

Analysis of ADAMTS, MMPs, Versican and Related Proteoglycans in Origin and Progression of BRONJ

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Abstract

Bisphosphonate-related osteonecrosis of the jaw (BRONJ) is a complication basically associated with dento-alveolar surgical procedures in patients receiving intravenous and oral bisphosphonate therapy for various malignancies and bone-related conditions. So far, the pathogenesis of BRONJ is assumed to be related to oral surgical traumas to dento-alveolar structures, which have already limited bone-remodelling capacity due to the effects of bisphosphonate therapy. However, the etiology of the disease is still unclear, while the literature review of past studies is inconclusive. The aim of this paper is to review the literature and current evidences and to explore the possibility of association between changes in the expression level of ADAMTS (1, 4, 5, 9) “a disintegrin and metalloproteinase with thrombospondin motifs”, matrix metalloproteinases (MMPs), Versican, and other related proteoglycans in oro-musculoskeletal tissue, and the onset and progression of BRONJ. This paper outlines a huge body of literature indicating the key role of versican, aggrecan, bioactive degradation products of versican and aggrecan, ADAMTs and MMPs in bone repair, angiogenesis, and BRONJ pathogenesis, and demonstrating a strong clinical correlation between jaw necrosis and bisphosphonate therapy. The paper concludes that in order to establish a definitive causal relationship, there is a critical need of research investigating the expression and localization of these factors during the onset and progression of BRONJ by utilizing advanced analyzing techniques.