Australian Society of Orthodontists

University of Sydney

Drugs and Orthodontic Treatment

PART 1

Creating Brighter Futures

Drugs & Orthodontic Treatment (PART 1)

Many patients today are taking a range of medications and nutritional supplements that can influence orthodontic treatment. Any pharmacologic agent or supplement consumed by patients can reach the periodontal tissues through the circulation and thus interact with and influence a cell's response to orthodontic forces.[1] These agents may have the effect of potentiating or inhibiting tooth movement as well as exacerbating or reducing root resorption.[1]

Orthodontic tooth movement (OTM) is triggered by prolonged application of controlled mechanical forces. Various cell-signalling pathways are activated, ultimately leading to stimulation of periodontal ligament metabolism resulting in localised bone resorption and deposition.[2-4] Orthodontic tooth movement is a function of the periodontal ligament and alveolar bone that involves micro-scopic and macroscopic changes within the periodontal ligament, alveolar bone and dental pulp. It is well documented that inflammatory mediators, neurotransmitters, and growth factors, in addition to numerous other cytokines such as IL-1, play a vital role in orthodontic tooth movement as well as inducing pain and root resorption.[5-8] The main mediators involved in this complex process are:

TABLE 1. FACTORS AFFECTING BONE REMODELLING[9]

Hormones and Systemic Factors	Parathyroid hormone, Calcitonin, Insulin, Growth hormone, Vitamin D, Glucocorticoids, Sex steroids, Thyroid hormones
Growth Factors	Insulin-like growth factors 1 & 2, Transforming growth factor ß, Fibroblast growth factor, Platelet derived growth factor
Cytokines	Interleukin-1,4,6,11,18, Tumour necrosis factor, Osteoclast differentiating factor, Interferon-γ, Osteoprotegrin
Colony-Stimulating factors	M-CSF, G-CSF, FM-CSF
Others	Prostaglandins, Leukotrienes, Nitric oxide

Pharmacologic agents that alter or interfere with the inflammatory process will therefore have an effect on tooth movement and root resorption via the same mechanisms that allow inflammatory mediators to intervene. Several studies have investigated the effect of short and long term administration of drugs on orthodontic tooth movement.[10-12]

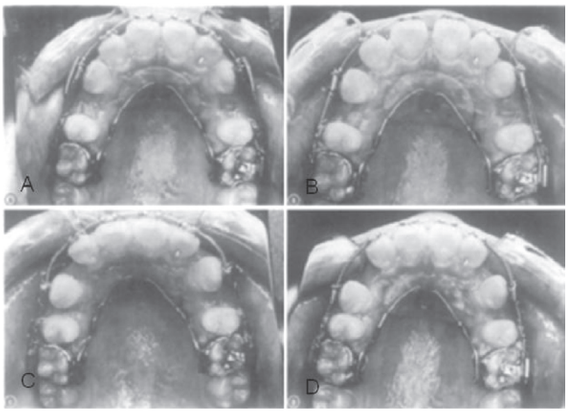
Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)

TABLE 2. GROUPS AND SUB-GROUPS OF NSAIDS[15]

GROUP	SUB-GROUP	BRAND NAMES
Salicylates	Aspirin Diflunisal	Aspirin, Acetal, Acetophen, Acetosal, Aspro and over 100 more Dolobid
Arylalkanoic Acids	Diclofenac Indomethacin	Voltaren, Voltarel, Diclon, Dicloflex, Difen, Difene, Cataflam, Pennsaid, Rhumalgan, Abitren Indocin, Indocid, Indochron
Arylpropionic Acids (profens)	Ibuprofen Flurbiprofen Naprelan	Nurofen, Advil, Brufen, Dorival, Panafen, Ibumetin, Ibuprom ANSAID Aleve, Anaprox, Naprogesic, Naprosyn, Naprelan
Oxicams	Piroxicam Meloxicam	Feldene Movalis, Melox, Recoxa, Mobic
Coxibs	Celexocib Rofecoxib Valdecoxib	Celebrex, Celebra Vioxx, Ceoxx, Ceeoxx Bextra

