Bisphosphonates

Fact file

September 2008

Bisphosphate treatment can result in serious complications which a dental practitioner should be aware of, particularly osteonecrosis of the jaw (ONJ). This fact file examines the evidence on bisphosphonates, ONJ and its treatment and management.

Bisphosphonates are used predominantly in the treatment of osteoporosis, but also are used in the treatment of cancer and other diseases. Bisphosphate treatment can result in serious complications which a dental practitioner should be aware of. Particularly, bisphosphonate treatment is associated with osteonecrosis of the jaw (ONJ). Patients taking bisphosphonates, and patients that have developed ONJ require particular consideration in their treatment.

What are bisphosphonates and what are they used for?

Bisphosphonates are used in the treatment of osteoporosis, Paget's disease, hypercalcaemia, and in patients with cancer, particularly those receiving anti-cancer drugs. In cancers that metastasize to the bone, bisphosphonates reduce the risk of complications, such as spinal cord compression, fractures and bone pain. Bisphosphonates bind to the bone osteoclasts, and inhibit their function so decrease bone reabsorption.

The large majority of prescriptions of bisphosphonates are for patients with osteoporosis. Osteoporosis is a significant problem in the UK, leading to 180,000 fragility fractures in the UK annually.[1]

Bisphosphonates currently used in the UK include etidronate, clodronate, alendronate, risedronate, tiludronate, ibandronate, pamidronate and zoledronate.[1]

Intravenous bisphosphonates

Patients with cancer who are also given bisphosphonates are usually given them in intravenous form. This is usually in higher doses than that given for other non-cancer conditions.[1] Pamidronate and zoledronate are available only in intravenous form, and ibandronate can be used orally or intravenously.

Oral bisphophonates

The majority of bisphosphonates are administered orally. Bisphosphonate therapy administered in this way forms part of the management of osteoporosis.

What is osteonecrosis of the jaw?

A recent working party appointed by the American Society for Bone and Mineral Research defined a confirmed case of bisphosphonate-associated osteonecrosis of the jaw (ONJ) as "an area of exposed bone in the maxillofacial region that did not heal within 8 weeks after identification by a healthcare worker, in a patient who was receiving, or had been exposed to, a bisphosphonate and had not had radiation therapy to the craniofacial region."[3]

The incidence of ONJ in oral bisphosphonate therapy for osteoporosis is low (between 1 in 10,000 to 1 in 100,000).[1] Cancer patients on high dose intravenous bisphosphonates however have a risk ranging from 1 in 10 to 1 in 100 patients, depending on the duration of the bisphosphonate treatment.[1]

The number of ONJ cases is increasing and there are three potential reasons for this:

- Growing awareness of the condition through increased case reporting in the literature
- Increased prescribing of more potent bisphosphonates
- Increasing use of and duration of prescribing of these drugs.

Features of ONJ include localised pain, numbness and altered sensation, loosening of teeth, spontaneous exfoliation, soft tissue infection and swelling, exposed jaw bone, bone sequestration, extra-oral sinuses.[2]

Risk factors for ONJ

Risk factors for ONJ include:[1]

- Bisphosphonates (especially intravenous)
- Length of bisphosphonate therapy exposure
- Cancer and anti-cancer treatments
- Dental extractions
- Oral bone surgery
- Intra oral trauma
- Poorly fitted dental appliances
- Glucocorticoid use
- Smoking
- Alcohol abuse
- Periodontal/dental disease

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Current recommendations for patients taking bisphosphonates

The table below summarises the current recommendations for bisphosphonate patients, as summarised by Arrain and Masud[1] from the Report of the American Society for Bone and Mineral Research Working Party.[3]

