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Featured Review Article

Recent Advances in Orthodontic Retention Methods: A Review article

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ABSTRACT

Importance: Retention is an integral part of orthodontic treatment. Various biomedical agents, methods, and techniques have been introduced over the past 2 decades that could be useful in orthodontic retention. This review focuses on the underlying mechanisms and uses of these biomedical agents, lasers, vibrational therapies, and the most recent types of mechanical retainers. This review is also intended to serve as a resource for orthodontic researchers and clinicians. For researchers, it should facilitate further investigations into the clinical applications of the various agents and methods. For clinicians, it provides an up-to-date summary of new approaches that might be used in the future.

Observations: Several biomedical agents, including osteoprotegerin, bisphosphonates, bone morphogenic proteins, and relaxin, were reviewed. The applicability of low-level laser therapy (LLLT) and mechanical vibration also were evaluated, along with the modifications that have been introduced in conventional retention appliances.

Conclusion and Relevance: Among biomedical agents evaluated in this review, RANKL inhibitor agents, particularly denosumab, hold the greatest potential for future applications in orthodontic retention. In addition, LLLT has been associated with faster periodontal ligament maturation, especially if it is used with conventional retention methods, which might shorten the time required for retention after orthodontic treatment. Mechanical vibration has shown osteogenic effect on bone, even though it failed experimentally to inhibit relapse. Importantly, these new biomedical agents and techniques were mainly investigated experimentally, and further studies are required to confirm or refute their clinical applicability for orthodontic retention.

1. Introduction

The retention protocols and appliances used in orthodontics have witnessed a major changes in recent years with the incorporation of biological agents and adjunctive procedures, along with conventional approaches [1–4]. Review articles detailing conventional approaches, which compare and discuss the most commonly used retainers (e.g., fixed lingual retainers, removable thermoplastic retainers, and acrylic retainers) [5–7], along with a recent systematic review that comprehensively compared different commonly used retention protocols (fixed vs. removable, fixed vs. fixed, and removable vs. removable retainers) [8] exists in the literature. No previous publication has reviewed and synthesized current advances in orthodontic retention methods, which includes biological agents, low-level lasers, and newer retention protocols and designs. Thus, a review is deemed necessary to update the clinical community on the potential application of these newer materials and methods. Moreover, understanding these advances will help shape the future of orthodontic retention research by clarifying the potentials and limitations of each investigated agent, material, or technique.

Orthodontic biological research has developed greatly over the past 20 years. Multiple biological agents, such as osteoprotegerin (OPG), relaxin, bone morphogenic proteins (BMPs), and chemical agents, such as bisphosphonates (BPs) and simvastatin, have been investigated experimentally to determine whether they could be used to inhibit tooth movements and improve postorthodontic stability. The ability of low-level laser therapy (LLLT) and mechanical vibration devices to enhance postorthodontic stability also has been studied [9–11]. There also have been clinical studies evaluating composite resin retainers and introducing new retainer designs [12,13]. The aim of the present review was to evaluate current

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proposals in orthodontic retention, focusing on new materials and techniques that might serve as potential adjuncts or replacements for current retention protocols. The literature was systematically searched using MEDLINE (through PubMed) and ProQuest databases, covering both the published and unpublished literature that reported in English between 1996 and 2016. The review is presented in three sections: biomedical agents, laser and vibrational therapies, and mechanical retainers (Table 1).

2. Biomedical agents

The biological and pharmacological agents that have been investigated in orthodontics typically target factors that control bone metabolism. The ability of various hormones, cytokines, growth factors, and therapeutic agents to inhibit tooth movements has been well studied. This section discusses the biological mechanisms of action of various biomedical agents, focusing on their potential orthodontic applicability and suitability for further investigations.

2.1. Osteoprotegerin

OPG is an endogenous competitor protein that counteracts the resorptive action of RANKL (receptor activator of nuclear factor kappa-b ligand) by blocking it from binding to RANK. RANKL is a member of the tumor necrosis factor (TNF) superfamily actively involved in remodeling of bone and the periodontal ligament (PDL). It is considered essential for osteoclast differentiation, function, and survival [14]. Bone resorption is activated by binding of RANKL to RANK, another (TNF) family receptor that is present on osteoclast cells and their precursors [15]. Again, the role of OPG in the RANK-RANKL-OPG triad is to counter the action of RANKL. As a result, binding of OPG to RANKL produces an inhibitory effect on bone resorption, with profound reductions in osteoclast numbers (up to 95% reductions in osteoclasts have been reported in animal models during orthodontic tooth movement) [16,17]. The RANKL:OPG ratio is considered an important factor in bone metabolism, with increases and decreases of this ratio associated with bone resorption and formation, respectively.

