Dental note

Osteoporosis treatment and medication-related osteonecrosis of the jaws

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Antiresorptive drugs are used widely for the prevention and management of primary and secondary osteoporosis. The bisphosphonates[1] and newer drugs such as denosumab[2] have been associated with osteonecrosis of the jaws. This condition is characterised by the presence of exposed, non-healing bone for more than eight weeks in the absence of radiotherapy or other pathology in the jaws. Extraction of teeth has been identified as the trigger factor in 60–87% of cases.[1,3-5] Dentoalveolar surgery has also been identified as a trigger[1] and is considered a major risk factor for osteonecrosis.[6]

When osteonecrosis occurs with antiresorptive therapy, it is termed medication-related osteonecrosis of the jaws (MRONJ).[6] There has been much debate over the incidence of MRONJ associated with bisphosphonate use. A widely quoted paper by the American Society for Bone and Mineral Research said it was rare, at between 1 in 10 000 and less than 1 in 100 000 patient-treatment years.[7] Detailed independent studies that take into account dental extractions have reported a much higher incidence at around 1 in 1000 patients.[3,8] When the duration of oral bisphosphonate therapy is taken into account, the incidence has been found to double to 2.1 in 1000 patients for those with four or more years of drug exposure.[8] A recent UK national survey[4] over a two-year period estimated that the incidence in a population of postmenopausal women with osteoporosis was between 1 in 1262 and 1 in 4419.

The incidence is much higher in cancer patients on antiresorptive drugs, with the risk being 1 in 15 for extractions in patients on intravenous bisphosphonates.[3] Compared to patients receiving monthly intravenous antiresorptive therapy for metastatic bone disease, multiple myeloma or giant cell tumours of bone, the 6-monthly or 12-monthly intravenous regimens used for patients with osteoporosis have a lower incidence of MRONJ.[6]

An Australian case-control study[9] investigated 950 consecutive patients taking oral bisphosphonates for osteoporosis who underwent dental extractions. There were four cases of MRONJ versus none in a control group of patients not taking bisphosphonates. All four cases had a low bone turnover as assessed by a fasted C-terminal crosslinking telopeptide (CTX) concentration of less than 150 pg/mL immediately before dental extraction. The incidence in patients with a CTX value less than 150 pg/mL was 1 in 45. All the affected patients were aged 70 or above and had chronic health problems requiring medication but which did not affect bone healing. No patients were immunocompromised, taking corticosteroids or undergoing cancer chemotherapy.

The exact pathogenesis by which antiresorptive therapy may result in MRONJ is unclear. Several mechanisms have been proposed[6,10] including anti-osteoclast activity, inhibition of angiogenesis, uncoupling of osteoblast–osteoclast activity in jaw bones, and soft tissue toxicity. Reduction of bone cellularity and vascularity may not support hard or soft tissue healing following dental extraction. This can lead to exposure of avascular bone which is readily colonised by oral bacteria. These mechanisms may also explain why MRONJ can occur spontaneously when normal function (eating or toothbrushing) traumatises the thin mucosa overlying jawbone exostoses or the mylohyoid ridge of the mandible, or when dentures are ill-fitting and traumatise the oral mucosa. Local factors such as periodontal disease or periapical pathology, and systemic factors such as corticosteroid use may contribute to the risk of MRONJ.[6]

The management of MRONJ is problematic and patients do not respond well to established protocols used for the treatment of osteomyelitis or osteoradionecrosis.[10] Patients may benefit from drug withdrawal until the area of osteonecrosis heals.[1] For patients with exposed or necrotic bone who are asymptomatic and have no evidence of infection, antibacterial mouth rinses are indicated. Patients with soft tissue infection require treatment with broad-spectrum antibiotics such as penicillin, cephalexin or clindamycin.[10] With time, the dead bone will sequestrate and should be removed without exposing uninvolved bone.[6] Treatment is dictated by the clinical stages of MRONJ and should be provided by an oral and maxillofacial surgeon. The MRONJ staging system developed by the American Association of Oral and Maxillofacial Surgeons[6] is the one used most commonly to guide treatment strategies and is available online.

Patients with osteoporosis who are to begin antiresorptive drug therapy by either the oral or intravenous route should be informed by their medical practitioner of the potential risks of MRONJ. They should also be informed of the need to ensure optimal oral health so as to prevent dental and periodontal disease which might require extraction of teeth in the future. Before starting treatment, the patient should therefore be seen by a dentist for a comprehensive oral examination.

Australian[11] and American[6] guidelines recommend that any teeth requiring extraction should be removed and dental caries and periodontal disease treated to ensure optimal oral health, and that the patient is dentally fit, before beginning antiresorptive therapy. During therapy, it is important that the patient's oral health is monitored regularly by their dentist. The less invasive treatments such as restorative dentistry, endodontics and non-surgical periodontal therapy are not risk factors for MRONJ and may also be used as safe alternatives to extractions if clinically feasible.

For patients on oral bisphosphonates who are to undergo dental extractions or other dentoalveolar surgery, a low bone turnover as shown by CTX testing may be used as a trigger to cease drug therapy until the fasted CTX exceeds 150 pg/mL.[11] Such cessation of therapy is termed a 'drug holiday'. In contrast with this approach, American guidelines[6] recommend a blanket two-month drug holiday before invasive dental procedures for patients with more than four years exposure to oral bisphosphonates. Drug holidays for osteoporotic patients should only be instituted following discussion with the patient's treating physician. The risk of MRONJ should be weighed against the risk of fracture on a case-by-case basis.

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