

Management of Bisphosphonate-Related Osteonecrosis with a Topical Antioxidant Gel

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Introduction:

Bisphosphonates used to treat bone diseases by inhibiting osteoclastic activity have become standard therapy in the management of patients with multiple myeloma and metastatic cancer of the bone. Increased doses, especially via intravenous administration however, increase the patient's risk of developing osteonecrosis. Bisphosphonate-related osteonecrosis of the jaw (BRONJ) is localized death of bone tissue in the jaw associated with bisphosphonate medications. Treatment of BRONJ is complicated and has, up to now, centered on controlling pain and infection and careful debridement of necrotic bone with unpredictable results. A topically applied antioxidant gel shows promise as a well-tolerated novel treatment for BRONJ.

Background:

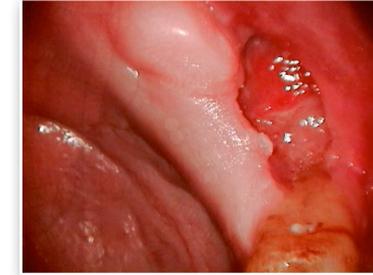
- ❖ Signs of bisphosphonate-related osteonecrosis of the jaw (BRONJ) include exposed and necrotic bone in the mandible or maxilla that may be accompanied by pain, infection, or osteolysis.¹
- ❖ BRONJ is defined as exposed bone in the maxillofacial region that has persisted for more than eight weeks in a patient with no history of radiation therapy to the jaws and is currently being or has previously been treated with a bisphosphonate.¹
- ❖ Underlying systemic conditions such as diabetes, obesity, renal dialysis or low hemoglobin increase risk of incidence.²
- ❖ Incidence of osteonecrosis in bisphosphonate-treated cancer patients is reported to be 0.8% - 1.2%,³ but occurrence can pose serious systemic health risks and quality of life issues.
- ❖ Occurrence of BRONJ appears directly related to the total dose of bisphosphonate administered.⁴
- ❖ Trauma, inflammatory oral disease and dentoalveolar surgery increase risk, with approximately 60% of reported cases occurring after tooth extraction or other dental surgery.
- ❖ Current treatment of BRONJ centers on controlling pain and infection and careful debridement of necrotic bone when necessary. Extensive resection is not consistently helpful and may worsen the condition.¹

Patient 1:

- ❖ 56 year-old male
- ❖ In remission from Stage IV non-small cell adenocarcinoma of the lung with bone metastases
- ❖ History of Aredia® (pamidronate), IV administration for eight rounds, monthly cycle
- ❖ Osteonecrosis: left maxillary quadrant following extraction of tooth #14



Presentation



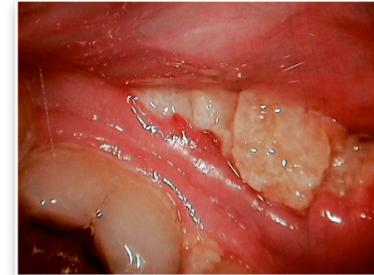
7 weeks, 4 days



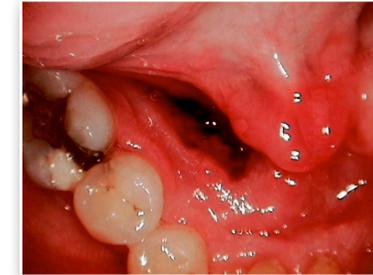
Exfoliated bone

Patient 2:

- ❖ 59 year-old male
- ❖ Stage IV non-small cell adenocarcinoma of the lung with bone metastases
- ❖ History of Zometa® (zoledronic acid), IV administration for six rounds, monthly cycle
- ❖ Osteonecrosis: right mandibular torus, no dental surgery



Presentation



7 weeks



Exfoliated bone

Patient 3:

- ❖ 66 year-old female
- ❖ Stage IV clear cell renal cell carcinoma with bone metastases
- ❖ History of Zometa® (zoledronic acid), IV administration for eight rounds, irregular cycle
- ❖ Osteonecrosis: right mandibular quadrant from area of second premolar to ascending ramus



Presentation



7 weeks



13 weeks

Clinical Procedure:

Three patients treated with intravenous bisphosphonate therapy within the past 12 months and presenting with an area of osteonecrosis were followed. Each patient was instructed to clean the area of necrotic bone with aqueous chlorhexidine gluconate 0.12% and apply a topical antioxidant gel twice daily. Each was seen biweekly for follow-up. Two patients experienced resolution of the necrotic bone. The third expired before the end of the study but exhibited significant improvement prior to her death.

Rationale for Treatment:

Bacterial infection triggers the release of cytokines and initiates an inflammatory process. Phagocytosis of bacteria by polymorphonuclear neutrophils leads to the release of additional cytokines, thus increasing levels of reactive oxygen species and consequently the oxidative stress in surrounding tissue.⁵ Topical application of antioxidants (AOs) has been shown to reduce oxidative stress. It was theorized that combining AOs with the antimicrobial treatment regimen for BRONJ might have a positive effect on the healing process by simultaneously addressing the effects of bacterial infection and oxidative stress.

Conclusion:

Antioxidants topically applied to areas of BRONJ represent a component of treatment that when combined with antimicrobial agents may promote healing. The treatment is non-invasive and well-tolerated by patients. No deleterious side effects of the antioxidant gel were reported. Further research is needed to explore the promise that antioxidants may hold as an effective component of therapy for BRONJ and to understand the mechanism of action at the cellular level.

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