ORIGINAL ARTICLE

Orthodontic tooth movement after inhibition of cyclooxygenase-2

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Introduction: The purpose of this study was to compare the effects of a conventional nonsteroidal anti-inflammatory drug, diclofenac (Voltaren [Novartis, Barcelona, Spain]), and a specific cyclooxygenase-2 (COX-2) inhibitor, rofecoxib (Vioxx [MSD, Madrid, Spain]), on the inhibition of dental movement induced with a coil-spring orthodontic apparatus in rats. **Methods:** Tooth movement was measured on the lateral cranial teleradiographs of 42 male Wistar rats in 6 experimental groups: (1) 50-g coil spring and 2 rofecoxib injections of 1 mg per kilogram of body weight; (2) similar orthodontic procedure and 2 diclofenac injections of 10 mg per kilogram of body weight; (3) the same orthodontic treatment and 0.9% saline-solution injections; and (4), (5), and (6) 100-g coil appliance and the same pharmacological treatment as 1, 2, and 3, respectively. **Results:** The difference in tooth movement, measured in the control animals after 10 days of 50 or 100 g of orthodontic force application, was not statistically significant. Reduction in tooth movement in 50-g traction groups reached statistically significant differences; both rofecoxib or diclofenac were effective in inhibiting dental movement. The comparison of the 3 groups treated with 100 g of force also reached statistical significance. Both rofecoxib and diclofenac significantly inhibited dental movement, partially in the case of rofecoxib and totally in the case of diclofenac. Nevertheless, no statistically significant difference was found between the effects of rofecoxib and diclofenac. **Conclusions:** There is no substantial advantage in using selective COX-2 inhibitors compared with nonspecific COX inhibitors to avoid interference with tooth movement during orthodontic treatment in rats. (Am J Orthod Dentofacial Orthop 2006;129:402-6)

Tooth implantation in mammals, or gomphosis, consists of a system of collagen fibers connecting the radicular cement to the surrounding alveolar bone. Gomphosis allows some mobility of the tooth in the alveolar cavity. This, together with the alveolar periodontal bone plasticity, is the basis for orthodontic movement. When a force of adequate duration and magnitude is applied to a tooth, complex histological responses occur in the alveolar bone, predominantly osteolysis on the pressure side accompanied by small amounts of bone formation and the contrary on the opposite side, where tension stress develops.[1]

The mechanism of activation for the osteoclastic response is not yet totally understood. Mediation by the locally produced prostaglandins (PGs) has been suggested by Wong et al.[2] Yamasaki et al[3] demonstrated that the local injection of prostaglandin E-1 (PGE1) and prostaglandine E-2 (PGE2) into the submucosa overlying orthodontically treated teeth in monkeys doubled the rate of dental displacement. In rats, exogenous PGE2 injected over an extended period of time enhances the amount of orthodontic tooth movement, according to Leiker et al.[4] Yet, the in-vitro direct effect of PGs on bone resorption[5,6] and their increase in periodontal tissues that have undergone orthodontic stress have been demonstrated.[7] Acetominophen, a weak inhibitor of cyclooxygenase-1 and cyclooxygenase-2 (COX-1 and COX-2) that also reduces the levels of urinary PGs after systemic administration,[8,9] showed no effect on orthodontic tooth movement in rabbits.[10] Moreover, although PG synthesis seems to participate in the mechanism of tooth movement,[11,12] recent research also suggests that orthodontic forces that generate bone remodeling induce the synthesis of cytokines IL-1 beta and IL-6, and that these cytokines might play an important role in bone resorption.[13]

Early stages of orthodontic treatment are generally

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accompanied by an acute inflammatory process including periodontal vasodilation and some discomfort or pain, related to the stimulation of periodontal nerve endings.[14] These responses have great individual variability.[15]

The use of analgesics such as nonsteroidal anti-inflammatory drugs (NSAIDs) that inhibit the release of PGs and stop inflammation are effective in the treatment of pain related to orthodontic treatment.[16] Nevertheless, the extended use of NSAIDs is inappropriate for orthodontic discomfort, because, as research and clinical experience suggests, their use could slow down tooth movement.[11,12]

PG production during the inflammatory process depends on the enzymatic degradation of arachidonic acid through the constitutive isoform of COX-1 and the inducible isoform of COX-2 pathways. COX-1 produces PGs that protect the gastrointestinal mucosa.[17-19] The selective inhibition of COX-2 produces anti-inflammatory effects, causing less injury to the gastrointestinal mucosa than the nonselective NSAIDs.[20-23] Consequently, the use of selective COX-2 inhibitors is increasing, replacing conventional NSAIDs, especially for chronic inflammatory conditions.

