What's new for the clinician?

Summaries of and excerpts from recently published papers

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1. Risk of developing BRONJ among patients exposed to intravenous bisphosphonates following tooth extraction.

Bisphosphonate-related osteonecrosis of the jaws (BRONJ) is a recognised risk factor when extractions are performed on patients who are on a regime of bisphosphonates, especially when the drug is intravenously administered. This project investigated the incidence of BRONJ amongst patients who were at such risk.Most authors agree that between 50% and 60% of the occurrence of all BRONJ are related to dental interventions, especially extractions. Hence the current admonition that the recommendations of the American Association of Oral and Maxillo-Facial Surgeons should be heeded.

A prospective study included 36 patients and 62 tooth extractions. All patients had been treated or were currently being treated with zoledronic acid (Zometa, Novartis). The indications for extraction as opposed to more conservative approaches included intense pain, extreme mobility, and progressive and persistent infection. A prophylactic programme was instituted after each patient had signed an Informed Consent document. Amoxicillin with clavulanic acid was administered at the rate of 875 mgs amoxicillin and 125 mg clavulanic acid every eight hours. The regime was instituted two days before and continued through to 15 days after, the extraction(s).As an alternative when allergy to [penicillin was recorded, clindamycin was administered , 300 mg every eight hours. The extractions were completed with minimal trauma, maximum preservation of ti=ssue , frequent use of chlorhexidine mouthwash and most sites were sutured with double zero silk. Mouthwashes were continued at home three or four times a day for fifteen days.

Teeth were categorised into three types:
Type One: mobile, single root, simple removal
Type Two: ankylotic tooth with multiple roots, difficult extraction.
Type Three: Complicated extraction, with ostectomy or flap raising.

Comprehensive details of each case were recorded with special emphasis on the duration of the zoledronic acid regime including length of time of taking the drug.

The progress of the extraction site was monitored at 15 days after extraction and at one, two, three and four months. Each case was assessed as:

- closed socket
- normal healing with no exposed bone but open socket
- bone exposure (asymptomatic)
- infection, exposed bone (symptomatic).

The resulting data were subjected to comprehensive statistics, including regression analysis to identify possible relationships of the assorted variables. The incidence of BRONJ in relation to the number of extractions in the sample was 14.5 % after four months whilst in relation to the number of patients the incidence of the disease was 23.5%. One patient showed persistent infection and sequestrations leading to a mandibulectomy.

Amongst those patients with ongoing Zometa treatment, 18.2 % suffered BRONJ whilst those who suspended the drug at the time of extractions recorded an incidence of 26.1%.

There were no significant findings regarding sutured versus non sutured sockets, periodontal versus carious conditions or previous BRONJ. However it may be prudent to observe the lamina dura which may be sclerosed as a result of bisphosphonate impregnation and present a condion referred to as Stage One Osteonecrosis.

Given the high risk of BRONJ, patients are advised to seek conservative treatment in preference to extractions. When extractions are unavoidable it may be prudent to utilise controlled root extrusion techniques to minimise trauma. Other options include low frequency laser therapy which has a biostimulating effect on soft tissues, or a piezoelectric scalpel and platelet rich plasma.

Following the protocol of minimal trauma and adequate antibiotic protection, the incidence of BRONJ is shown to be low. It may be that patients suffering a bone disease such as multiple myeloma may be more susceptible to BRONJ, and it is known that more prolonged duration of administration of the drug is linked to an increased occurrence of BRONJ.

There are other factors related to the occurrence of BRONJ and more research will contribute to a further understanding of this unhappy possible consequence of extractions. A final note is that the regime of oral administration of bisphosphonates is associated with a much lower incidence of BRONJ.

Reference

1. Sanchis J M, Bagán J V, Murillo J, Diaz J M and Asensio L. Risk of developing BRONJ among patients exposed to intravenous bisphosphonates following tooth extraction. Quintesence International. 2014; 45 (9):769-77

2. Retrospective analysis of 27 cases of bisphosphonate related osteonecrosis of the jaw treated surgically or non surgically

The pathogenesis of BRONJ is related to the potential of BPh's as powerful inhibitors of osteoclastic activity and promoters of osteoclast apoptosis, resulting in decreased bone resorption and increased bone formation. These properties are valuable in the treatment of diseases in which intense bone resorption occurs, but their anti-angiogenetic properties lead to reduced bone vascularity, and reduced healing in the jawbone hence the risk of BRONJ.

The treatment of BTRONJ has remained difficult and identification of the most effective regime remains controversial. The authors undertook a study of 27 cases treated with a variety of strategies. There were amongst the sample 30 sites in the mandible and ten in the maxilla. Treatment was determined according to severity of the condition and the general health of the patient, but the general routine started with conservative management with a daily antimicrobial mouthwash, using 0.1% or 0.2% chlorhexidine. Where infection was evident, antibiotic therapy was prescribed, amoxicillin or clindamycin, for two weeks. Patients having Stage Two or Stage Three BRONJ (Exposed bone with pain and sepsis and, in Stage Three, having sequestra, fistula, and osteolysis) were scheduled for surgery to remove necrotic bone and loose teeth, followed by curettage. Gelfoam impregnated with tetracycline was placed when primary closure of the wound was not possible. In more severe instances, alloplastic bone substitute with tetracycline was inserted and covered with an absorbable collagen membrane as a guided bone regeneration technique. Stage Four BRONJ, having pathologic mandibular fractures, received radical segmental resection and immediate reconstruction using a mandible plate. Postoperative protocol determined that sutures were not removed before 14 days after surgery and patients were observed daily for the first week, weekly for the first month, once a month for the next six months and every three months thereafter.

Possible clinical signs and symptoms of BRONJ were sought. Pain, swelling, non-healing mucosal ulcer, recurrent abscess or fistula formation, exposed necrotic bone and/or changes in the periodontal health of adjacent teeth such as widening of the periodontal space or osteosclerotic lamina dura or loosening. Successful treatment was defined as complete healing with no exposed bone, necrosis, no swelling or pain. Unsuccessful treatment was recorded when there were sites without complete healing or if signs of recurrence of BRONJ were observed.

Twenty two patients were treated surgically and five non surgically. Twenty five patients (93%) and 27 sites (90%) were successfully treated with a mean period of healed BRONJ of 14 weeks (range 6 to 68 weeks). Three cases were deemed unsuccessful. One case was in a patient where myeloma had involved the mandible. In 21 sites of BRONJ, successful results were recorded after removal of necrotic bone and loose teeth. Guided Bone Regeneration (GBR) was successful in all 21 sites.

This series demonstrates that surgical treatment was effective in 21 patients and 23 sites. Non surgical treatments were delivered to six patients and four of these managements were successful.

Regular long term follow up after BRONJ is essential. Relapse or recurrence remains a possibility. The authors emphasise that early radiological diagnosis of BRONJ is often not possible as radiographic images do not show the real extent of the problem. All members of the health care team, including dentists, should be aware of the effects of bisphosphonates, including the disadvantages. Their use can be of considerable benefit to those suffering osteolytic forms of skeletal cancer. In osteoporosis, the drug is valuable in preventing fractures . Hence discontinuing the therapy involves a considered decision.

Although this series records a high success rate, the definitive treatment of BRONJ remains challenging and prevention through avoiding extractions and other triggers is infinitely preferable.

Reference

Lu, S-Y, Liang, CC, Lin, L-H.Retrospective analysis of 27 cases of bisphosphonate related osteonecrosis of the jaw treated surgically or non surgically.Journal of Dental Sciences, 2014; 9:185-94.