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Antihistaminic drugs affect bone metabolism in orthodontic tooth movement in rats

Introduction: Histamine receptor antagonists are widely used drugs for treatment of several allergic conditions and gastric acid secretion, targeting H₁ and H₂ receptors respectively. To study potential effects on bone, an orthodontic tooth movement model (OTM) in rats was used.

Aim: The aim of study was to determine the mechanism of antihistaminic action in osteoclast and osteoblast activation and expression of histamine receptors by H₁ antagonist cetirizine and H₂ antagonist famotidine.

Materials & Method: We used different groups of Wistar rats: control group (n=16), appliance-only group (n=16) and cetirizine (n=16) and famotidine groups (n=16). Each animal was fitted with a superelastic closed-coil spring appliance and treated daily with saline solution or antihistaminic drug for 42 days. Tooth movement was measured weekly from day 0 to day 42. Gene expression levels of bone turnover markers cathepsin K, osteocalcin and histamine receptors were determined by means of real-time polymerase chain reaction. Histologic samples were analyzed by using histomorphometry.

Results: Cetirizine decreased the amount of OTM from day 28 onward (P<0.01), and it also decreased osteoclast volume density (P<0.001). An increase in alveolar bone volume density was observed in the cetirizine group (P<0.01) compared with the control group. The gene expression level of histamine H₁ receptors was significantly higher on days 14 and 42 (P<0.01). Famotidine decreased the amount of OTM and the gene expression of H₂ receptors during the late stage of tooth movement (P<0.001).

Conclusion: It seems that histamine plays an important role through histamine H₁ receptors only in initial stage of orthodontic tooth movement, probably through its pro-inflammatory action. H₂ antagonists could play a role during the late stage of OTM in rats. Therefore, H₁ and H₂ receptor antagonists could interfere with bone metabolism, which is important also due to interaction of those drugs especially when multidrug therapy is applied.

Biography

Gorazd Drevenšek has his expertise in Pharmacology and obtained his PhD degree in Medical Sciences, both from the Faculty of Medicine at University of Ljubljana. He started his research in Cardiovascular Pharmacology, in ischemic and reperfusion injuries. His focus is on pharmacological and toxicological evaluation of various drugs and natural compounds as potential cardio- and neuro-protectants. His laboratory and research skills comprise methods used in isolated organs, in vivo animal pharmacology studies and human studies. As one of the "in vivo" research models, his team developed a model of "orthodontic tooth movement in rats", thus studying bone modelling in "in vivo" animal condition. Research with this model has been published in several dental and bone journals. His present engagement is with psychopharmacology-oriented research. He teaches Psychopharmacology, Psychopharmacology of Mental Disorders and Molecular Basis of Neurodegenerative Diseases. He conducts research in pharmacology, toxicology, neuroscience, and is heading the Laboratory for Cardiovascular Pharmacology in the Faculty of Medicine at University of Ljubljana.

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