Abstract

Orthodontic tooth movement results from the response of the periodontal tissue to orthodontic forces, which leads to modeling and remodeling of the surrounding alveolar bone. The endocrine system is responsible for hormonal secretion, being closely related to the central nervous system, as it diversifies its functions through the hypothalamus and pituitary glands. It controls physiological processes and maintains homeostasis. The neuroendocrine system is responsible for adaptation to environmental changes. Also, the nervous system may provide a correct organic response, of primary type, with the release of neurotransmitters or, if the stimulus prevails, the endocrine system secretes hormones. This is especially important in dentistry because many of the patients attending dental clinics face stressful situations. Awareness is therefore necessary on the risks and difficulties that may arise during the dental and orthodontic management of patients with endocrine disorders and most common oral manifestations.

Keywords: endocrine, hormone, orthodontics

INTRODUCTION

The term ‘endocrine’ refers to endocrine or ductless glands, because they secrete physiologically-active substances (hormones) directly into the blood stream. Hormones are secretory products of the endocrine glands released directly into the circulation in small amounts, in response to a specific stimulus. On their delivery in circulation, they respond to the target cells or organs [1].

Protein hormones and catecholamines act through intracellular enzymes. The hormone, which acts on a target cell, is called the first messenger. In combination with the receptor, it forms the receptor-hormone complex. This, in turn activates the enzymes of the cell and causes formation of another substance, called the second messenger or the intracellular hormonal mediator, making the effects of the hormone to be manifested inside the cells [2].

The most common second messenger is cyclic AMP (cyclic adenosine 3’5’monophosphate or cAMP). On the membrane of most of the target cells, receptor proteins called G-proteins are present. The hormone binds with the receptor coupled with the G-protein, to form a receptor hormone complex. This complex activates the enzyme adenyl cyclase, which is also present in the cell membrane. Most of the adenyl cyclase protrudes into the cytoplasm of the cell from the inner surface of the cell membrane. The activated adenyl cyclase converts the ATP of the cytoplasm into cAMP, called the second messenger, which performs the hormonal actions inside the cell; by stimulating some enzymes like protein kinase A, it produces the response, as a function of the target cells through these enzymes [1-2].

The thyroid and steroid hormones act on the genes of the target cells. As soluble lipids, hormones can easily enter the target cells and bind with the receptor in either cytoplasm (steroid hormone) or nucleus (thyroid hormone), forming the hormone receptor complex. This complex enters the nucleus and gets attached to chromatin. The complex reacts with DNA, stimulates transcription (i.e., formation of mRNA), then it enters the cytoplasm, where it directs the ribosomes to synthesize specific proteins (translation). These proteins may be enzymes, structural proteins and receptor proteins of secretory proteins.

Orthodontic tooth movement results from the response of the periodontal tissue to the orthodontic force, which leads to modeling and remodeling of the surrounding alveolar bone. The response is considered to occur through the
activation of specific signaling pathways, many of which are known, all acting to ultimately result in tooth movement. The rate at which tooth movement occurs depends on the ability of these pathways to realize bone metabolism by the two main cell types responsible for tooth movement: osteoblasts and osteoclasts [3-5].

GROWTH HORMONE (GH)

GH is a protein hormone, secreted by the acidophils of the anterior pituitary gland. GH secretion is pulsatile, secretory bursts occurring especially at early hours of sleep and throughout the night. GH has no specific target organ. It is an anabolic hormone to which every organ system responds, considered in the present study being craniofacial growth and its relation with the orthodontic treatment. Apparently, it has no direct action upon bones, acting through a substance called somatomedin. GH stimulates the liver to secrete somatomedin and is the main regulator of childhood and adolescent growth. Undersized children secrete less GH than the tall ones. GH pulse amplitude is increased in growth spurt, with simultaneous increase in plasma IGF-I concentrations. These values often increase to as high as 50ng/ml after depletion of the body stores of proteins and carbohydrates during prolonged starvation [1-5].

Dental development

Dental delay is always less pronounced than height or bone delay. Dentition seems to be harmoniously delayed, so that all studied components of dental development (primary root resorption, secondary tooth formation and eruptive movement) display the same degree of retardation. GH influence on growth starts after 9 months of age, so that the effect on the growth of primary teeth is very little known.

GH deficiency

Children show big skull with babyish face, however their intelligence is normal for their age. Cephalometric studies in such children have shown small sizes of the anterior and posterior cranial bases and smaller mandibular dimensions, small posterior facial height, and small posterior mandibular height. Hypersecretion leads to gigantism in the young ones and to acromegaly in adults, which is usually caused by a pituitary adenoma.