Due to its antiresorptive effect, increased OPG levels result in a significant increase in bone mineral density and bone strength [18,19]. This shift of balance in bone metabolism toward bone formation is thought to result from the transient secondary effects of OPG on endogenous parathyroid hormone, which helps to maintain normal serum calcium levels and increase bone density and strength [20]. In medicine, OPG has been used to treat rheumatoid arthritis, osteoporosis, and other bone-related disorders [21–23]. The effectiveness, safety, and tolerability to OPG treatment has been studied in a randomized clinical trial on healthy postmenopausal women [24], which showed that it was well tolerated, and its effect was rapid, sustained, and reversible.

Table 1
Effects of biomedical agents, LLLT, and mechanical vibration on bone and PDL

Biomedical agent	Biological effect
Osteoprotegerin	Inhibits bone resorption and accelerates PDL maturation
Bisphosphonates	Inhibit bone resorption
Bone morphogenic proteins	Stimulate bone and PDL formation
Relaxin	Stimulates PDL turnover
Simvastatin	Stimulates bone formation
Strontium ranelate	Stimulates bone formation and inhibits bone resorption
LLLT	Stimulates both PDL and alveolar bone remodeling
Mechanical vibration	Inhibits bone resorption

LLLT, low-level laser therapy; PDL, periodontal ligament.

In orthodontics, OPG has been investigated to prevent relapse and enhance anchorage. Several experimental studies have shown that local or systemic injections of OPG inhibit orthodontic tooth movements and reduce relapse [16,17,25–30]. Keles et al. [16], who experimentally compared the effects of systemically injected OPG and BP on bone resorption and teeth movements, showed greater reductions in osteoclast numbers and lesser molar movements with OPG than BP. The same effects were also reported after localized OPG injections (5 mg/kg injected twice weekly for 3 weeks) [28]. These differences between the two agents were related to the fact that BP must be incorporated into the bone matrix to inhibit osteoclast activity [31], and OPG blocks RANK-RANKL binding, as well as differentiation of pre-osteoclasts to osteoclasts. Furthermore, BPs act only on active osteoclasts, whereas OPG inhibits osteoclast formation, function, and survival [32] (Fig. 1).

Additionally, OPG affects the amount of incisor retraction to molar anchorage loss. Different doses of OPG applied locally (0.5 mg/kg or 5 mg/kg), have been experimentally assessed [25]. The ratios of incisor retraction to molar anchorage loss were 2.3 to 1.0 mm, 2.0 to 1.0 mm, and 5.2 to 1.0 mm in the control, low-dose, and high-dose groups, respectively. Schneider et al. [27] also reported greater inhibition of molar than incisor movement with a higher dose of OPG. They showed no detrimental effects of OPG on PDL cells.

In addition, OPG inhibits bone loss in both lipopolysaccharide and ligature-induced periodontitis [33,34]. There was a faster PDL maturation with OPG [26], without any epithelial tissue abnormalities [28]. Rapid maturation of PDL and inhibition of bone resorption, the properties exhibited by OPG, are considered desirable after orthodontic treatment. Moreover, local injection of OPG appears to induce endogenous OPG expression in periodontal tissues, with no signs of severe inflammation [17,29,35]. Furthermore, OPG has been reported to inhibit external root resorption due to inhibitory effects on cementoclasts. The external root resorption repair ratio was significantly increased in the OPG group (75.7%), compared with 37.1% in the control group [35]. At the cellular level, immunohistochemical analyses of osteolytic markers, such as RANK, Runt-related transcription factor-2 (RUNX-2), Vimentin, acid-sensing ion channel 2 (ASIC2), transient receptor potential cation channel subfamily V member 4 (TRPV4), matrix metalloproteinases (MMPs), and tissue inhibitor of metalloproteinase, indicating decrease in bone remodeling, with no changes in type I collagen expression, the major

