Bisphosphonate related osteonecrosis of the jaw: A minipig large animal model.

Abstract:
Bisphosphonate related osteonecrosis of the jaw (BRONJ) is rare but potentially severe, and the etiopathology and risk factors are poorly defined. To date, it has not been possible to induce BRONJ in a large animal model, a shortfall this study aims to redress. Ten two-year-old adult Göttingen minipigs were split into two groups. Five pigs (group 1) were administered intravenously a weekly dose of a bisphosphonate (zoledonate 0.05mg/kg body weight, approximating the oncologic dose in humans) and five pigs (group 2) served as controls. After 6 weeks, tooth extractions were performed in the upper and lower jaw (both groups) and the bisphosphonate administration continued for a further 10 weeks (group 1 only). Clinical and blood parameters were monitored throughout the entire experiment; thereafter, the jaw-bones were subjected to macroscopic, radiological (CT) and histological investigations. Whilst the extraction sites in the control group healed within two weeks, all animals in the bisphosphonate group exhibited exposed bone and impaired wound healing, indicators that are synonymous of macroscopically advanced osteonecrosis. Radiological and in particular histological investigations confirmed the presence of BRONJ in the animals from group 1. This paper demonstrates that the administration of bisphosphonates, in
combination with tooth extractions, induces BRONJ in a minipig model. The ability to study BRONJ in miniature pigs, animals with a bone structure not dissimilar to humans, may improve our knowledgebase regarding the etiopathology, the prophylaxis and potentially uncover new therapies of BRONJ.

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