Gigantism

A cephalometric study was done on two female patients suffering from gigantism, due to GH excess. The anterior facial heights appeared as the largest cephalometric dimensions, followed by posterior facial height. Acromegaly-s serum levels of IGF-I in these patients were very high, the mean value being 10-fold higher than in normal adults. Mandibular growth is gradual and often noticed by the dentist when crossbite was developed. The calvarium, hands and feet grow by bone apposition. The tongue grows, and a general visceral growth has been also documented. The cartilaginous tissue gets larger, the ribs are thicker and the costochondral cartilage appears hypertrophic. The hypertrophic articular cartilage and the growth of chondrocytes in the articular cartilage may cause acromegalic arthropathy. Mandibular growth in acromegaly results from both appositional growth and hypertrophic changes in the condylar cartilage. [6-9]

INSULIN

Insulin is a polypeptide hormone secreted by the beta cells of the Langerhans islets of the pancreas. A normal non-obese man secretes approximately 50U/day, with a basal plasma insulin concentration of 10-50 microns/ml. Its main function is to maintain the blood glucose level. Insulin deficiency produces a clinical state called diabetes mellitus, while its excess leads to hypoglycemia. Diabetes mellitus is diagnosed in 3-4% of the population treated in our day-to-day orthodontic practice. The orthodontic practitioner should have a basic knowledge and understanding of this disease and of its impact on the oral cavity, as well as of its consequences upon the dental treatment. [1,10]
Orthodontic considerations

Informed on the oral complications induced by diabetes mellitus, the dental practitioner should consider them when treating a DM patient; the key to any orthodontic treatment is a good medical control. No orthodontic treatment should be performed in a patient with uncontrolled diabetes. There is no treatment reference with regard to fixed or removable appliances. A good oral hygiene is especially important when fixed appliances are used, as they may increase plaque retention, which could more easily cause tooth decay and periodontal breakdown. Daily rinses with fluoride-rich mouthwash can provide further preventive benefits. Candida infections may also occur in the oral cavity, so that they should be well monitored. Diabetes-related microangiopathy can occasionally appear in the periapical vascular supply, resulting in unexplained odontalgia, percussion sensitivity, pulpitis, or even loss of vitality in sound teeth. Especially in orthodontic treatments involving force application for moving teeth over a considerable distance, the practitioner should regularly check the vitality of the teeth involved. It is advisable to apply light forces and not to overload the teeth [11].

Holtgrave and Donath, who studied the periodontal reaction to orthodontic forces, evidenced retarded osseous regeneration, weakening of the periodontal fibers and microangiopathies in the gingival areas. In adults, before starting the orthodontic treatment, the orthodontist should obtain a full-mouth (periodontal) examination and evaluation of the need for periodontal treatment. The periodontal condition should be improved before staring the treatment and should be monitored regularly. Maintaining a strict oral hygiene is important, by a proper use of toothbrush, interdental toothbrush and chlorhexidine mouthwash. To minimize the neutralizing effect of toothpaste on the chlorhexidine molecule, an at least 30-min interval should be left between tooth brushing and chlorhexidine rinse.

As no upper age limit for orthodontic treatments is any longer valid today, the practitioner will see both type1 and type2 DM patients. Type2 patients can be considered more stable than type1 ones, as hypoglycemic reactions are more frequent in these patients. If a patient is scheduled for a long treatment session, he or she should be advised to eat a usual meal and take the medication as usual. At each appointment, the orthodontist should confirm the meal and medication, to avoid a hypoglycemic reaction in the office. DM patients with good metabolic control, without local factors, such as calculus, and with a good oral hygiene, have a similar gingival status as the healthy ones, consequently they can be treated orthodontically [12-14].

THYROXIN HORMONES (TH)

TH lack in a specific target organ may affect every organ and system and every biologic process. Thyroid disorders are common and affect craniofacial and dental structures. The dental and craniofacial retardation manifested under prolonged hypothyroid conditions differs from the isolated lack of GH. The main difference is the cranial vault, which shows growth retardation in hypothyroidism, and reduced facial height in children with prolonged untreated hypothyroidism. Thyroxin administration seems to lead to increased bone remodeling, increased bone resorptive activity and reduced bone density. Thyroid hormones increase osteoclastic bone resorption in neonatal mouse calvarium by stimulation of prostaglandin synthesis [14].

PARATHORMONE (PTH)

It is a polypeptide hormone secreted by the parathyroid glands, which increases serum calcium by releasing calcium from the bone. Possibly, it may enhance orthodontic tooth movement by the local use of PTH. The discrete removal of the alveolar bone prior to force application may reduce resistance to tooth movement, permitting a selective tooth movement [15].