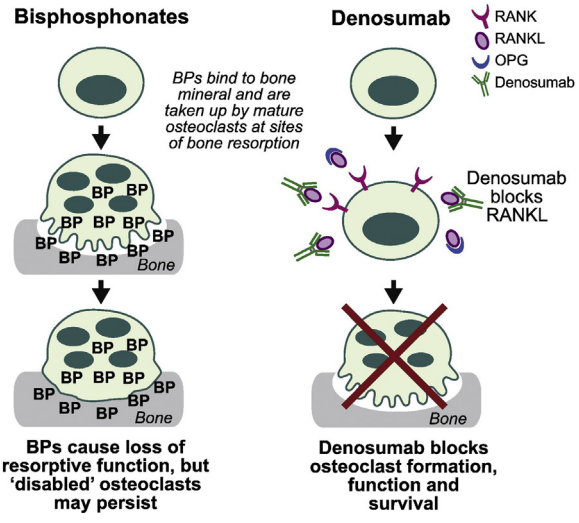

Fig. 1. BPs and denosumab mechanism of action on osteoclasts. Adapted with permission from Baron R, Ferrari S, Russell RG. Denosumab and bisphosphonates: different mechanisms of action and effects. Bone 2011;48:677–92. © 2010 by Elsevier.

component of PDL structure [28,29]. In addition, micro computed tomography analyses have shown that OPG significantly increases bone volume fraction (BVF) in the molar furcation area [26], and enhances trabecular bone mineralization [26–29,35].

The effects of locally delivered OPG appear to be more profound in alveolar bone than in long bones. Several studies have shown no effect on long-bone remodeling, based on bone mineral density and BVF, even though alveolar bone showed increases in bone formation [17,27,35]. Systemic effects of locally delivered OPG, assessed by serum tartrate-resistant acid phosphatase 5b assay, have been reported [26]. The difference between these experimental studies probably relates to the animal models and protocols that were used. Possible rapid uptake of OPG at the injection site, in response to orthodontic force and subsequent cellular activities, might be another reason.

Although OPG holds some advantages over BPs, there are some concerns regarding its use. One potential side effect is the development of anti-OPG antibodies that could neutralize endogenous OPG. In addition, the potential of OPG to block TRAIL (TNF-related apoptosis-inducing ligand) protein and interfere with normal immune mechanism should not be overlooked [22]. Because of these concerns, any clinical evaluation of this new protocol in orthodontic retention should consider using denosumab, a monoclonal antibody against human RANKL. Denosumab has the same effect on bone as OPG [32], but does not develop anti-OPG antibodies because it is structurally different (Fig. 2). Moreover, it does not show any binding affinity to TRAIL or other TNF family members [36]. Denosumab was developed to increase the duration of RANKL inhibition and increase patients' compliance. The sustainability of denosumab is a favorable feature for orthodontic retention purposes. Denosumab is applied every 6 months, as compared with monthly applications with OPG. A single dose of denosumab has been shown to produce a more efficient, sustainable effect that is safe, reversible, and well tolerated [37]. Denosumab has been approved by the Food and Drug Administration for use in adults and skeletally mature individuals [38].

2.2. Bisphosphonates

BPs are commonly used to treat osteoporosis and other bone-related disorders [39]. Although there are different types of BPs, the most commonly tested in orthodontics are pamidronate and zoledronate [16,28,40]. Both of these drugs have the same mechanism of action; they decrease bone resorption by inhibiting osteoclastic activity [39]. BPs get incorporated in the bone mineral due to their high affinity to calcium ions. When osteoclasts attempt to resorb bone, they undergo apoptosis because BPs block their enzymatic activity [41]. The decrease in osteoclastic activity and, subsequently, bone resorption, inhibits alveolar bone loss in experimental periodontitis [42], and improves the outcome of conventional periodontal therapy [43].

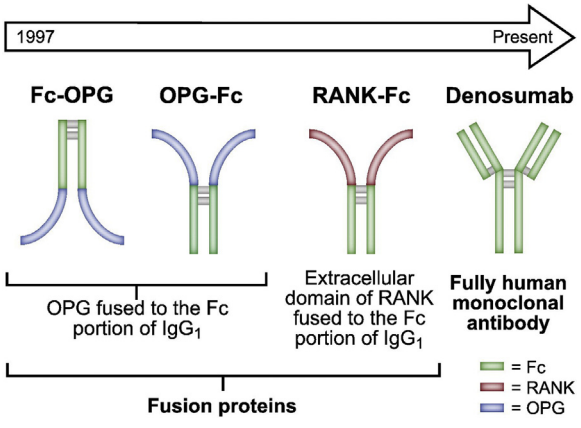

Fig. 2. History of RANKL inhibitors development. Adapted with permission from Baron R, Ferrari S, Russell RG. Denosumab and bisphosphonates: different mechanisms of action and effects. Bone 2011;48:677–92. © 2010 by Elsevier.