The main purpose of this study was to compare the effect of a conventional NSAID (diclofenac) and a specific COX-2 inhibitor (rofecoxib) on the inhibition of dental movement induced with a coil-spring orthodontic apparatus in rats.

MATERIAL AND METHODS

Forty-two male Wistar rats from the vivarium of the University of Oviedo in Spain, with an average weight of 350 g at the beginning of the experiment, were used. The animals were exposed to the standard 12-hour light/dark cycle. To minimize the risk of appliance displacement during mastication, they were fed ad libitum with soft food (finely ground standard pellets).

The force (50 or 100 g) was generated by a unilateral closed-coil spring that was stretched between the maxillary left first molar and the incisor. The teeth were prepared with perforation holes (buccolingually for the molar and distomesially for the incisor).

The animals were killed by carbon dioxide inhalation and decapitated 10 days after the orthodontic appliances were placed. The magnitude of tooth movement was blindly determined by the same person on lateral cranial teleradiographic images of each animal. An intraoral radiographic apparatus (Siemens Heliodent 70, Bensheim, Germany) was used with Kodak DF-50 radiographs (Ostifildern, Germany) and a specially constructed craniostat. Cephalometric measurement was based on the cephalometric system of Ruf and Pancherz[24] by using, as the horizontal reference, the longitudinal cranial plane defined by the most anterior point of the nasal bone and the most posterior point of the squama occipitalis and, as the vertical reference, a plane defined by the most superior point of the parietal bone and the most inferior point of the tympanic bone (Fig 1). Outline definition was used to minimize location errors. The distance between the first and second molar determined by 2 parallel lines to the parietal-tympanic plane, 1 on the most posterior point of the posterior border of maxillary first molar crown and the other on the most anterior point of the anterior border of the maxillary second molar crown, was deemed the mesial tooth movement after orthodontic treatment.

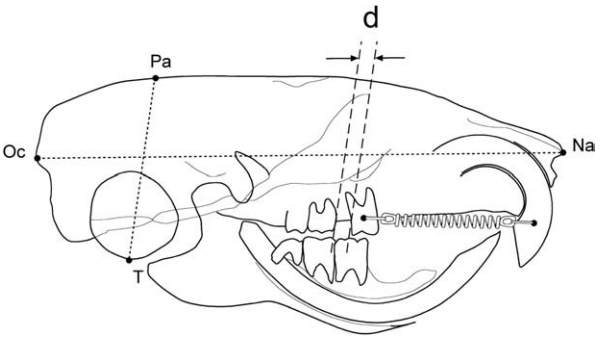

Fig 1. Landmarks on traced lateral cephalometric radiograph. *Na,* most anterior point of nasal bone; *Oc,* most posterior point of *squama occipitalis*; *Pa,* most superior point of parietal bone; *T,* most inferior point of tympanic bone.

Rofecoxib (Vioxx [MSD, Madrid, Spain]) was freshly prepared for each injection by dissolving 25-mg tablets in 12.5 mL of 0.9% saline solution. Diclofenac sodium (Voltaren [Novartis, Barcelona, Spain]) was used as a commercial solution of 25 mg/mL.

The animals were divided into 6 experimental groups of 7 rats. Group 1 (R-50): the rats underwent 50-g coil spring implantations and received 2 injections of 1 mg per kilogram of body weight of rofecoxib in the maxillary gingiva, close to the first molar, 1 on the day of implantation and again after 3 days. Group 2 (D-50): with a similar implantation procedure, the rats received 10 mg per kilogram of body weight of diclofenac. Group 3 (control) (C-50): the rats received the same orthodontic treatment and 0.9% saline-solution injections. Group 4 (R-100): the rats were implanted with a 100-g appliance and received the same rofecoxib treatment as R-50. Group 5 (D-100): the rats were implanted with a 100-g appliance and received the same diclofenac treatment as D-50. Group 6 (control) (C-