Bisphosphonate-associated osteonecrosis of the jaw

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In 2003, the first reports describing osteonecrosis of the jaw in patients receiving bisphosphonates were published.[1] About 95% of these cases occurred among cancer patients receiving high-dose intravenous bisphosphonates. Approximately 5% of the reported cases have been in osteoporosis patients receiving low-dose bisphosphonate therapy.[2]

The Canadian Task Force on Osteonecrosis of the Jaw, with representatives from medical, surgical, and pathology disciplines, has developed Canadian consensus practice guidelines for bisphosphonate-associated osteonecrosis of the jaw.[3] These guidelines are based on a systematic review of the literature.

Osteonecrosis of the jaw is an uncommon condition with many recognized causes. Traditionally, it has been associated with head and neck irradiation. It can also occur in the presence of periodontal disease, local malignancy, chemotherapy, glucocorticoid therapy, or trauma.[1-6] Recently, however, high-dose intravenous bisphosphonates have been identified as a risk factor for osteonecrosis of the jaw among oncology patients. Low-dose bisphosphonate use in patients with osteoporosis or other metabolic bone disease has not been causally linked to the development of osteonecrosis of the jaw.

Bisphosphonates have been widely used in the management of osteoporosis and metabolic bone disease. They have proven to be effective in reducing the risk of fracture and have recently been shown to improve mortality.[7] They are valuable in the management of skeletal complications of malignancy, namely metastatic bone disease and hypercalcemia of malignancy, and are a key treatment option for cancer patients with metastatic disease.[8-14]

The mechanism by which bisphosphonates might contribute to the development of osteonecrosis of the jaw is not well understood. Osteonecrosis of the jaw can occur in patients who are not taking bisphosphonates and in patients without traditional risk factors.

Diagnosis

If exposed bone is present in the maxillofacial region for more than 8 weeks in the absence of radiotherapy to the jaw in a patient who has been on bisphosphonate therapy, the diagnosis can be confirmed clinically. It is important to exclude other conditions that can present similarly. These include local malignancy, trauma, periodontal disease, and lingual mandibular sequestration and ulceration.[15] Lingual mandibular sequestration and ulceration is a spontaneous sequestration that was described before the availability of amino bisphosphonates. It is a self-limiting process that spontaneously heals within 3 days to 12 weeks.[16]

Incidence

Among cancer patients receiving high-dose intravenous bisphosphonates, osteonecrosis of the jaw is dependent on dose and duration of therapy,[17-20] and has an estimated incidence of 1% to 12%.[17,21-24] Among osteoporosis patients, bisphosphonate-associated osteonecrosis of the jaw is rare and the incidence might not be greater than the natural background incidence of the condition. Postmarketing data and observational studies indicate an estimated incidence of less than 1 case per 100 000 person-years of exposure to oral amino bisphosphonates.[25]

Prevention and treatment

All patients receiving bisphosphonate therapy should ensure that they maintain good oral hygiene and follow the Canadian Dental Association recommendations of semiannual visits to their dentists.[26] Quitting smoking and limiting alcohol intake should be encouraged. Before starting intravenous bisphosphonate therapy for a cancer patient, a detailed examination and panoramic x-ray scans of the oral cavity should be completed. If an invasive procedure is necessary while on high-dose intravenous bisphosphonate therapy, the bisphosphonate treatment should be interrupted, if medically possible, and any essential dental work should be completed (**Figure 1**[26]). Ideally, bisphosphonate therapy should be stopped during the healing period.[27,28]

For osteoporosis patients requiring urgent oral surgery, interruption of bisphosphonate therapy is recommended during the healing period. If surgery is not urgent, then bisphosphonate treatment can be discontinued for several months before the planned procedure and restarted when healing is complete.[29,30]

Treatment of osteonecrosis of the jaw currently focuses on addressing local pain, treating secondary infection, and ensuring adequate nutritional intake and appropriate dietary supplementation (using a feeding tube, if necessary). It is recommended that surgery be limited to removing necrotic debris.[31]

Conclusion

Bisphosphonate-associated osteonecrosis of the jaw is an important condition seen most commonly in oncology patients receiving high-dose intravenous

Figure 1. Bisphosphonate-associated osteonecrosis of the jaw following a palliative resection of the mandible with insertion of a reconstruction plate: *Progressive tissue necrosis has resulted in continued exposure of the bone and reconstruction plate, despite attempts to keep the wound clean.*

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bisphosphonates. Low-dose bisphosphonates given either orally or intravenously in osteoporosis patients have not been causally linked to the development of osteonecrosis of the jaw. A temporal relationship between high-dose intravenous bisphosphonates and osteonecrosis of the jaw exists in cancer patients.

As the condition can occur spontaneously in the absence of known risk factors and the background incidence is not known, it is important to ensure that all patients maintain good dental hygiene and see their dentists semiannually. Prospective data will provide a greater understanding of the pathogenesis and the true incidence of osteonecrosis of the jaw occurring in association with bisphosphonates, as well as the background incidence of spontaneous osteonecrosis of the jaw.

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Acknowledgment

The development of the Canadian guidelines on osteonecrosis of the jaw was funded by the Canadian Association of Oral and Maxillofacial Surgeons' Foundation for Continuing Education and Research. The Canadian Task Force on Osteonecrosis of the Jaw comprises the following members: **Aliya A. Khan, George K.B. Sandor, Edward Dore, Archibald D. Morrison, Mazen Alsahli, Faizan Amin, Edmund Peters, David A. Hanley, Sultan R. Chaudry, David W. Dempster, Francis H. Glorieux, Alan J. Neville, Reena M. Talwar, Cameron M. Clokie, Majd Al Mardini, Terri Paul, Sundeep Khosla, Robert G. Josse, Susan Sutherland, David K. Lam, Robert P. Carmichael, Nick Blanas, David Kendler, Steven Petak, Louis Georges Ste-Marie, Jacques Brown, A. Wayne Evans, Lorena Rios, Brian Lentle,** *and* **Juliet E. Compston.** *The consensus practice guidelines have been endorsed by the following national and international societies: the Canadian Association of Oral and Maxillofacial Surgeons, the Canadian Society of Endocrinology and Metabolism, the Ontario Society of Oral and Maxillofacial Surgeons, the Canadian Academy of Oral and Maxillofacial Pathology and Oral Medicine, the American Association of Clinical Endocrinologists, the International Bone and Mineral Society, and the International Society of Clinical Densitometry.*

Competing interests

Dr Khan *is a consultant for Amgen, Novartis, Merck, Lilly, Procter & Gamble, and Servier, and has received research support from Merck, Novartis, and Procter & Gamble.*

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Punch biopsy

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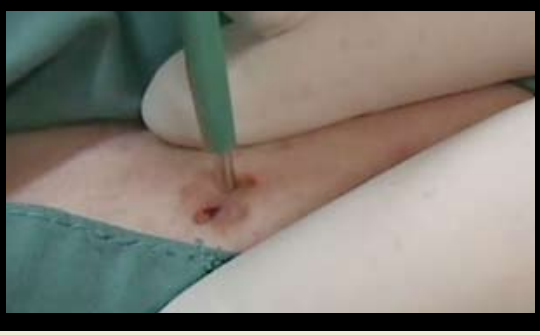

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Competing interests
None declared

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