BMC Pharmacology

Meeting abstract



# Endothelin-1 increases osteoclastic bone resorption via endothelin A receptors during orthodontic tooth movement in rats

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*from* 15th Scientific Symposium of the Austrian Pharmacological Society (APHAR) Joint meeting with the Hungarian Society of Experimental and Clinical Pharmacology (MFT) and the Slovenian Pharmacological Society (SDF)
Graz, Austria. 19-21 November 2009

Published: 12 November 2009

*BMC Pharmacology* 2009, **9**(Suppl 2):A64 doi:10.1186/1471-2210-9-S2-A64

This abstract is available from: http://www.biomedcentral.com/1471-2210/9/S2/A64



## Background

The involvement of the endothelin signaling system during orthodontic tooth movement has not been explained yet. Therefore, the aim of this study was to determine the role of endothelins ET-1, ET-2 and ET-3 and both receptor subtypes $ET_A$ and $ET_B$ during all the three phases of orthodontic tooth movement in a rat model.

## Methods

The study was performed on male Wistar rats (n = 85). Orthodontic tooth movement was induced by a closed coil spring (F = 25 cN), which was placed between the upper left first molar and the upper incisors. The effects of the endothelin system were investigated using tezosentan, a non-selective endothelin antagonist, and TBC3214, a highly selective $ET_A$ antagonist. Measurements of the distance between the upper left first molar and the ipsilateral incisor were performed on a weekly basis for 6 consecutive weeks. After that, the animals were sacrificed and tissue samples of the maxilla were taken for further biochemical and histological evaluations.

## Results

Tezosentan increased tooth movement ($p < 0.01$). The opposite effect was shown using TBC3214, which decreased tooth movement ($p < 0.01$). On day 14, gene expression levels for ET-1 ($p < 0.05$) and ET-3 ($p < 0.001$) were increased compared to day 0. On day 28, a down-regulation of ET-3 was observed when compared to day 0 ($p < 0.001$). On day 42, ET-1 ($p < 0.001$) and ET-3 ($p < 0.01$) gene expression levels were strongly up-regulated, while ET-2 gene expression level was down-regulated ($p < 0.01$) when compared with day 0. The immunoreactivity of $ET_A$ and $ET_B$ significantly decreased on day 14 ($p < 0.001$) and increased on day 28 ($p < 0.001$). Alveolar bone volume was significantly higher in the TBC3214 group compared to the appliance only group ($p < 0.001$). Osteoclast volume was significantly lower in the TBC3214 group compared to the appliance only group ($p < 0.05$).

## Conclusion

ET-1 and ET-3 are the endothelin isopeptides, which are involved in all three phases of orthodontic tooth movement. However, ET-1 is the predominant physiological form functioning during the late phase of orthodontic tooth movement. Gene and protein expression levels indicate that the major signaling pathway during the late phase of orthodontic tooth movement mainly involves $ET_A$ receptors. During this phase ET-1 increases osteoclastic bone resorption via $ET_A$.