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Abstract

Bisphosphonates (BPs) are drugs that act primarily to inhibit osteoclast activity and bone resorption, used in many clinical conditions associated with excessive bone resorption. Aim of this review is to investigate the effects of BPs on orthodontic tooth movement. All selected studies showed that orthodontic tooth movement is reduced after BPs administration, with not clear effect on root resorption. Orthodontists should be aware of the effect of bisphosphonates on tooth movement and evaluate patients taking BPs before starting any orthodontic treatment.

Introduction

Bisphosphonates (BPs) are drugs that act primarily to inhibit osteoclast activity and bone resorption. BPs are a class of drugs prescribed for various skeletal disorders / osteopenic conditions (Paget's disease, osteoporosis, malignancy metastasis to the skeleton, multiple myeloma, osteogenesis inperfecta etc.,) associated with excessive bone resorption.[1-2]

They are considered the ?rst-line of therapy in the treatment of osteoporosis and are the most commonly prescribed like bone anti-resorptive agents.[1-2]

BPs are synthetic analogues of inorganic pyrophosphates. In pyrophosphate structure oxygen is bonded with phosphates (P-O-P), while the oxygen molecule is replaced with carbon atom (P-C-P) in bisphosphonate structure. The P-C-P bondage gives resistance to enzymatic degradation and strong affinity to calcium hydroxyapatite of the bone structure.[3]

BPs are classified into two sub types, based on the presence of Nitrogen atom; they are Nitrogenous BPs - N-BPsÂ (Zoledronate, Alendronate, Pamidronate, Risedronate, Ibandronate etc.,) and Non-Nitrogenous BPs - Non-N BPs (Clodronate, Etidronate, Tiludronate etc.,). The presence of Nitrogen gives more potency to N-BPs. NBPs acts on osteoclasts by inhibiting protein synthesis and induction of apoptosis by the production isoprenoid compounds (farneyl / pyrophosphate and geranyl / genanyl /pyrophosphate) in mevalonate pathway.[4]

In clinical dentistry, patients under BPs treatment should be tackled carefully when considering for dental procedures (extraction, implant placement, periodontal surgery etc.,) and also orthodontic treatment (extraction therapy, excessive force application, miniscrews placement etc.,) because they can be at the risk to develop â€œBP related osteonecrosis of the jawâ€• due to the anti-vascular activity of BPs [5-6]. In such patients conservative procedures like non extraction orthodontic treatment, mild force application, avoiding orthognathic surgeries etc., are preferable. In clinical orthodontics, few cases were reported with reduced orthodontic tooth movement, increase relapse tendency, late duration of treatment in patients which are taking BPs.[7]

Orthodontists have observed that tooth move at different rates and that there is an extensive variability in individual response to orthodontic treatment due to drugs and â•„ or systemic factors which can change bone remodeling. It has been seen that drugs such as bisphosphonates can reduce the rate of orthodontic movement through their actions on bone metabolism, principally the inhibition of bone resorption. Orthodontists should be very careful with patients using bisphosphonates. [8]

Aim of this study is to analyze the effects of BPs therapy on orthodontic tooth movement and the potential use of them to improve orthodontic anchorage.

Methods

A systematic review of literature has been performed on the principal medical databases: PubMed (Medline) and Scopus. Used keywords were: bisphosphonates, tooth movement, orthodontics in order to identify all articles about the correlation between bisphosphonate therapy and tooth movements. After a careful analysis, 26 articles were selected.Â

Review

Many studies documented reduction of orthodontic tooth movements due to BPs therapy.[9]

All studies were in vivo in animals.

There is general consensus in selected papers that orthodontic tooth movement is reduced after BPs administration. [10-24]

Studies by Liu, Igarashi and Adachi used similar models and protocols, and applied expansion forces of between 120 and 165 mN.[10-12] They reported a significant decrease in orthodontic tooth movement after subperiosteal injections adjacent to the molar under study (topical administration) or after subcutaneous injections (systemic administration). Comparing these three studies risedronate appears to be the most effective in reducing orthodontic tooth movement, followed by 4-amino-1-hydroxybutylidene-1,1-bisphosphonate (AHBuBP), then clodronate.

A recent study by Franzoni showed that both alendronate sodium and zoledronic acid reduce orthodontic teeth movement but this effect is much greater with zoledronic acid.[25]

The reduction in orthodontic tooth movement relapse that several authors found[10,11,15]Â could be explained by the decrease in osteoclasts[10,20Â] and structural changes (undulating margins, cytoplasmic polarity) and resorptive functions[14,16], significantly reducing the subcellular localization and expression of H(+)-ATPase and cathepsin K during orthodontic movement[16].

Analyzing if BPs administration has an influence on root resorption, the literature reviewed is contradictory about this. Some studies evidenced the reduction of root resorption after BPs administration[11,12,14], but another study found that showed root resorption on the side under pressure and the side under tension in 1-hydroxyethylidene-1,l-bisphosphonate-treated rats, but only on the side under pressure in untreated animals[13].

Regarding the effects on mid-palatine suture, a study showed that the combination of the administration of a local bisphosphonate injection with mechanical retention give a much safer retention of rapid palatine expansion.[17]

The tooth movement reduction induced by BPs administration may be beneficial for anchorage procedure; to address the problem of anchorage loss, topical or systemic administration of BPs could be considered as they decelerate the tooth movement. Therefore, if we could use pharmacological agents to prevent undesirable tooth movement it would reduce the retention duration and also provide better orthodontic force system. However, the results from animal studies need to be verified on patients in trials before they could be suggested for clinical use.

Due to the increasing number of older patients requiring orthodontic treatment, the number of patients with a medical history including BPs treatment is increasing.[26]

Some recommendations to orthodontists for patients taking bisphosphonates were proposed by Zahrowski.[7] Â He suggested to obtain detailed patient information about bisphosphonate administration regarding the duration of treatment, the dose, and the frequency of use. This should be followed by a careful evaluation of the bene?ts vs. the risks of orthodontic treatment by ?rst assessing whether the patient is at high or low risk for inhibition of orthodontic tooth movement or more serious medical complications such as osteonecrosis. It may be prudent to prohibit orthodontic treatment to high-risk patients. For low-risk patients, if orthodontic treatment is considered appropriate, plans should be assessed and modi?ed to include compromises such as avoiding or minimizing elective surgery and extractions, favoring interproximation over extractions, minimizing tooth movement, minimizing pressures on tissues during treatment and retention, and limiting treatment to facilitate the possible need for early discontinuation of treatment.Â

Conclusions

Bisphosphonates administration is associated with reduction of orthodontic tooth movement. Itâ€™s not still clear about the influence of this therapy on root resorption. The tooth movement reduction induced by BPs administration can be beneficial for anchorage but this effect needs to be evaluated in clinical human studies before using bisphosphonate in clinical practice. Orthodontists should be aware of the effect of bisphosphonates on tooth movement and evaluate patients taking BPs before starting any orthodontic treatment.

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