Australian Society of Orthodontists

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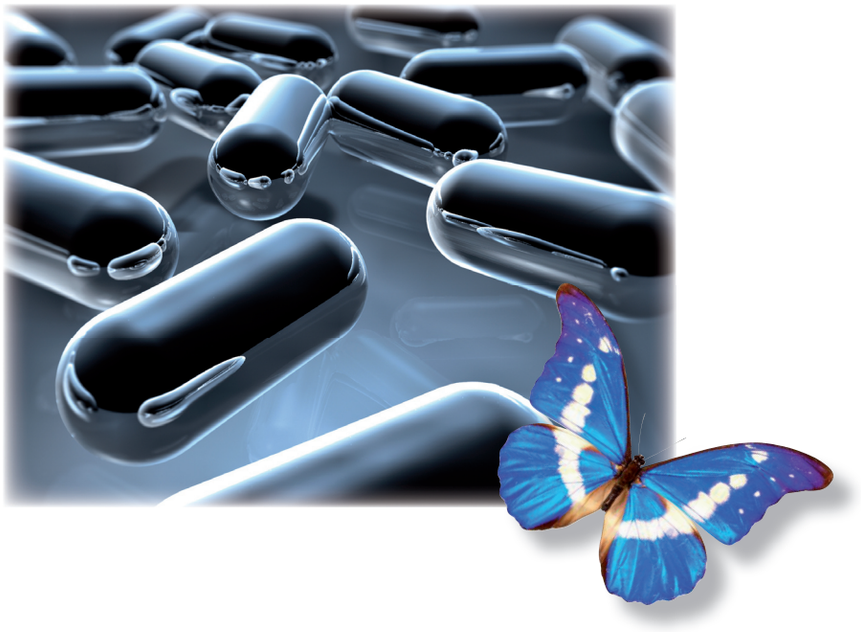

Drugs and Orthodontic Treatment

PART 2

Creating Brighter Futures

Drugs & Orthodontic Treatment (PART 2)

PART 1 reviewed the effects of Non-Steroidal Anti-Inflammatory drugs as well as Corticosteroids on orthodontic tooth movement (OTM) through their role as mediators in bone metabolism.

PART 2 will review a range of relevant medications and dietary supplements.

Anti-convulsants

Seizure disorders are characterised by sudden involuntary time-limited alterations in neurologic function resulting from abnormal electrical discharge of cerebral neurons.[14] The treatment of these conditions involves polypharmacy with multiple anti-convulsant medications. The drugs which are important to orthodontic treatment are Valproic acid, Phenytoin and Gabapentin.

Valproic acid has the potential to induce gingival bleeding and Phenytoin induces gingival hyperplasia making application of orthodontic mechanics and oral hygiene practices more difficult. Gingival hyperplasia has also been reported with sodium valproate and ethosuximide.[21] Gabapentin produces xerostomia which compromises oral hygiene.[14] However, there is consensus in the literature that treatment of a patient with a controlled seizure disorder does not present a major problem.[21]

Calcium and calcium regulators

Calcium plays a very important role in tooth movement and bone remodelling. Calcium homeostasis is regulated not only by dietary intake but by hormones such as Parathyroid Hormones, Thyroid Hormones (Thyroxin, Calcitonin), Sex Hormones (oestrogens) and Vitamins (Vitamin D3).

Parathyroid Hormone (PTH)

This hormone is secreted by the parathyroid gland. It increases the concentration of calcium in blood which stimulates bone resorption. Pathologic conditions of this gland will result in Hypoparathyroidism or Hyperparathyroidism.

PATHOLOGY	DEFINITION	TREATMENT	EFFECT ON OTM
Hypoparathyroidism	Lack of actvie PTH	• Vitamin D • Calcium Supplementation	Inhibits bone resorption
Primary Hyperparathyroidism	Overproduction of PTH PTH which results in high serum Ca+ levels	• Surgical removal of the gland • Medication with Bisphosphonates	Stimulates bone resorption
Secondary Hyperparathyroidism	Hypocalcaemia increases production of PTH	• Vitamin D supplementation • Phosphate binders	Stimulates bone resorption

TABLE 1 Continuous elevation of PTH leads to bone loss but intermittent short elevations of this hormone can be anabolic for bone, increasing mass, density and strength.[22] OTM is stimulated by PTH in a dose-dependent manner.[23,24]

Thyroid Hormones

Thyroid hormones are able to promote bone maturation and resorption. They directly stimulate osteoclastic activity and also have an indirect effect through insulin-like growth factor.

Thyroxin (T4) affects intestinal calcium absorption and is indirectly involved in bone turnover. Therefore, hyperthyroidism or thyroxin medication can lead to osteoporosis. L-Thyroxin has been recommended to reduce root resorption because it increases the resistance of cementum and dentine to clastic activity.[25,26] Exogenous thyroxin has been shown to increase the rate of OTM in rats, on a dose dependant basis, resulting in reduction of the extent of root resorption.[27] Clinical applications of these drugs still need to be clarified.

Calcitonin hormone is used to treat postmenopausal osteoporosis, hypocalcaemia, and Paget's disease. Although this hormone is related to bone remodelling and calcium homeostasis, no experimental data are available on its effect on OTM.

Oestrogens

Oestrogens inhibit the production of cytokines involved in osteoclast activation and bone resorption.[28] Decreased oestrogens after menopause are linked to the development of osteoporosis. Currently, osteoporosis is being treated with a specific oestrogen receptor modulator (Raloxifene), which has an oestrogenic effect on bone. Research found that the rate of OTM was inversely related to oestrogen serum level.[29,30] Therefore oestrogen supplementation might slow OTM however there are no experimental studies on exogenous oestrogens and their effect on OTM.