Studies evaluating the effect of BPs, delivered systemically or locally, on tooth movements, showed positive results (close to the effects of OPG) [16,28,40,44,45]. A single dose of BP in rats reduced osteoclast numbers on the alveolar surfaces, with aggregations mainly in vascular canals [40]. The same study found no changes in osteoblasts, osteocytes, or PDL fibroblasts [40]. Increased osteoclast numbers also have been reported with long-term BP treatment, which might have been a reaction to osteoclast apoptosis [41].

BPs may provide an adjunctive retention therapy in orthodontics, especially with single-dose applications. However, the use of BPs for orthodontics purposes, either for retention or anchorage control, should be weighed against the long period of time that BPs can affect bone resorption. More importantly, BPs increase the risk of BP-related osteonecrosis of the jaw, especially when other dental procedures (i.e., extraction of wisdom teeth, implant placement) must be performed. However, single doses of BP in orthodontic experimental models have shown no signs of BP-related osteonecrosis of the jaw [28]. This issue would be less of a concern if the effects of BPs were reversible, as with RANKL inhibitors OPG or denosumab. Another issue is the long-term effects of BPs on craniofacial growth [46,47]. Local application of BPs in experimental animals has, so far, not been shown to have effects on overall growth or tibial growth [45]. Any further orthodontic investigations on BPs should consider their efficacy, effectiveness, and long-term safety.

2.3. Bone morphogenic proteins

BMPs are growth factors that induce bone, cartilage, and PDL formation [48,49]. BMPs act locally at the site of application. They are often incorporated in dried bone matrix and used to repair defects. BMP effects on bone and surrounding tissues are only temporary [49]. In other words, the regenerative effects of BMPs are limited to the matrix size and the BMP bioactivity period. BMPs have been used in orthopedic treatments [50], oral surgery [51], and regenerative periodontal therapy [52].

In orthodontics, a pilot study assessed the role of BMPs in improving postorthodontic stability [53]. Favorable effects on incisor stability and regeneration of surrounding tissues were reported. However, there was evidence of hypercementosis and focal fusion of root and alveolar bone, which could develop into ankylosis. Further experimental studies are necessary to rule out the risk of ankylosis, and confirm the current effects on stability and root resorption.

2.4. Relaxin

Relaxin hormone is known to play a role in various physiologic processes [54]. It has been shown to have stimulatory effects on PDL collagen metabolism [55] and collagenase production, as reflected by elevated expression of MMP1 and MMP8, and increases collagen degradation activity in the PDL [56,57]. Based on the hypothesis that increased collagen metabolism will alleviate the rebound of PDL fibers, and subsequently tooth relapse, the effects of relaxin on posttreatment stability were investigated. Experimental studies showed that relaxin injections reduce the percentage of relapse in orthodontically moved teeth [56,57]. Clinically, relaxin showed no effects on the rate of tooth movement and subsequent relapse. A randomized trial evaluating the maxillary incisors of patients treated with a sequence of programmed aligners (Invisalign Align

Technology, California) showed no differences in the tooth-movement rates or relapse between the relaxin and placebo groups [58]. Relaxin treatment also requires frequent administrations because of its rapid turnover, which makes it inconvenient for both the patients and orthodontist.

2.5. Simvastatin

Simvastatin, a member of the statin drug family, is known to reduce cholesterol levels and thought to prevent cardiovascular diseases. It also has anabolic effects on bone, mainly by osteogenesis promotion, osteoblast survival, and inhibition of osteoclast activity through the RANK-RANKL-OPG pathway [59]. In orthodontics, simvastatin has been experimentally evaluated for its effects on stability of teeth. The simvastatin group showed 40% less relapse than the control group, after 4 weeks of daily systemic injections [60]. This was associated with increases in bone formation and decreases in bone resorption, as indicated by increased OPG and decreased RANKL expression in the PDL. Another experimental study showed less, but not statistically significant, relapse of orthodontically moved teeth in the treated group than in controls [61]. In brief, simvastatin seems to have favorable effects on bone metabolism in experimental studies. However, this agent requires daily applications due to its short half-life, which makes it an unfavorable agent for further clinical application.

