PB150

Olmesartan decrease inflammation, oxidative stress and protein loss bone in experimental periodontitis.

Aurigena Araújo4,5, Tatiana Souza2, Raimundo Araújo Jr2,3

1UFRN (Department of Biophysics and Pharmacology, UFRN, Post graduation program Public Health / Post graduation program in Pharmaceutical Science), Natal, RN, Brazil, 2UFRN (Post graduation program Health Science), Natal, RN, Brazil, 3UFRN (Post graduation program in Functional and Structural Biology/Post graduation program Health Science/Department of Morphology), Natal, RN, Brazil, 4UFRN (Post graduation program Pharmaceutical Science), Natal, RN, Brazil, 5UFRN (Post graduation program Public Health), Natal, RN, Brazil

Olmesartan, an angiotensin II type 1 receptor (AT1) blocker, has also been investigated and found to inhibit the expression of TNF-α (Li et al. 2004). The mechanism of inhibiting the expression of TNF-α by olmesartan-induced can be very interesting to study in the context of periodontal disease because studies have shown, beyond doubt, that the plaque bacteria that are necessary for initiating periodontal disease drive a chronic inflammatory response in periodontal tissues (Deo & Bhonga 2010). The objective of this study is to investigate the participation of inflammatory and oxidative stress mediators, and the effects on the expression of MMP-2, MMP-9 and RANKL/RANK/OPG pathway in the response to treatment with olmesartan, an angiotensin II type 1 receptor (AT1) blocker.

Male Wistar albino rats were randomly divided into five groups of ten rats each: (1) non-ligature with water/NL, (2) ligature with water/L, (3) ligature with 1 mg/kg olmesartan/OLME 1mg/Kg (4) ligature with 6 mg/kg olmesartan/OLME 6mg/Kg and (5) ligature with 10 mg/kg olmesartan/OLME 10 mg/kg. All groups were treated with olmesartan or the vehicle by gavage daily for 10 days. The experimental protocol for experimental procedures and animal treatment was approved by the Animal Ethics Committee (number 28/2012) of the Federal University of Rio Grande Norte. Following the treatment course, the periodontal tissue of the animals was analyzed by histopathology and immunohistochemistry to determine the expression of COX-2, MMP-2, MMP-9, and members of the RANKL/RANK/OPG pathway, and by Elisa and Spectroscopic assay to determine of the levels of IL-1β, IL-10, TNF-α, myeloperoxidase (MPO), malonaldehyde (MDA), and glutathione (GSH). Analysis of variance followed by Bonferroni’s test was used to calculate the means.

The concentrations of MPO and MDA were reduced in the group that received 6 mg/kg olmesartan (p < 0.05). In addition, the group that was treated with 6 mg/kg olmesartan showed a decreased level of IL-1β (p < 0.05), and all doses of olmesartan resulted in decreased levels of TNF-α (Figure 1). Furthermore, treatment with 6 mg/kg olmesartan led to down-regulation of the expression of COX-2, MMP-2, MMP-9, RANKL, and RANK and to up-regulation of the expression of OPG (Figure 2).

These findings suggest that olmesartan 6mg/Kg reduces the inflammatory process and bone loss by down-regulating MMPs and RANKL in osteoblasts and by up-regulating OPG.

### Figure 1

Levels of IL-1β, IL-10 and TNF-α, group

Non-Ligated (NL), Ligated (L) and in groups treated

with 1 mg/kg, 6 mg/kg and 10mg/kg olmesartan


Figure 2 Photomicrographs of the periodontal tissue of rats on Experimental Periodontitis (EPD) that were treated with olmesartan showing immunoreactivity to MMP-2, MMP-9, COX-2, RANK, RANK-L, and OPG. Rats that were subjected to saline treatment (Non-Ligated group) are shown in (A, D, G, J, M, and P); rats that were subjected to EPD (Ligated group) are shown in (B, E, H, K, N, and Q); and rats subjected to EPD and treated with 6 mg/kg olmesartan are shown in (C, F, I, L, O, and R). (100 × magnification; scale bar = 100 µm).