Bisphosphonates and their clinical implications in dentistry

Tashmita Dhiman¹, Geetanjali², Jaspreet Singh Gill³, Ramneet Birring⁴

ABSTRACT

This review article describes the pivotal role played by bisphosphonates in the development of osteonecrosis of the jaw in patients on these drugs. It briefly describes the diverse bone diseases for which bisphosphonates are the prescribed drugs. The occasional but devastating adverse effect of these drugs has been prescribed as Bisphosphonates Related Osteonecrosis of the Jaw (BRONJ). As this condition is debilitating and difficult to treat, all efforts should be made to prevent its occurrence in patients at risk. Furthermore, pathogenesis and risk factors for BRONJ are described along with preventive measures and Management protocol for the same.

KEYWORDS: Bisphosphonates, Osteonecrosis, Dentistry

INTRODUCTION

Bisphosphonates are drugs that reduce bone resorption by hindering the formation, recruitment and function of osteoclasts. They are used in the treatment of many malignant and non malignant conditions as follows¹²:

Non-malignant:
- Osteoporosis
- Pagé’s disease
- Osteogenesis imperfecta
- Fibrous dysplasia
- Primary hyperparathyroidism.
- Cystic fibrosis

Malignant:
- Multiple myeloma
- Breast cancer
- Prostate cancer
- Bone metastatic lesions
- Hypercalcemia of malignancy

Commonly used bisphosphonate drugs:
- Zoledronic acid (Zometa)
- Alendronic acid (Fosavance)
- Risedronate sodium (Actonel)
- Etidronate disodium (didronel)
- Disodium pamidronate (Aredia)
- Sodium clodronate (Bonefos, Loron)
- Ibandronic acid (Bondronat, bonvia)

Bisphosphonates have a positive effect on quality of life of patients by decreasing or delaying onset of disease or treatment complications like bone fractures and bone pain.

However they accumulate at sites of high bone turnover such as in the jaw. This reduces bone turn over and bone blood supply leading to death of bone termed osteonecrosis or Bisphosphonate related osteonecrosis of jaw (BRONJ).

CLINICAL IMPLICATIONS IN DENTISTRY

BRONJ (Bisphosphonate Related Osteonecrosis of Jaw): It is defined as exposed, necrotic bone in maxilla or mandible that has persisted for more than eight weeks in patients taking bisphosphonates and where there has been no history of radiation therapy to the jaw. Symptoms of the condition can vary and may include pain, soft tissue infection and swelling, numbness, paraesthesia, exposed bone and delayed healing. BRONJ is seen to occur rarely in patients and therefore bisphosphonate drugs should not be considered as a contraindication for patients undergoing dental treatment.⁵

Also, till date there is no evidence to support that BRONJ risk will be decreased if the patient refrains from taking bisphosphonates temporarily or even permanently prior to invasive dental procedures since the drugs may persist in the skeletal tissues for years.

Modes of administration of bisphosphonates is an important determinant/risk factor of BRONJ. It has been seen that bisphosphonate taken i.v for malignancy is most commonly associated with production of ONJ. Risk of ONJ in patients taking oral bisphosphonate is low but has been reported.

Percentage of patients receiving bisphosphonates for management of malignancy who develop ONJ is between 4% and 10%. Around 60% cases arise after 1000 extractions or dentoalveolar surgery. Mandible is more susceptible than maxilla.

How to cite this article:
**MANAGEMENT OF PATIENTS TAKING BISPHOSPHONATES**

Management of patients taking bisphosphonates has been described as follows:

1. **Prevention:** Reducing risk factors: Patients should be strictly counselled to stop smoking. Prior to performing any surgical procedures, patient’s oral hygiene and periodontal health should be improved taking appropriate measures for the same.

2. **Use of Chlorhexidine mouthwash:** All patients should be told to rinse with chlorhexidine mouthwash twice daily for a week before extractions are done. Till date no evidence proves that taking antibiotics pre and post-operatively significantly prevents the occurrence of BRONJ. Just before performing extractions, the area should be irrigated/wiped with chlorhexidine. Its advisable to avoid raising flaps and use atraumatic technique as far as possible. Whenever possible, primary soft tissue closure should be achieved so that faster healing takes place. Patients should be instructed to rinse mouth with chlorhexidine twice daily for 2 months, 24 hrs post-operatively and should be reviewed regularly to monitor healing.