2.6. Strontium

Strontium (Sr^{+2}) ion, which resembles calcium (Ca^{+2}), has a high affinity for bone. Strontium ranelate is promoted as a dual-action bone agent [62]. Strontium stimulates the calcium-sensing receptors and leads to the differentiation of pre-osteoblasts to osteoblasts, which increases bone formation. Moreover, strontium stimulates osteoblasts to secrete OPG, which reduces osteoclast differentiation and decreases bone resorption [63]. Strontium ranelate is used to treat osteoporosis and other bone-related disorders.

In orthodontics, the inhibitory effects of strontium chloride, which acts similarly to strontium ranelate, have been demonstrated experimentally [64]. Local delivery of strontium chloride around expanded molars in rats every other day for 3 weeks reduced the amount of tooth movement and improved the osteoblasts-to-osteoclasts ratio. It is important to note that restrictions on the use of strontium ranelate have been recently issued by the manufacturer and the European Medicine Agency, because of the risk of adverse cardiovascular events [65]. For this reason, strontium is an unsuitable agent for further orthodontic investigations.

Briefly, among the biomedical agents reviewed, the RANKL inhibitor agent (denosumab) has been shown as the most favorable agent for its potential application in orthodontic retention. It has favorable reversible effects on bone metabolism that might be helpful after orthodontic treatment. However, further investigations are required to confirm these findings. Other biomedical agents, such as BPs and BMPs, require further experimental evaluations. Agents such as relaxin, simvastatin, and strontium are unsuitable for further orthodontic investigations as per the critical evaluation of the published literature.

3. LLLT and mechanical vibration devices

3.1. Low-level laser therapy

LLLT or cold lasers have been investigated in orthodontics for accelerating tooth movements [9,11], relief of pain associated with activation of orthodontic appliances [11,66], and as an adjunctive tool in dental retention. A recent systematic review was unable to identify any clinical studies that evaluated the effects of LLLT on relapse prevention after orthodontic treatment [11].

From a biological perspective, LLLT has biostimulatory effects on the submucosal cellular environment, thought to be due to photostimulation of the cell metabolism and increased cellular activity [67,68]. The suggested cellular mechanisms of lasers include increases in cell membrane permeability and Ca^{+2} influx, increases in ATP production and cellular activity, and increases in pro- and anti-inflammatory cytokines [69,70]. In addition, LLLT increases the blood flow in exposed soft tissue area through vasodilation. This accelerates the repair and remodeling processes of the PDL, mainly by upregulating MMPs and collagenases.

LLLT has shown favorable regenerative effects on the PDL during relapse and retention [71]. In an experimental orthodontic model, LLLT was applied daily in both labial and palatal root areas of the maxillary incisors. There was a significant increase in MMP (collagen degradation biomarkers) levels and a decrease in tissue inhibitor of metalloproteinase (MMPs endogenous inhibitors) levels in the LLLT group than in the relapse and active control groups. In addition, collagen synthesis was notably higher when LLLT was applied as an adjunct to fixed orthodontic retainer, compared with LLLT alone. This happened because LLLT stimulated both PDL and alveolar bone remodeling. Maintaining the stationary position of teeth appears to be a key factor in using LLLT for retention purposes.

The effects of LLLT on relapse tendency after orthodontic tooth movement have also been assessed in experimental orthodontic models [72]. There was no significant difference in relapse rates between the LLLT and control groups. As previously indicated, the position of teeth must be maintained to increase LLLT-induced collagen synthesis in the PDL relative to its degradation, and consequently accelerate PDL tissue recovery. As such, conventional retention methods or other potential bone-directed biological retainers should be evaluated as adjuncts to LLLT.

The effects of LLLT on short-term rotational relapse prevention in orthodontically de-rotated maxillary incisors have also been clinically investigated [73]. The conventional circumferential supracrestal fiberotomy, erbium-doped yttrium aluminium garnet (Er:YAG) laser–aided fiberotomy, and LLLT have shown similar effects on rotational relapse prevention. These findings were also described in an experimental study using dogs [74]. The highest relapse of rotated mandibular incisor happened during the first week after orthodontic forces were stopped. After 3 months, there was still less relapse in the LLLT (32 J/cm^2) group than the control group. On the other hand, Kim et al. [75], using an incisor rotation model in beagles, found greater relapse in their LLLT (4–6 J/cm^2) group (56.8%) than in their laser-aided circumferential supracrestal fiberotomy (14.5%) group, or in the control group (41%). These contradictory findings are probably related to differences in laser application protocols. Laser biostimulatory effects occur at low energy densities. The highest activity of colony-forming units was observed at a dose of 1 J/cm^2, whereas high-energy doses (35 J/cm^2) are associated with bio-inhibitory effects [76].

