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Bisphosphonate and its impact on orthodontic tooth movement

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Abstract

In orthodontic treatment, mechanotherapy is needed to move the teeth. It is a challenge for the dentist to maximize the desired tooth movement without losing anchorage. Some experts have proposed a mechanical device to prevent the loss of anchorage, but it is still common to lose anchorage and cause side effects such as root resorption, white spots, caries, gingivitis and others. The use of bisphosphonates is recommended for the control of relapse and even for establishing pharmacological anchors. Bisphosphonates are pharmacological agents used to treat osteoporosis patients. This pharmacological agent is a potential bone resorption inhibitor. So, the use of bisphosphonates can be useful for orthodontist to control anchorage movement. Many literatures have begun to discuss the use of BP in orthodontic treatment patients. This review article aims to analyze the literature that discusses the influence of BP on orthodontic tooth movement.

Keywords: Bisphosphonate; Orthodontic Tooth Movement; Anchorage; Root Resorption

1. Introduction

In orthodontic treatment, mechanotherapy is needed to move the teeth. There is something that needs to be considered in orthodontic mechanotherapy, namely the anchoring function. It is a challenge for the dentist to maximize the desired tooth movement without losing anchorage. Some experts have proposed a mechanical device to prevent the loss of anchorage, but it is still common to lose anchorage and cause side effects such as root resorption, white spots, caries, gingivitis and others. [1,2]

In orthodontics, the use of bisphosphonates is recommended for the control of relapse and even for establishing pharmacological anchors. Bisphosphonates are pharmacological agents used to treat osteoporosis patients. This pharmacological agent is a potential bone resorption inhibitorIn orthodontic treatment, loss of anchorage (mesial movement of the anchor teeth) and relapse after treatment can occur.[3] Many literatures have begun to discuss the use of BP in orthodontic treatment patients. This review article aims to analyze the literature that discusses the influence of BP on orthodontic tooth movement.

2. Bisphosphonates

Bisphosphonates are drugs used in bone metabolic diseases such as osteoporosis, bone disease and bone pain caused by cancer. BP has the effect of inhibiting osteoclast activity and reducing bone resorption. BP has unique pharmacological characteristics unlike other drugs, its half-life can be more than 10 years.[4]

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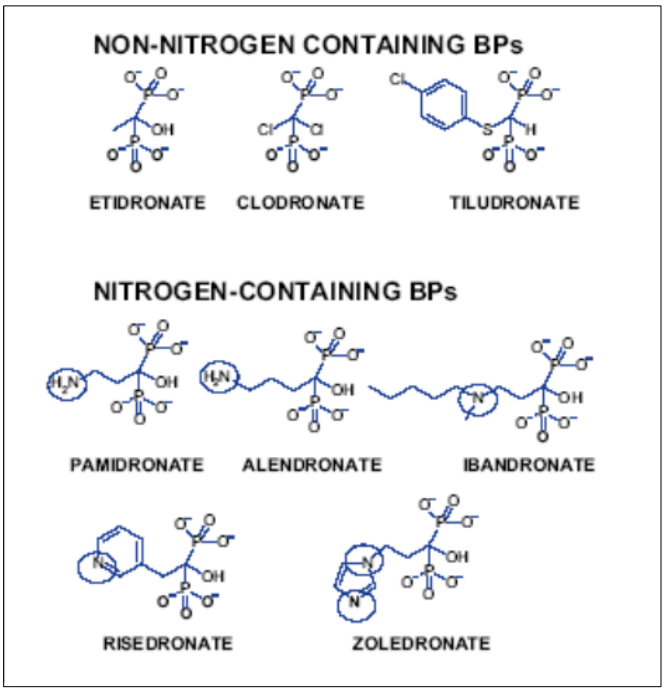

Figure 1 Bisphosphonate structure[5]

2.1. Pharmacological aspects of bisphosphonates

The structure of BP is related to its pharmacological activity, basically BP is an analogue of inorganic pyrophosphate. BP has a Phosphate-Carbon-Phosphate chemical structure, which is resistant to solvent enzymes and can bind to Hydroxyapatite bone crystals.[7]

There are 2 (two) types of Bisphosphonates, namely Bisphosphonate Nitrogen and Bisphosphonate Non-Nitrogen as shown in Figure 2 below.[8] (See Figure 2).

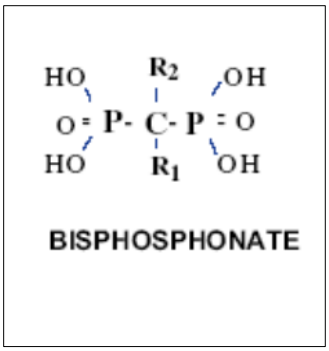

Figure 2 Types of bisphosphonates

Early generation Bisphosphonates (Etidronate and Clodronate) are Non-Nitrogen Bisphosphonates which have low bone resorption inhibitory potency. In contrast, Bisphosphonate Nitrogen (Pamidronate, Ibandronate and Zoledronic Acid) is a 100-10,000 times higher inhibitor of bone resorption.[8]

Bone resorption is inhibited by induction of osteoclast apoptosis.[6] The nitrogen type prevents the lipid lipidation process by inhibiting the production of isoprenoid compounds in the mevalonate pathway. This type is more potent than the non-nitrogen type.[10] Meanwhile, non-nitrogen BP works by inhibiting protein synthesis and inducing osteoclast apoptosis. Both of them inhibit bone resorption but through different pathways. Incorporation of BP by osteoclasts can induce apoptosis or programmed cell death.[12] BP can interfere with the 3-hydroxy-3methyl-glutaryl pathway. Bone metabolism in patients taking BP in the long term may be impaired, because its pharmacological effects only wear off after a long time, considering that its half-life is more than 10 years.[13]

Accumulation of high concentrations of BP in bone tissue can inhibit endothelial proliferation and reduce new capillary formation, this reinforces the characteristics of BP, namely, antiangiogenic.[14] Caution should be exercised because excessive accumulation of bisphosphonates in alveolar bone can predispose to avascular necrosis due to decreased new capillary formation. and endothelial cells.[15]

BP can also prevent osteoclast-activating factors such as RANKL, which are major mediators of osteoclast differentiation, activation and survival.

