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Short Communication

Current Concepts about the Effects of Statins on Tooth Movement

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Abstract

A class of drugs, namely statins, enhances osteogenesis and suppresses bone resorption, which could represent a plausible biological mechanism to minimize orthodontic relapse. It also seems to represent a major concern, once the tooth movement could be arrested in patients taking statins for a long period. One reasonable explanation is the inhibition of osteoclastogenesis through the overexpression of osteoproteogerin, followed by the inhibition of the binding between RANK and RAKL (RANK ligand). On the other hand, some authors have recently argued that statins cannot produce significant clinical effects on tooth movement, suggesting the need for further studies in this field. Besides, it should be noted here that some of the adverse effects of statins, including the stimulation of endochondral ossification, are a major concern. This short communication aims to present the current concepts on statins modulation of bone turnover and its effects on tooth displacement during orthodontic treatment.

Keywords: Tooth Movement; Osteoprotegerin; Receptor Activator of Nuclear Factor-Kappa B Ligand; Atorvastatin

Orthodontic tooth movement (OTM) is characterized by changes in the alveolar bone micro-environment, in which quimiockynes, cytokines and growth factors orchestrate osteoclastic bone resorption and osteoplastic bone neoformation [1] In osteoclastogenesis, the signaling between Receptor Activator of Nuclear Factor Kappa B (RANK) located in pre-osteoclastic cells' membrane and its ligand–RANKL–present in osteoblast membrane or extracellular matrix (ECM) seems to be crucial for osteoclast differentiation and survival. However, the RANK/RANKL interaction can be inhibited by a third protein, i.e., osteoproteogerin (OPG), which will compete with RANK to bind RANKL, thus, preventing the viability of osteoclastic cells [2-4]. In this context, laboratory studies have suggested that OPG over-expression is a plausible mechanism to regulate osteoclastic cell differentiation during orthodontic tooth movement, leading

to a reduction in tooth displacement [5-9]. Although it is far early to consider these data clinically, interesting researches are currently being carried out in this field.

Based on this background, statins, a group of drugs widely used to lower cholesterol levels, also seems to affect bone turnover. Statins inhibit osteoclastic resorption that seems to occur through three distinct paths: (a) anti-inflammatory effects [10], (b) suppression of Nuclear Factor Kappa B pathway7, [11-12], and (c) inhibition of small GTPases [13-14]. Several studies have demonstrated that statins bone modulation is a plausible mechanism to reduce orthodontic tooth movement and relapse [5-8]. One of the main biological mechanisms associated with this finding is the over-expression of OPG protein in the periodontal tissues [5]. In contrast, recent studies have also suggested that, although statins can affect alveolar bone turnover, this was not associated with a clinical reduction of tooth movement [9]. This is a topic of controversy in the literature [5-9], and further studies are needed to confirm whether statins can affect tooth movement clinically.

Furthermore, it is important to emphasize that a plausible impairment of tooth displacement related to drug consumption, during or after the orthodontic treatment, could represent a clinical concern or even a scientific advance. Firstly, considering the widespread usage of statins as the main drug for cholesterol lowering [15-16], it could be inferred that the tooth movement would be arrested during orthodontic treatment of individuals taking these drugs, which would affecting the treatment time. On the other hand, the inhibition of tooth movement induced by drug modulation of bone turnover could be the first step to control and reduce orthodontic relapse through a non-invasive pathway.

Recently, two experiments were developed in our laboratory [5-6] that revealed a novel finding: during orthodontic tooth movement and relapse, statins (atorvastatin) can inhibit osteoclastogenesis transiently (after 7 days of tooth movement and after 14 days of tooth relapse). Thus, it is suggested that after this initial period, an in vivo compensatory mechanism is activated, which surpasses the action of statins and stimulates osteoclasts differentiation [14]. It could also be hypothesized that statins would act only during the early stages of the inflammatory process and that, over the time, it would lose its effects as the bone micro-environment re-established its physiological condition. However, even on considering this transient effect of statins on osteoclastogenesis, our results highlight the clinical relevance of these findings as orthodontic relapse and tooth movement were significantly inhibited [5-6].

With respect to the side effects of statins, studies have suggested a possible action of these drugs on endochondral ossification of long bones [5,17,18]. Researchers have indicated that short-term drug administration could contribute to an increase in Growth Plate Cartilage Thickness (GPCTh) and Hypertrophic Zone Thickness of chondrocytes (HzTh) [5,17]. However, the long-term drug administration seems to have no significant effects on the measurements of these same parameters (GPCTh and HzTh) [6]. These findings are based on preclinical studies and far away from any clinical extrapolation.

Finally, the future applications of cellular and molecular biology to control the rate of tooth displacement during orthodontic treatment seem to be foreseeable. In this scenario, drug modulation of periodontal tissues turnover would be an interesting alternative, representing a sophisticated method, in contrast to the currently used invasive surgical techniques.

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