In summary, LLLT at high-energy settings (35 J/cm^2) has shown inhibitory effects on the relapse of teeth. However, further clinical investigations are necessary to determine if LLLT can be used in orthodontic retention. Standardization of protocols, better understanding of LLLT effects at different energy settings, and its effects with and without retainers, are needed. Currently, it appears that LLLT alone is not a helpful tool in relapse prevention. However, if LLLT is used as an adjunct to conventional retention methods, there might be more rapid maturation of the PDL and less time required for retention.

3.2. Mechanical vibration

Mechanical vibration is thought to inhibit bone turnover by stimulating osteocytes, which are known as a mechanosensors that orchestrate the bone-remodeling process by releasing soluble factors that affect both osteoclasts and osteoblasts [77]. Osteocytes, which comprise 90% to 95% of the adult skeleton, respond to changes in hydrostatic pressure, fluid flow, and mechanical stretching or stimulation [78]. With mechanical vibration, osteocytes respond by releasing factors that inhibit osteoclast formation. A 50% reduction in RANKL levels has been reported with 60-Hz vibration [77]. In addition, mechanical vibration has been shown to reduce prostaglandin-E2 levels by approximately 60% [77]. Because prostaglandin-E2 is known to stimulate osteoclast differentiation, a reduction in its levels would theoretically be expected to reduce the numbers of osteoclasts.

In orthodontics, mechanical vibration has been mainly evaluated as a tool to accelerate tooth movements. Only a few experimental studies have evaluated its effects on relapse prevention. In a tooth-movement model [79], mechanical vibration (at 60 Hz) was associated with an increase in rates of tooth movement, and, surprisingly, increase in RANKL expression and osteoclast number. However, this study used expansion springs, where the rate of tooth movement could be influenced by skeletal expansion and other biomechanical limitations. On the other hand, another experimental study showed that mechanical vibration (at 30 Hz) had a significant inhibitory effect on tooth movement [80]. This inhibition in tooth movement was associated with reductions in osteoclasts, and increases in BVF. The anabolic effect of mechanical vibration on alveolar bone also has been reported in animal models [81].

Clinically, mechanical vibration has shown no effects on rates of tooth movement. Two randomized trials [82,83] showed no effects on rates of tooth movements or alignment with vibrational device. One randomized trial [84] showed increase of 0.37 mm per month (1.16 mm per month, control 0.79 mm per month) in upper canine retraction. However, this study showed great variability in rates of teeth movement and monthly rates of retractions that were not markedly different from expected rates. In short, using mechanical vibration for teeth movement acceleration seems counterintuitive to its biological effects on bone metabolism.

From a retention perspective, mechanical vibration (at 30 Hz) has shown no favorable effects on relapse prevention in experimental studies evaluating orthodontic tooth movement [85]. However, it is important to realize this was an experimental study on mice, where the bone response is not the same as in humans. Furthermore, the study used a molar protraction model, which does not match with the clinical scenario in postorthodontic retention. Even though relapse was not reduced, there was a noticeable improvement in BVF and tissue density. The thickness and integrity of collagen fibers of the PDL were improved. Moreover, there were reductions in osteoclast numbers and sclerostin expression from osteocytes (sclerostin expression is associated with reduction in bone formation). The effects of mechanical vibration on orthodontic retention remains uncertain, and further investigations are necessary to explain the current findings.

Briefly, application of mechanical vibration as an adjunctive tool in orthodontic retention is a new technique that requires further investigation. From a biological perspective, mechanical vibration has shown favorable anabolic effects on bone remodeling, which could be advantageous for stability after orthodontic treatment. In addition to the cost of the appliance, compliance is required with such approach.

