PRESENCE OF TUMOUR NECROSIS FACTOR-α AND TUMOUR NECROSIS FACTOR RECEPTOR 1 IN ASEPTIC ROOT RESORPTION

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Abstract

The osteoclast antagonist osteoprotegerin (OPG) can hypothetically offer molecular control over the process of orthodontic root resorption. Unpublished work investigating OPG in a rat model found no inhibitory effect on osteoclasts and odontoclasts when given at a dosage of 2.5mg/kg. It was hypothesised that traumatically induced periodontal ligament (PDL) inflammation produced mediators and cytokines with the ability to stimulate clast cell differentiation and antagonize the effects of OPG. A pilot study conducted in 2006 found Tumour Necrosis Factor Alpha (TNF-α) to be present to a greater extent in OPG-treated rats. It was concluded that TNF-α may moderate OPG effectiveness. The present study investigated the presence of TNF-α and its receptor Tumour Necrosis Factor Receptor 1 (TNFR1) in a PDL sterile inflammatory model. Dry ice was applied for 15 minutes to the upper right first molar crown of 18, eight-week-old male Sprague-Dawley rats. These were evenly divided into experimental and control groups. The experimental group was injected with OPG at a dose of 2.5 mg/kg of body weight. After seven days, the rats were sacrificed and their maxilla processed for immunohistochemical identification of TNF-α and TNFR1. Results showed root resorption to be present in varying amounts and locations. Reparative processes appeared greater in the OPG-treated rats, often with the presence of an ankylotic union. Immunolabelling showed the presence of TNF-α and TNFR1 in the sterile inflammation of the periodontium, mainly in the interradicular area. There appeared to be more noticeable labelling in OPG-treated rats. The results indicated that TNF-α and its receptor TNFR1 were present and may modify OPG effectiveness by offering

an alternative pathway for osteoclastc formation, thereby challenging the potential anti-resorptive effects of OPG. Results from immunohistochemical reactions are strongly influenced by technical and interpretative problems and, in some instances, may result in false positive or negative outcomes. Differences in results were obtained between the pilot study and the current study conducted three years apart using the same animal material and immunohistochemical protocol. The pilot study conducted in 2006 investigating the presence of Tumour Necrosis Factor alpha (TNF-α) found positive staining in an induced sterile inflammation animal model. The current study using the same animal material in 2009 found a remarkable difference in results. In 2006, a multispecies detection kit was used and no antigen retrieval was required. Results showed a strong, generalised, positive staining for TNF-α within the periodontal ligament. At the end of this study, the unused tissue was packaged and stored for a period of three years. In 2009, the same tissue and antibody were used in a parallel immunohistochemical investigation but no positive result was found. The original protocol was reviewed and the antibody concentration and antigen retrieval was optimised with a new staining protocol being developed. Results showed diffuse positive staining in six of the nine specimens. It was concluded that other processing and storage factors were involved in the loss of antigenicity during the time period between studies.

Declaration

This work contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution to Linda Curl and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text.

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Dr. Linda Gayle Curl

Dated

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