2.2. Pharmacokinetic aspects of bisphosphonates

Pharmacokinetics is the study of drug activity in the human body including absorption, distribution to tissues, metabolism and elimination.[16] Bioavailability is the fraction of a drug that reaches the systemic circulation after oral intake and depends on the amount absorbed and the amount that passes through the liver metabolism. The bioavailability of oral bisphosphonates is very low, usually less than 2%.[17]

Once BP is in the bloodstream, it can bind to hydroxyapatite in the bone matrix and residual drug is excreted through the kidneys. In general, 50-60% is bound to bone, and the remainder will be excreted through the kidneys within a few hours.

After the drug binds to bone, BP is considered inactive until bone remodeling occurs. BP leads to osteoclasts and rebounds to other areas with hydroxyapatite exposed or eliminated by the kidney. When directed towards osteoclasts, BP can inhibit cell function and shorten the lifespan of these cells. The amount of drug removed from the bone depends on the rate of bone turnover.

3. Orthodontic Teeth Movement

The basis of orthodontics is that teeth move within the alveolar bone when a force is applied. Various local and systemic factors such as age, nutrition, drug consumption and so on can affect orthodontic tooth movement. Such as bisphosphonates which have a mode of action that can interfere with osteoclast activity, so that it can affect dental care including inhibiting tooth movement, interfering with wound healing and triggering osteonecrosis.

Zahrowski said that in order to treat pro orthodontic patients who are undergoing BP therapy, counseling and treatment modification should be provided as needed, then the patient must be given information about possible side effects, after signing the informed consent treatment can only be started.[4]

While in orthodontics, the pharmacology of BP can alter bone physiology and may interfere with treatment. Then the most important thing is that it can trigger the occurrence of osteonecrosis. The risk of this osteonecrosis depends on the dose, duration and method of application. Patients with intravenous BP and malignant disease are at higher risk than patients with oral BP and benign disease

Several investigators reported a decrease in post-orthodontic relapse. This can be explained because BP causes a decrease in osteoclasts and there are structural changes in the cells including cytoplasmic polarity. This can reduce subcellular localization and expression of H+-ATPase and cathepsin K during orthodontic treatment.[19]

In an in vitro study by Liu et al, decreased tooth movement can reduce stress on the periodontal ligament. Lower levels of PGE2, COX2 and ribonucleic acid as receptor activator of NF-kappa beta indicate a slowed resorption pathway.[20]

3.1. Root resorption

Root resorption after local administration of BP showed a decreased effect on root resorption. In a study by Igarashi et al, it was found that there was a reduction in the occurrence of root resorption after systemic or topical BP administration. This depends on the dose applied. In this study, local subperiosteal injections were performed every 3 days for 21 days which was carried out during orthodontic treatment starting on day 7. Histologically, there were morphological changes of osteoblasts including loss of polarity and increased number of nuclei, no evidence of improvement or healing of resorption. root after BP administration after administration was discontinued.[21]

3.2. Rapid palatal expansion

RPE is an orthodontic process indicated for constricted maxillary arches. Orthodontic appliances are used for sutural expansion. Sutures undergo remodeling including deposition, resorption and changes in fiber orientation. Clinically, to

maintain the stability of the results obtained, various retainers were used to maintain the position of the teeth and allow the periodontal tissues to reorganize after the maxillary expansion procedure. By using BP, its mode of action can help to prevent relapse after maxillary expansion procedures.[22]

In a 2004 study, investigators recommended a combination of local administration of BP with mechanical retention to achieve maximal retention. In this study, RPE was performed on 44 wistar rats. This group received the RPE procedure, in the group with local BP injection, the result was a reduced relapse rate of only 6% while in patients without injection the relapse presentation was 25%. The high affinity of BP for hydroxyapatite crystals is an important factor in reducing bone resorption that occurs in relapse. Histological examination revealed that there was a decrease in multinuclear giant cells in the group given BP injection. Warita et al reported that topical application of BP can also inhibit tooth movement and reduce the number of multinuclear giant cells on the pressure side.[23]

4. Conclusion

- In patients on BP therapy, orthodontic treatment may be longer due to inhibited bone turnover.
- Root resorption in the orthodontic field is of great concern. BP has proven that it can reduce the amount of root resorption in animal studies. This can be an additional therapy for orthodontists in order to reduce orthodontic tooth movement that can trigger root resorption.
- Maximum retention can be achieved during the study, namely by mechanical retention and BP administration after the mechanical expansion procedure. However, more clinical evidence is needed before it can be used pharmacologically in orthodontics.
- To help resolve the problem of anchor loss, topical or systemic administration of BP can be considered as a barrier to orthodontic tooth movement. Then if the orthodontist uses this pharmacological agent to prevent unwanted tooth movement so as to reduce the retention duration and also provide a better orthodontic strength system. Even so, it is necessary to carry out further research on experimental animals before giving it to patients.

In conclusion, more clinical studies are needed to provide scientific evidence regarding the effect of BP on orthodontic tooth movement. In the field of orthodontics, the therapeutic use of BP must be done carefully because there are still many pros and cons.

Compliance with ethical standards

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Disclosure of conflict of interest

There are no conflicts of interest.

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