Orthodontic patients often take analgesics for the relief of pain during treatment[13] with NSAIDs being the most common group of medications.[14] They are also prescribed for numerous inflammatory and autoimmune conditions such as rheumatoid arthritis and for the prevention of cardiovascular disease and colorectal cancer. When used in the treatment of chronic disease, such as arthritis, relatively high doses are prescribed, whereas low dose prescriptions are given for long-term preventive effects.[15] NSAIDs act by inhibiting the production of prostaglandins, through their inhibition of the cyclooxygenase enzyme (COX) which exists in two forms. The first, COX-1, is present in many tissues and releases prostaglandins that are responsible for normal cellular activity such as the synthesis of eicosanoids which play an important role in homeostatic function in the gastric mucosa and platelets. COX-2 on the other hand is induced by pro-inflammatory mediators and releases prostaglandins involved in inflammation and pain signalling.[16]

Prostaglandins are important to orthodontic treatment since they mediate the inflammatory response in the PDL following orthodontic force application, facilitating tooth movement. Prostaglandins have been linked with bone resorption as well as bone apposition.[7] Experiments with local prostaglandin injections have demonstrated an increased rate of tooth movement (CASE 1). While emphasising the important role of prostaglandins in tooth movement, the procedure was not widely adopted as the injection of Prostaglandins was painful.[17]



Case 1: Case from Yamasaki et al showing canine distalization on the RHS injected with PGs while the LHS was injected with vehicle only (control). A, at 0 day. B, 1 month. C, at 3 months. D at 7 months[17]

Numerous studies have demonstrated that NSAIDs effectively reduce the pain and discomfort caused by activation of orthodontic appliances. Ngan et al were the first to compare the effectiveness of various drugs for the management of orthodontic pain, concluding that ibuprofen is more effective than aspirin in controlling pain.[18] While studies testified to the effectiveness of NSAIDs they also indicated that they may affect tooth movement by inhibiting or at least reducing the associated inflammatory and bone resorptive process.[14] This is thought to result from inhibition of COX activity, leading to altered vascular and extracellular matrix remodelling, causing a reduction in the pace of tooth movement.[14] Animal studies evaluating the effects of relatively short administrations of NSAIDs such as acetylsalicylic acid, flurbiprofen, indomethacin, and ibuprofen, showed a decrease in the number of osteoclasts, due to the role of prostaglandins in the differentiation and stimulation osteoclasts.[15]

Given that conventional NSAIDs have the potential to reduce tooth movement, the possibility of using selective COX-2 inhibitors to relieve pain without inhibiting tooth movement has been examined. Selective COX-2 inhibitors have the advantage of having a strong anti-inflammatory effect without the gastric irritation caused by conventional NSAIDs.[19] De Carlos et al investigated the effect of a selective COX-2 inhibitor, rofecoxib, compared with a conventional NSAID, diclofenac, on tooth movement in rats.[11] They found that both inhibited tooth movement but inhibition was only partial in the use of rofecoxib. Furthermore, they found that not all COX-2 inhibitors have the same effect. In studying the effects of three different COX-2 inhibitors, rofecoxib, celecoxib and parecoxib they showed that while rofecoxib inhibited tooth movement, celecoxib and parecoxib did not. Celecoxib had the least effect on tooth movement and therefore the authors recommended its use to control pain associated with orthodontic treatment (FIGURE 1). The use of NSAIDs during orthodontic tooth movement has been questioned due to the possibility of compromised tooth movement by inhibition of the inflammatory reaction.