4. Mechanical retainers

This section of the review is intended to provide an overview of changes that have been introduced in existing conventional retention appliances. All the modifications address one or more drawbacks of retainers, including metal allergies, esthetics, oral care, and risk of failure. The modifications usually involve changes in the materials used to make the retainers. There were different fiber-reinforced composite (FRC) retainers investigated in orthodontics, which include both glass fiber–reinforced retainers [12,86–90] and polyethylene ribbon–reinforced retainers [89–92].

Glass fiber–reinforced retainers have been shown to have higher failure rates (51%) than multistranded stainless-steel wire retainers (18%). In addition, a higher modified gingival index and greater bleeding on probing were noted in the glass fiber–reinforced retainers than in the multistranded retainers. Shorter survival times and more adverse effects were associated with these modified retainers. Overall, worsening of the periodontal conditions was significantly greater in both retainer groups than in the controls [12,86]. In addition, in vitro analyses showed similar fatigue resistance and debonding forces among metal and fiber-reinforced retainers [89]. Polyethylene (PE) ribbon–reinforced composite also has been used for retention [93]. In a clinical study [91], PE-reinforced retainers showed higher failure rates over a 2-year retention period than multistranded wire retainers. In fact, the average survival time of PE-reinforced retainers was 12 months, compared with 24 months with multistranded wires. It seems that FRC retainers, regardless of the type of fibers used, have poorer survival rates than metal retainers. More deleterious effects on the periodontal tissues also have been reported with fiber-reinforced retainers. The advantages of fiber-reinforced over metal retainers include the elimination of nickel allergy and, perhaps, improved esthetics.

Finally, other innovative designs and materials have been investigated as alternatives to existing metal retainers. These creative designs include magnetic retainers [94], flossable ceramic retainers [95], lingual spurs [96], nickel-titanium wires [13], and light polymerized composites [97].

As shown previously, modifications to existing retainers to overcome inherent limitations will probably help in specific situations (e.g., nickel allergy), but they will not address the main reason why retainers are used after orthodontic treatment. FRC retainers have higher failure rates and more detrimental effects on PDL than conventional metal retainers. Therefore, the use of FRC retainers should be limited to the indicated cases, if fixed retention is preferred for specific clinical situation. Furthermore, orthodontic research should shift its focus toward targeting the biological mechanisms responsible for relapse.

5. Clinical implications and future research

Orthodontic tooth movements involve both mechanical stimulation and biological response. Currently, only mechanical retention is used after orthodontic treatment, with the intention of holding teeth in their new positions until the supporting tissues remodel. Biological intervention makes it possible to accelerate tissue recovery after treatment and reduce or eliminate the need for mechanical retention. Among the biomedical agents reviewed, denosumab (RANKL inhibitor agent) holds the greatest potential for further orthodontic clinical investigation. There are a variety of posttreatment benefits that could be gained from this agent. First and foremost is its potential use as a biological retainer. Denosumab might be expected to be particularly helpful in preventing relapse of impacted canines that have been aligned, extraction spaces that have been closed, and teeth that have been extruded. From a

biological perspective, this agent could be applied whenever relapse occurs due to uncontrolled bone resorption. In addition, denosumab might have a favorable effect on root resorption after orthodontic force is discontinued [98]. Finally, and perhaps most importantly, biological retainers such as denosumab do not rely on patient compliance and limit the complications associated with traditional retainers. However, further investigations of these agents are required to determine their clinical applicability and develop protocols for their use.

The favorable effects of LLLT on PDL recovery rates could shorten retention time. However, LLLT has not been investigated clinically for its effects on relapse prevention after orthodontic treatment. Any further clinical investigation should consider LLLT as an adjunct to conventional retention methods, rather than using it alone. Mechanical vibration, as a relapse-prevention strategy, requires further experimentation to determine its inhibitory effects and improved PDL recovery after orthodontic treatment. Presently, there is no support for mechanical vibration to be used clinically for orthodontic retention.

6. Conclusions

- Several biomedical agents, such as OPG, BPs, and BMPs, exhibit favorable effects on bone metabolism that could help hasten the tissue-recovery process after orthodontic treatments. Further research is necessary to determine the clinical applicability of these agents for orthodontic retention.
- LLLT accelerates the remodeling process of the PDL tissues, which could be helpful in reducing posttreatment retention time. Further clinical evaluations of LLLT used in conjunction with conventional retainers are needed.
- Low-frequency mechanical vibration (at 30 Hz) has shown favorable anabolic effects on bone metabolism and periodontal tissues. However, further investigations are required because the effects on relapse prevention remain unclear.

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