	Patients with osteoporosis or other non-malignant disease taking bisphosphonates >3yrs	Patients with malignancy, starting or already receiving bisphosphonates
Dental regime	Regular dental visits, oral health maintenance	Regular dental visits, oral health maintenance – 6 to 12 monthly dental exams or as clinical/dental status demands
Dental exam pre-bisphosphonate therapy	No - as risk of ONJ is low no additional dental examination is needed or change to routine dental care. However, where there has been a lack of previous, routine, dental care, a dental checkup should be undertaken with any dental treatment, especially acute treatment, being addressed before patients begin a bisphosphonates prescription.	Yes – before starting IV bisphosphonates for bone metastasis. Invasive dental procedures, if needed, should be carried out and healing completed before starting bisphosphonates if the patient's clinical treatment allows. Liaise with physicians/oncologists. If not possible, need careful follow up of surgical sites.
Extractions	Extractions are not contra-indicated as risk of ONJ low. Root treatment preferable , coronally unrestorable can amputate to root level after root treatment seal. If extract, best to carry out atraumatic extractions and careful socket follow up – refer if chronic exposed bone.	Avoid extractions wherever possible as increased risk of ONJ – root treatment preferable and if coronally unrestorable can amputate to root level after root treatment and seal. For periodontally affected teeth – only extract if excessive mobility and aspiration risk. Symptomatic teeth in an area of exposed bone that is already exposed and necrotic can be extracted as established necrotic process will not be exacerbated by this. If unsavable, e.g. vertical root fracture and extraction needed, very careful follow up of surgical site important.
Periodontal disease	Perio surgery is appropriate if it reduces or eliminates bone disease. Can carry out modest bone contouring	Perio surgery is not recommended. Non-surgical perio treatment only.
Dentures	Need good fitting dentures	Good fitting dentures possibly with soft lining to prevent trauma
Endodontics	Avoid apical surgery. Conventional orthograde endodontics recommended rather than extraction where possible. Good coronal seal maintenance important.	Avoid apical surgery. Conventional orthograde endodontics recommended rather than extraction where possible. Good coronal seal maintenance important.
Implants	Currently not contra-indicated if taking bisphosphonates but prudent to gain informed consent which should be documented (risk assessment)	Not recommended and avoid elective surgery such as tori removal.

It is important to note that antibiotic prophylaxis is not recommended for any of the above situations. Should chronic bone exposure occur, referral to an appropriate specialist is essential.[3]

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Preventive measures

Good oral hygiene and regular routine dental examinations and hygiene are vital. Preventive measures also include preventive dentistry with caries control, avoiding invasive periodontal procedures or dental implant placement using soft liner on dentures. Preventive use of chlorhexidine mouthwash is recommended. [5]

Once ONJ has developed there are a number of ways of managing the condition. These are summarised in the table below, again taken from the paper by Arrain and Masud in which they summarised the Report of the American Society for Bone and Mineral Research Working Party.

Pain	Must be dealt with first appropriately
Infection	1. Oral rinses such as 0.12% Chlorhexidene 2. If there is infection systemic antibiotics are given 3. Maintain an infection-free oral environment (especially in multiple myeloma patients being considered for stem cell transplantation)
Surgical treatment	1. This should be delayed or conservative 2. Sharp edges removed to stop soft tissue and trauma 3. Loose boney sequestra removed with exposure of uninvolved bone 4. Segmental jaw resection may be needed for symptomatic patients with large segments of necrotic bone or pathological fracture
Altering bisphosphonate therapy regime	Some experts suggest stopping bisphosphonate therapy in cancer or osteoporosis patients with established ONJ if the patient's clinical situation allows. No published data yet to suggest this helps. The half life of bisphosphonates in the skeleton is high. Recommendation is to look at clinical situation, e.g. for aggressive skeletal metastatic disease one may continue bisphosphonates. For mild skeletal disease or for therapy for prevention of metastases can consider discontinuation. Discussion with patient's physician/oncologist is important.
Other considerations	1. In advanced ONJ in patients with limited ability to eat additional nutritional supplements important, e.g. tube feeding 2. Hyperbaric Oxygen: effectiveness of this procedure has not been established

References

[1] Arrain Y and Masud T. Recent recommendations on bisphophonate-associated osteonecrosis of the jaw. *Dental Update* May 2008; 35:238-2 2

[2] Rogers S. Jaw-necrosis increase. *BDA News* 2007; Vol 20 No. 3 March 2007

[3] Barker K and Rogers S. Bisphosphate-associated osteonecrosis of the jaws: A guide for the general practitioner. *Dental Update* 2006; 33:270-275

[4] Khan AA, Sandor GK, Dore E, Morrison AD, Alsahli M, Amin F, Peters E, Hanley DA, Chaudry SR, Dempster DW, Glorieux FH, Neville AJ, Talwar RM, Clokie CM, Al Mardini M, Paul T, Khosia S, Josse RG, Sutherland S, Lam DK, Carmichael RP, Blanas N, Kendler D, Petak S, St-Marie LG, Brown J, Evans AW, Rios L, Compston JE. Canadian consensus practice guidelines for bisphosphonate associated osteonecrosis of the jaw. *Journal of Rheumatology* 2008.

[5] Khosla S. et al. Bisphosphonate-associated osteonecrosis of the jaw: Report of a task force of the American Society for Bone and Mineral Research. *Journal of Bone and Mineral Research* 2007; Volume 22, Number 10 2007

For further background papers and resources, please refer to:

http://www.library.nhs.uk/oralhealth/ViewResource.aspx?resID=285289&tabID=289

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