P035

Bone modelling during orthodontic tooth movement is regulated by osteoclastic and osteoblastic stimulation via ET_A receptors and osteoclastic inhibition via ET_B receptors

I Štokelj[1], T Marinko[1], A Meh[1], S Sprogar[2], G Drevenšek[2], M Drevenšek[1], M Yanagisawa[3]. *[1]University Medical Centre Ljubljana, Department of Orthodontics, Slovenia, [2]University of Ljubljana, Faculty of Medicine, Department of Pharmacology and Experimental Toxicology, Slovenia, [3]UT Southwestern Medical Center Dallas, Howard Hughes Medical Institute, USA*

INTRODUCTION: Bone modeling is the key factor of orthodontic tooth movement (OTM). Many mediators, including endothelins are involved in the mechanism of OTM. The aim of the present study was to determine the role of endothelin receptors in the mechanism of orthodontic tooth movement by using highly selective ET_A receptor antagonist TBC3214 and animals with knock-out gene for ET_B receptor, since the selective ET_B receptor antagonists are not available for »in vivo« studies.

MATERIALS and METHODS. The study was performed on 50 animals (260-320g) which were divided into 4 groups: control group - male Wistar rats treated daily with saline (n=10), group 1 – male Wistar rats treated daily with ET_A receptor antagonist TBC3214 (TBC3214 rats; n=10), group 2: knock - out male rats for ET_B receptor gene and DβH gene inclusion (KOETB rats; n=15) and group 3: male rats with DβH gene inclusion (KOBWT rats; n=15). All animal were applied an appliance consisted of super-elastic closed coil spring between the upper left second molar and upper incisors. On day 35 the distance between the most mesial point of the upper left first molar and the most palatal point of the ipsilateral incisor at the gingival level was measured by digitronic caliper. Application of the appliances and measurements were done under general anaesthesia (ketamine 50 mg/kg; medetomidine 67 µg/kg; thiopental 3 mg/kg; all i.p.). Tooth movement was calculated by subtracting the distance between the teeth on each day of measurement from the distance between the teeth measured on previous week. On day 35 the rats were sacrificed and samples of the maxilla containing all three molars were taken for bone histological analysis.

RESULTS: Tooth movement in KOETB animals was significantly less on day 35 (0.9mm±0.12) when compared to control group* (2.4mm±0.23), TBC3214* (1.8mm±0.24) treated group and KOBWT animals ** (1.24±0.27)(* $p<0.001$; **$p<0.05$). Alveolar bone volume covered by osteoblasts on pressure side was not significantly different in KOETB animals (4.7%± 1.2) compared to KOBWT animals (5.0%±1.6) and control animals (6.3%±1.2), but significantly higher in the animals treated with TBC 3214(10.3±1.7) ($p<0.05$). Alveolar bone volume covered by osteoclasts was significantly higher in KOETB animals (1.3%±0.12) then in animals treated with TBC 3214 (0.80%±0.2) and KOBWT animals (0.63± 0.10) ($p<0.05$).

CONCLUSIONS: ET_A receptors mediate mainly osteoclastic bone resorption thus TBC3214 treated animals expressed the largest OTM, while ET_B knock – out animals showed the highest density of osteoclasts in bone tissue, so ET_B receptors could inhibit mainly osteoclastic bone resorption during OTM in rats. The amount of OTM was less in ETB knock-out animals then in TBC3214 treated animals probably due to their influence on osteoblastic density and their activity.