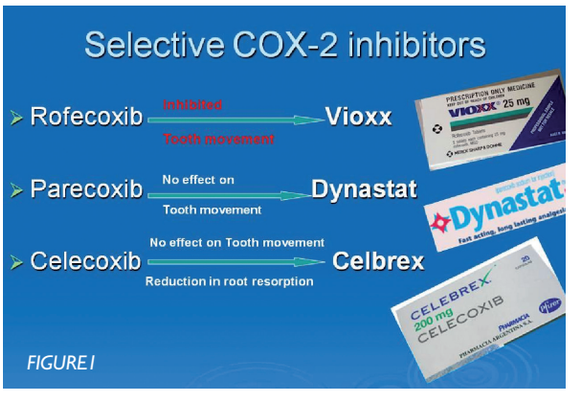


FIGURE 1

BRIGHTER FUTURES

Australian Society of Orthodontists

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Paracetamol (acetaminophen) is another commonly used analgesic which differs from the NSAIDs as it lacks anti-inflammatory properties. Paracetamol blocks a third isoform, COX-3, which is expressed only in the brain and the spinal cord and consequently has minimal effects on prostaglandin synthesis. Studies with paracetamol in animals show that it does not affect the rate of OTM, suggesting that it could be the analgesic of choice for managing pain associated with orthodontic therapy.[13]

Corticosteroids

Corticosteroids are prescribed for various inflammatory and autoimmune conditions, including rheumatoid arthritis, dermatitis, allergies, and asthma. They are also used as immunosuppressive medications after organ transplantation.[15] Corticosteroids are a class of steroid hormones, produced in the adrenal cortex.[15] There are two main types – Glucocorticoids and Mineralocorticoids. Glucocorticoids are more relevant to orthodontics as they affect metabolism and have anti-inflammatory and immunosuppressive activity. They are also involved in bone physiology, but their mode of action is not yet completely elucidated. Their anti-inflammatory effect is based on the indirect blocking of phospholipase A2 and suppression of the synthesis of both COX-1 and COX-2. This leads to inhibition of the synthesis of prostaglandins and leukotrienes. Their immunosuppressive action is due to the inhibition of interleukins and IFN-gamma.[15] The cited side effects of long term steroid therapy include disturbances in mineralised tissue metabolism and wound healing, discrepancies in chondrogenesis and osteogenesis, bone loss and osteoporosis.[14]

Corticosteriod treatment has been shown to interfere with the rate of orthodontic tooth movement and tissue reaction in animal studies.[20] Only a few authors have examined the effects of glucocorticoids on OTM, and no studies were found dealing with mineralocorticoids. The glucocorticoids that have been studied are cortisone, prednisolone, and methylprednisolone.[15] Rat studies on acute and chronic corticosteroid treatment revealed that the rate of tooth movement is increased in the chronic group. Force application resulted in a significant increase in the relative extension of resorption, indicating that the orthodontic force level should be reduced and controlled more frequently in patients on chronic steroid therapy.[14] Acute corticosteroid ingestion reduces bone turnover and therefore it has been suggested that orthodontic treatment should be postponed until treatment has ceased.[21]

Special mention needs to be given to the chronic use of steroids by asthmatics using inhalers. Clinicians need to be aware of their usage as it can result in oral candidiasis and xerostomia. Patients with a history of asthma have been reported to be at a higher risk for developing excessive root resorption during the course of orthodontic treatment.[14] This has been attributed to the fact that asthma involves periodic production of large amounts of pro-inflammatory cytokines in the airway mucosa and the skin. Primed leukocytes derived from these tissues may travel through the circulation into the extravascular space of the tissues surrounding orthodontically treated teeth, increasing the incidence of root resorption.

Summary

Bone metabolism allows orthodontic tooth movement. Anything that effects this may either promote or inhibit tooth movement. In some cases this may be beneficial, for example, by increasing stability after active treatment has concluded; or be detrimental, for example by slowing down the rate of space closure following extractions. An understanding of a patient's medications is crucial.

The next edition of **Brighter Futures**, (Drugs and Orthodontic Treatment - PART 2) will examine additional classes of pharmacologically active substances and review their effects on orthodontic treatment.

REFERENCES AVAILABLE ON REQUEST