CALCITONIN

It is a peptide hormone secreted by the interfollicular or C-cells in the thyroid gland, also called thyrocalcitonin. Thyrocalcitonin flows
into the bloodstream and attracts calcium to the bone, thus reducing serum calcium. It also inhibits bone resorption by reducing the number of osteoclasts. Calcitonin is used in the treatment of hypercalcemia and in osteoporosis; because of its physiological role, it is considered as inhibiting tooth movement. Consequently, a delay in the orthodontic treatment can be expected [1,15].

**VITAMIN-D$_3$**

Vitamin-D and its most active metabolite, vitamin-D$_{3}$, together with parathyroid hormone and Calcitonin, regulate the amount of calcium and phosphorus in the human organism. It promotes intestinal Ca$^{2+}$ and PO$_4^{-3}$ absorption. Vitamin-D$_3$ increases bone mass and thus reduces fractures in osteoporosis patients. Considering its beneficial effects on bone tissue, it may be assumed that it inhibits tooth movement [16,17].

**SEX-STEROIDS**

A slight increase in the growth rate is seen at the age of 6-8 years in most children, possibly due to an increased GH and IGF-I production, which is stimulated by adrenal androgens. During puberty, an increase in GH production is seen in boys and girls. Several lines of evidence indicate that this increase is sex-steroid dependent. The sex-steroids here involved are adrenal and ovarian androgens and ovarian and testicular estrogens. Plasma concentration of IGF-I shows a similar increase [18].

Estrogen directly stimulates the bone-forming activity of osteoblasts, so it is reasonably to expect a slower rate of orthodontic tooth movement. Androgens also inhibit bone resorption and modulate the growth of the muscular system. Thus, the excessive use of these drugs by athletes, in an attempt to achieve better athletic scores, may affect the duration and results of the orthodontic treatment.

**CORTICOSTEROIDS**

Hyperglucocorticoidism causes short stature and bone maturation, while increasing relative weight. Very small amounts of medication can decrease the growth rate. Skeletal IGF-I synthesis is decreased by cortisol, which has an inhibitory effect on bone collagen synthesis. In the process of tooth eruption, however, cortisone has a special effect, the eruption rate being accelerated [19-20].

**PROSTAGLANDINS (PGS)**

The precursor of PGs is the arachidonic acid, which is metabolized by cyclaseoxygenase (cox) enzymes. Experiments have shown that PGs may act as important mediators of mechanical stress during orthodontic tooth movement. They stimulate bone resorption by increasing the number of osteoclasts and by activating the already existing osteoclasts [21].

**LEUKOTRIENES**

These also exist metabolites of the arachidonic acid, produced when metabolized by the lipoxygenase enzyme. Leukotrienes may be also important mediators of orthodontic tooth movement. A study of Mohammed, Takikis and Dziak devoted to the role of inhibitors of leukotrienes synthesis in orthodontic tooth movement showed a significant reduction of orthodontic tooth movement. Consequently, the use of leukotriene inhibitors can delay the orthodontic treatment, whereas leukotrienes and PGs can have future clinical applications, causing enhanced tooth movements [22-23].

**BIPHOSPHONATES**

This class of pharmacological agents is characterized by their high affinity for calcified tissues. Biphosphonates are potent blockers of bone resorption, successfully used in the treatment of hypercalcemia, osteoporosis and, generally, in the treatment of metabolic bone diseases involving increased bone resorption. Inhibition of the osteoclastic metabolism is caused by a decrease in the number of osteoclasts, which may recommend it for anchoring and retaining teeth under orthodontic treatment. However, further studies
are required before any clinical application in orthodontics, for avoiding any possible systemic effects [24].

**FLUORIDE**

It is one of the several trace elements that affect hard tissue metabolism. It stimulates the growth and synthesis activity of osteoblasts and bone formation, and increases bone mass and mineral density. At clinical level, the mentioned findings suggest that the use of fluoride can influence the rate of orthodontic tooth movement. Even a very active preventive caries treatment with sodium fluoride (NaF) during orthodontic tooth movement can affect the duration of orthodontic therapy [22-24].

**NSAIDS (SALICYLATES)**

These non-steroidal anti-inflammatory drugs inhibit the cyclase-oxygenase (cox) activity. Salicylates’ action can be attributed to their inhibition of PG synthesis, which seems to play a significant role in bone resorption during orthodontic therapy. Therefore, it is not recommended to patients undergoing orthodontic treatment to take salicylates for long periods, as this might possibly prolongue the treatment [25].

**CONCLUSIONS**

Most of the studies on hormones have been done on rats, squirrels and monkeys and not on human beings; consequently, very little is still known on the effects of hormones on the development of face and craniofacial skeletal and on the rate of orthodontic tooth movement in humans. The role of endocrine disorders in orthodontics is still a great mystery for an orthodontic practitioner and further research is required to understand it better.

**References**