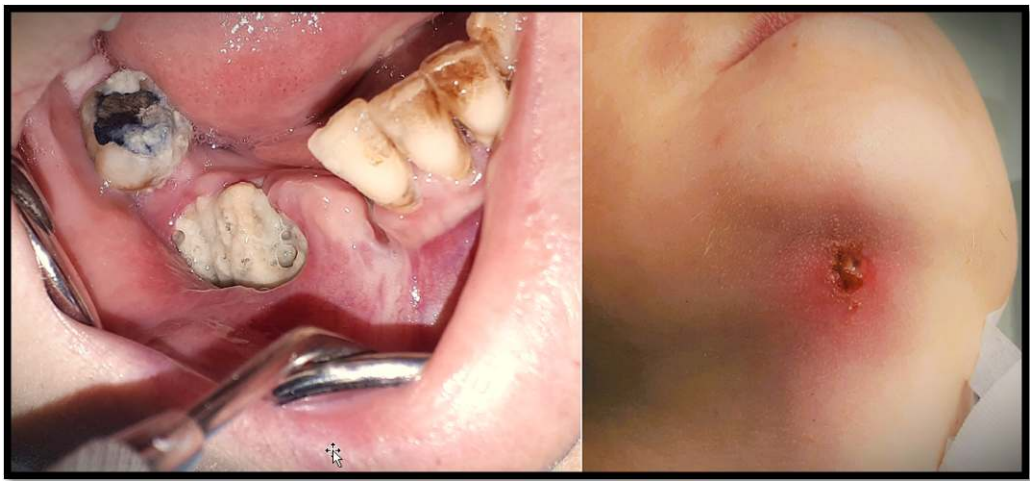

Figure 3. STAGE 3 Clinically exposed necrotic mandibular bone with signs of infection and the presence of an extraoral fistula in an oncology patient undergoing intravenous bisphosphonate therapy, occurring as a complications of tooth extraction.
(A case presentation from personal casuistry)

bone in 36 patients treated with intravenous bisphosphonates. He referred to the phenomenon as a "growing epidemic" [18, 19]. Over time, researchers concluded that blood vessel atrophy resulted from the toxic effects of bisphosphonates on osteoclasts. This led to the replacement of the term "avascular bone osteonecrosis" with "bisphosphonate-related osteonecrosis of the jaw (BRONJ), which more accurately reflects the cause [19].

Many cases of osteonecrosis are observed fallowing tooth extractions. Surgical procedures such as wisdom tooth extraction, torus removal, periodontal surgery, and implant placement are strongly contraindicated during bisphosphonate therapy [21, 22].

Preventive dental check-ups and timely treatment can significantly improve a patient's quality of life, reduce the risk of complication, and prepare patients for procedures fallowing modern standardized protocols [4]. The primary goal of preventive measures is to avoid interruptions in oncology therapy, because interruptions can lead to severe health consequences [4]. Research has shown that even one day of interrupted oncology therapy reduces a patient's chance of recovery ba 1-2% [4]. Additionally, recent studies indicate that 50% of patients in Stage 0 of the disease progress to higher stages with clinically evident osteonecrosis [16].

More research is required into many aspects of bisphosphonate induced osteonecrosis, such as the pathogenesis and risk factors – including the role of dental infections and extractions – and the best approaches to prevention, diagnosis and management [27, 28].

The decision to perform dental interventions on oncology patients who are already undergoing bisphosphonate therapy- whether they are at risk of developing osteonecrosis or already exhibit clinical manifestations of the disease- must be approached through a multidisciplinary evaluation. This requires close collaboration between dentist and oncologist overseeing the patient's treatment. It is crucial to evaluate whether the planned dental interventions offer more benefits than risks and whether it could further jeopardize the patient's already fragile health.

Timely dental check –ups and adequate oral cavity rehabilitation are essential for protecting oncology patients from severe and often irreversible complications that may arise after the introduction of bisphosphonate therapy.

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Declaration of interest

The author declares that there is no conflict of interest.

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