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**Zoledronic Acid Modulate Inflammatory Response Induced by Orthodontic Force**

A. N. Bergamo<sup>1</sup>, L. F. Duffles<sup>1</sup>, R. C. Casarin<sup>2</sup>, C. Stolf<sup>2</sup>, L. A. Silva<sup>1</sup>, R. A. Segato<sup>1</sup>, P. Nelson-Filho<sup>1</sup>

<sup>1</sup>Department of Pediatric Dentistry, University of São Paulo - Ribeirão Preto School of Dentistry, Ribeirão Preto, São Paulo, Brazil, <sup>2</sup>Department of Periodontology, University of Campinas - Piracicaba School of Dentistry, Piracicaba, São Paulo, Brazil

**Objectives** Force applied during the orthodontic movement promotes the release of inflammatory and angiogenic mediators. Zoledronic acid (ZOL) modulates inflammatory response. Aim was to evaluate inflammatory and angiogenic response under orthodontic force after ZOL administration.

**Methods** C57BL/6J mice with six-week-old (6w\_ZOL) and twelve-week-old (12w\_ZOL) received ZOL or PBS (6w\_PBS and 12w\_PBS). Maxillary right side received force, left side was control side. After 12 days of orthodontic force IL-10 and VEGF were evaluated by LUMINEX analysis. COX2 and PGE\_EP2 expression was analysed by immunohistochemistry assay. ANOVA, Pearson correlation were applied by JMP ( $\alpha=0.05$ ).

**Results** Quantitative digital analysis (QuPath software) showed that ZOL modulates the inflammatory mediator COX2 under loading, levels were higher in 6w\_PBS than in 6w\_ZOL, 12w\_ZOL and 12w\_PBS ( $p<0.05$ ). PGE\_EP2 presented a higher count to 6w\_PBS without significance ( $p>0.05$ ). IL-10 was modulated by ZOL on control side, the higher levels were observed in 6w\_PBS comparison with 6w\_ZOL, 12w\_ZOL and 12w\_PBS ( $p<0.05$ ). The movement side showed higher levels in 6w\_PBS group than 12w\_ZOL ( $p=0.0124$ ). VEGF levels showed higher values on the control side to the 6w\_PBS among all other groups ( $p<0.05$ ). The movement side presents higher levels to 6w\_ZOL than 12w\_ZOL and 12w\_PBS ( $p<0.05$ ). A strong correlation between VEGF, PGE\_EP2 ( $p=0.0237$ ) IL-10 ( $p=0.0323$ ) was observed in 12w\_PBS group. A strong correlation between displacement and IL-10 ( $p=0.0430$ ) in 12w\_ZOL group.

**Conclusions** COX2 decreased expression in experimental groups on the movement side. Levels of IL-10 and displacement teeth were lowest in 12w\_ZOL which presents a strong correlation between teeth displacement and IL-10. 12w\_ZOL presents lower levels of VEGF, and this angiogenic mediator has a correlation with PGE\_EP2 and with IL-10, indicating that ZOL decreased the levels of VEGF affecting the PGE\_EP2 and IL-10 protectors' inflammatory mediators. ZOL modulated most expressively the 12-week-old mice and decreased anti-inflammatory cytokine, vascular endothelial factor, and teeth displacement.