2. **Management of patients on oral bisphosphonates:** Treatment recommendations are similar to those for patients not taking medications as described below:

   **Restorative and Prosthetic dentistry:** All restorative procedures may be carried out. Till date no evidence proves that malocclusion or occlusal forces significantly increase the risk of BRONJ. Prosthetic appliances should be adjusted for fit to avoid mucosal irritation.

   **Periodontal diseases:** Treatment protocols are similar to those for the general population.

   **Oral and Maxillofacial Surgery:** In such cases, conservative surgical technique, with primary tissue closure, should be considered when extractions or surgery are necessary.

   Patients may use a chlorhexidine-containing rinse immediately before and after surgical procedures. Systemic antibiotic therapy may be considered for preoperative prophylaxis or if there is evidence of infection.

   **Endodontics:** If the tooth is salvageable, endodontic treatment is preferred to extractions or surgical manipulation.

3. **Management of patients receiving IV bisphosphonates:**

   Before the i.v bisphosphonate therapy is started, the patient is should undergo a dental evaluation by a qualified dental professional and dental recall examinations should be performed throughout the course of bisphosphonate therapy. The frequency of such examinations will be dictated by the patient’s clinical and dental status. Its also important to identify patients who pose the following risk factors for BRONJ: patients who have had oral bone surgery and/or dental extractions; patients having poorly fitting dentures or other appliances; any kind of trauma in the mouth; tori or other bony exostoses; pre-existing dental or periodontal disease; older age (>65yrs); prolonged exposure to bisphosphonate therapy; concomitant use of estrogen or glucocorticoids; comorbid conditions; alcohol or tobacco use.

   If the patients situation permits, invasive dental procedures should be performed before the IV bisphosphonate therapy is started with follow up at 14-21 days to ensure complete healing at the surgical site. Following are the treatment recommendations for the patients:

   **Restorative and prosthetic dentistry:** Recommendations are same as those for patients taking oral bisphosphonates.

   **Periodontal considerations:** Scaling and Root planing (non surgical) are preferred to performing periodontal surgery. Only when absolutely necessary, surgical treatment can be performed to obtain access to root surfaces.

   **Oral and Maxillofacial Surgery Considerations:** Mostly, nonsurgical endodontic or periodontal therapy is preferred to extractions, unless there is a risk of aspiration. Also, invasive dental/veolar surgical procedures such as reduction of tori, implant placement and extraction of asymptomatic teeth should be avoided. However, whenever an extraction or surgery is necessary, surgical technique used should be as conservative as possible with primary tissue closure.

   **Endodontic considerations:** It’s a preferred choice to perform endodontic treatment and save the tooth than to go for extractions or invasive surgeries. Manipulation beyond the apex is avoided.

4. **Management of patients affected with BRONJ:** In the early stages of BRONJ panoramic and periapical radiography may help in its detection. Computed tomography may also be used. However imaging is not required for patients with established clinical evidence of BRONJ.

   Incase there is pain, patient is prescribed with non steroidal anti inflammatory drugs or narcotic analgesics. Patient is advised to use chlorhexidine (0.12%) mouthwash or a similar oral antimicrobial rinse. Systemic antibiotic therapy may be prescribed if there is evidence of secondary infection. Establishing and maintaining good oral hygiene is essential.

   Management of affected bone–surgery should be minimised and only sharp bony edges removed. Antibiotics should be prescribed if there is evidence of infection around the exposed bone. Amoxicillin (500mg) is prescribed, its dosage being four times a day initially.
followed by twice a day for maintenance. Clindamycin (150-300 mg four times daily) can be prescribed alternatively (if allergic to penicillin) but it should be prescribed for use for not more than two weeks. Chlorhexidine mouthrinses should be done regularly four times a day. Topical application of chlorhexidine gel may be helpful.6

REFERENCES


Source of Support: Nil
Conflict of Interest: Nil