Vitamin D3 (1,25 dihydroxycholecalciferol)

Vitamin D promotes absorption of calcium and phosphate thereby regulating their serum concentration levels. It also promotes bone deposition, inhibits PTH release and promotes immunosuppression. Its deficiency may result from inadequate intake combined with insufficient sunlight exposure, eventually leading to impaired bone mineralization, rickets and osteoporosis. In addition, it can also lead to increased susceptibility to high blood pressure, periodontal disease, affective disorders and auto-immune diseases. Therapy for its deficiency involves dietary changes or taking vitamin D3 supplements.

Experiments on rats have shown that Vitamin D3 stimulates the rate of OTM in a dose dependent manner.[31,32] Physiologic doses do not stimulate bone resorption, however low supplemental administration does, possibly by stimulating osteoclast differentiation.[33] This effect could help stabilize orthodontic movement. Investigations have suggested that local application of vitamin D could facilitate regeneration of supporting tissue, particularly alveolar bone, after orthodontic treatment.[34,35]

Dietary calcium

Calcium is often prescribed as a dietary supplement for the prevention of osteoporosis in postmenopausal women. Experiments on animals have shown that a low calcium diet leads to a higher rate of OTM compared to a high calcium diet[36] and a control group.[37] There is also an increase in the number of osteoclasts and osteoblasts in rats with low calcium diet and therefore an increase in bone remodelling, where excessive bone resorption prevails over deposition.[38]

Bisphosphonates

This class of pharmacological agents selectively inhibits osteoclasts. They are used to treat and prevent metabolic bone diseases associated with excessive bone resorption such as osteoporosis, Paget's disease, bone metastases, and bone pain from some types of cancer.[39] These drugs are incorporated in the bone matrix and have an extremely long half-life of about 10 years or more. Bisphosphonates can therefore affect bone metabolism for many years after the patient has completed therapy. Long-term use of bisphosphonates may cause osteonecrosis, especially in the alveolar bone of the maxilla and the mandible.[39] Studies show a dose-dependent decrease in the rate of OTM following topical or systemic administration. Furthermore, it has resulted in reduced root resorption when used without a nitrogen atom (Clodronate).[40,41] Topical applications of bisphosphonate have been suggested as being useful in orthodontic anchorage and retention.[42] However it has also been reported that these drugs produce cementum surface alterations by inhibiting acellular cementum formation, thereby actually increasing vulnerability to root resorption.[1]

Further studies are required before these drugs can be used in clinical orthodontic therapy.

EFFECT OF SYSTEMIC FACTORS ON INDUCED TOOTH MOVEMENT

Systemic Factor	Effect on bone metabolism movement	Effect on tooth
Oestrogen	↓ Bone resorption	↓ Tooth movement
Thyroid hormones	↑ Rate of bone remodelling and bone resorption	↑ Tooth movement ↓ Root resorption
Parathyroid hormones	↑ Bone resorption	↑ Tooth movement
Vitamin D	↑ Rate of bone remodelling and bone resorption	↑ Tooth movement

TABLE 2[9]

Psychiatric medication

Orthodontic patients may suffer from psychiatric disorders such as attention-deficit / hyperactivity disorder, depression, eating disorder, and anxiety amongst others. Attention deficit /hyperactivity disorder is principally treated by central nervous system stimulants (Methylphenidate, dextroamphetamine, atomoxetine, etc) which may affect compliance and oral hygiene.[43]

Patients medicated with anti-depressants and mood stabilizers could present being overly concerned about their appearance while simultaneously being non-compliant. Benzodiazepines are often used for those suffering anxiety disorder or psychological stress. These patients may be more concerned about side effects and outcomes, but will utilize every chance to disrupt office visits.

BRIGHTER FUTURES

Australian Society of Orthodontists

Brighter Futures is published by the Australian Society of Orthodontists (NSW Branch) Inc. in conjunction with the Orthodontic Discipline at the University of Sydney.

The newsletter is intended to help keep the dental profession updated about contemporary orthodontics, and also to help foster co-operation within the dental team.

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Conclusion

Current orthodontic research aims to develop methods of increasing the tissue concentration of molecules promoting tooth movement, while simultaneously decreasing the concentration of unwanted elements which can produce harmful side effects.[14]

Researchers have injected prostaglandins locally at the site of orthodontic tooth movement to enhance the bone remodelling process and the pace of tooth movement. The main side effect associated with local injection of prostaglandins is hyperalgesia due to the release of noxious agents. Recent trends are directed toward combining local anaesthetics with prostaglandins to reduce pain when locally injected.

Certain drugs that inhibit tooth movement are being investigated for use in supplementing anchorage and prevention of relapse. Local injection of echistatin and RGD peptides has been trialled in rats to prevent tooth movement thereby enhancing anchorage.[14]

While many substances show promise for enhancing orthodontic therapy, the clinician must be aware of the potentially adverse effects of medications that patients may be taking if unfavourable side effects are to be avoided. Bisphosphonate therapy or vitamin supplements may be crucial. The value of a thorough medical history is increasingly significant as young and old alike are exposed to a greater range of therapeutic agents.

REFERENCES AVAILABLE ON REQUEST

EFFECT OF DRUGS ON INDUCED TOOTH MOVEMENT

Drug	Effect on bone metabolism	Effect on tooth movement
Non-steroidal anti-inflammatory drugs	↓ Bone resorption	↓ Tooth movement
Corticosteroids	↑ Bone resorption (CHRONIC USE)	↑ Tooth movement
Bisphosphonates	↓ Bone resorption	↓ Tooth movement
Acetaminophen	Unproven	No influence

TABLE 3[9]