AN ABSTRACT OF THE THESIS OF

Edward Henri El Asmar for Master of Science
Major: Pharmacology and Therapeutics

Title: Effect of third generation beta-adrenoceptor antagonists with vasodilating properties, carvedilol and nebivolol, on orthodontic tooth movement in rats.

Introduction: There are currently no drugs that can be used to reduce orthodontic treatment time. Carvedilol and nebivolol are third generation beta-adrenoceptor blockers with vasodilating properties attributed to enhanced nitric oxide synthesis. Survey of the literature revealed that nitric oxide enhances orthodontic tooth movement. Aim: Orthodontic movement of the two maxillary incisors, induced by the application of a spring exerting a divergent force of 40g, was studied under control conditions and after drug administration. The hypothesis was advanced that carvedilol and nebivolol may enhance orthodontic tooth movement by increasing availability of nitric oxide. Materials and methods: The study was conducted on four series of rats, control (N=9) and treatment with carvedilol (N=8), nebivolol (N=8) and propranolol as a beta-adrenoceptor blocker without vasodilating property (N=8). Tooth movement was gauged by measuring the internal and external distances between the incisors, before and after application of the spring, and 3, 7 and 10 days later. At day 10, the premaxillae were processed for histological examination. Differences in tooth movement, osteoblastic activity and bone resorption as well as capillary vascularization were assessed. Results and conclusions: The spring that was designed and constructed locally served the desired objective. Increases in the internal and external measurements at comparable periods revealed no significant difference, yet the internal measurement showed less variation and is considered more precise and reliable. Carvedilol increased the internal distance between the incisors by 0.11 ± 0.05 mm (P<0.05) at day 3 and by 0.29 ± 0.11 mm (P<0.01) at day 10 as compared to control series. Nebivolol consistently increased orthodontic tooth movement as compared to control at all periods, though not significantly due to the limited number of observations. Propranolol was without effect on tooth movement as compared to control. Carvedilol and nebivolol significantly enhanced tooth movement as compared to propranolol, implying that their effect is due to special properties other than beta-adrenoceptor blockade. All the drugs increased bone resorption, osteoblastic activity and vascularization, supporting the increased tooth movement confirmed by carvedilol and suspected by nebivolol. Confirmation of the role of nebivolol in tooth movement, the molecular mechanisms involved in the effect of carvedilol and the morphological changes of propranolol on bone structure deserve additional exploration.