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## Zer-011

### **Zoledronic acid promoted osteonecrosis of the jaws and can be attenuated by estrogen replacement therapy in senile female rats**

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Zoledronic acid (ZOL) is the most potent bisphosphonate used in the treatment of tumors, bone metastases and osteoporosis, however the long-term use of this drug is related to appearance of a pathologic condition, such as bisphosphonate-related osteonecrosis of the jaw (BRONJ) and the mainly risk factor is the creation of surgical wounds in the oral cavity. This study aimed to evaluate the action of zoledronic acid in the alveolar bone healing of senile wistar female rats submitted or not to the hormone replacement therapy (HRT) with estradiol (E<sub>2</sub>). During aging (18-20 months), the animals were submitted to HRT and received NaCl (0.15M) or ZOL (70 µg/kg), constituted the experimental groups CO (Corn oil)/NaCl; E<sub>2</sub> (17 β-estradiol; 300 µg/month)/NaCl; CO/ZOL and E<sub>2</sub>/ZOL. At 28 days after mandibular first molar extraction, it was obtained the blood of animals to biochemical analysis (Calcium, phosphorus, Alkaline phosphatase and serum TRAP) and the jaws to histologic and immunohistochemistry (TRAP, RANKL, OPG, MMP9 and CASP-3) analysis. The biochemical results showed a greater TRAP activity in E<sub>2</sub>/ZOL than CO/ZOL group (Bonferroni post-test -  $p < 0.05$ ). In the histological results its possible evidence the greater new bone formation, epithelialization of alveolar mucosa and bone vitality in the CO/NaCl and E<sub>2</sub>/NaCl groups. However, in the animals received ZOL were detected the BRONJ occurrence. On the other hands, the immunohistochemistry analysis signaling balance expressions of the proteins in the estrogen animals with or without ZOL treatment, however the ZOL group showed an increase MMP9 immunolabeling. Thus, we concluded that the treatment with ZOL associated with surgical wound, affect *bone turnover* providing the BRONJ occurrence and could be potentiated by aging and attenuated by HRT.

**Descriptors:** Bisphosphonates; Hormone Replacement Therapy; Osteonecrosis