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REVIEW ARTICLE

Effect of Growth Hormone on Orthodontic Tooth Movement: A Review

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ABSTRACT

Objectives: The purpose of the present review is to look into the impact of growth hormone on orthodontic tooth movement.

Sources and Data: To search for orthodontic treatment in elderly patients, a literature review of English papers was undertaken using Google Scholar, PubMed, and Scopus.

Conclusion: Growth hormones have a great importance in the growth of the face and craniofacial structures, also they affect tooth movement during orthodontic treatment, so orthodontists must have a background of knowledge about these hormones and their impact on the movement of the teeth before starting treatment because any defect in these hormones may negatively affect orthodontic treatment.

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INTRODUCTION

Growth hormone (GH) can be described as potent metabolic hormone secreted via the anterior pituitary gland cells and regulated through various pato-physiological and normal conditions. Its molecular structure is one 191 amino acid polypeptide chain with 2 di-sulphide bridges and a 22kDa[1] molecular weight, with a plasmatic half-life of 15min to 20min following intra-venous injection or secretion. Blood GH concentrations peak between 1 and 3 hours following subcutaneous or intramuscular injection and then decline to undetectable levels following 24 hours.[2]

The functioning of body organs is mediated by the nervous system, which activates the endocrinal system. Hypothalamus play the role of master orchestra, stimulates the pituitary glands, stimulating the endocrinal system. This endocrinal system constitutes endocrinal glands which facilitate the secretion of chemical mediators/hormones directly into the blood stream. The word hormones were first termed by Ernst Sterling in 1905, wherein he defined it as a chemical substance that excites the activities of cells and enhances the growth of various body parts.[3] Various hormones have a pivotal impact on the growth and development of various tissues and body organs. The growth hormone (GH) primarily assumes the role for linear somatic and craniofacial growth in infants.[4] GH secretion peaks in a predictable manner approximately one hour following the onset of the sleep with plasma levels ranging from 13–72 ng/mL, Discrepancy in secretion of GH would lead to severe growth abnormalities in children and adults, which would hamper the quality of life. On assessing the role of GH in the field of orthodontics, it induces orthodontic tooth movement by acting on specific signalling pathways thus activating certain cytokines to control the activity of osteoclasts and osteoblasts

for selective formation and remodeling of the bone.[5]
Regular collaboration with the endocrinologist is required to give effective care to orthodontic patients. An orthodontist might execute and plan therapy more efficiently if they are thoroughly aware of the patient's medical condition. Using appropriate appliances and planning mechanics can be aided by understanding potential dangers and physiological processes throughout orthodontic therapy.[6]

Impacts of the GH on the Craniofacial Growth

The depth and length of a face are abnormally small for the age of the child in Idiopathic Growth Hormone Deficiency, with the face preserving child-like convexity. Various researches found that mandibular total length (Gn-Cd) is shortened due to the small ramus height (Cd- Go). Furthermore, the maxilla is greatly decreased, and the mandible could be decreased similarly. The maxilla is frequently retrognathic, yet less so than mandible. In terms of cranial base size, various researches have found that posterior cranial base length is shorter compared with anterior cranial base (N-S) length. In contrast, GH replacement therapy reduces facial convexity, and its main impact appears to be on the condylar growth.[7]

Effect on Dental Development and Tooth Tissue

Height or bone delay is often less evident compared to dental delay. The dentition appears harmoniously delayed, with all of the examined components regarding the dental development (secondary tooth formation, resorption of the primary root, and eruptive movement) showing an identical level of retardation. The impact of the growth hormone on growth begins following nine months of age. Hence the impact on primary tooth growth is unknown.[8] At cellular level, odontoblast differentiation from the neural crest cells represents a lengthy process similar to osteoblast differentiation. As do bone morphogenetic proteins, growth hormone is known to increase the production of bone and hard tissues of teeth (cementum, enamel and dentine).[9] Those tissues have GH receptors, which can mediate local growth responses, which is discovered in future amelodentinal junction's distal cytoplasm.[10] IGF-I receptors have also been found in early rat molar tooth bud formation stages in vivo11. GH could be the main IGF-I expression regulator in the early phases of tooth formation. The GH mediates the mitogenic stimulus to the odontoblast lineage cells by epidermal growth factor (EGF) to differentiate into odontoblasts.[11]

Differentiation of odontoblast into various tooth structures like dentin, cementum and enamel, is mediated by IGF-1 and BMP 2. GH also increases the cell proliferation of inner dental epithelium, Hertwigs epithelial root sheath and dental papilla, which determines the root dimension and root shape. Hence GH affects the morpho differentiation and maturation status of tooth. However, it has least effect on the eruption of tooth.[12]

Mechanism of Action

GH is a non-fat soluble hormone. It mediates its action by binding to specific GH binding domain receptors(GHR) of target cells, initiating secondary messengers Inosine Triphosphate(IP3) activity, activates MAPK/ERK signalling pathway to enhance metabolic effects on cells.[13] GH also activates JAK-STAT signaling in the liver and pancreas to produce IGF-1, which has a stimulatory effect on the osteoblast and chondrocyte for the development of secondary ossification centres for endochondral ossification to promote the growth of bone.[14] Hence, the GH effect is mediated by GH and IGF-1, which have been cited as GH/IGF-1 axis. So Stomatomedin theory suggest that GH stimulates skeletal growth through the stimulation of IGF-1, which in turn stimulates longitudinal bone growth in an endocrine manner.[15] While Dual effector theory suggest that GH and IGF-1 act independently at various stages of endochondral maturation and differentiation. GH is stimulating the young pre-adipocytes at initial stages of development, while the IGF-I stimulates mature cells at later development stage.[16]

Corticosteroids

Corticosteroids are anti-inflammatory and immunosuppressive agents commonly used for treating pathological processes in dental and medical practice. As a result of their use, individuals undergoing orthodontic treatment could have changes in normal bone remodeling.[15] Hyperglucocorticoidism causes short stature and advanced bone maturation, yet it also causes an increase in relative weight. Small doses of medicine can slow down the growth rate. Cortisol inhibits bone collagen synthesis and reduces skeletal IGFI synthesis. Cortisone, on the other hand, has a unique action during tooth eruption. The rate of eruption has increased. The predominant action of corticosteroids on bone tissue appears to be direct osteoblastic function inhibition, resulting in a reduction in total formation of the bone. Increased PTH levels are generated by corticosteroid-induced obstruction of intestinal calcium absorption, resulting in decreased bone formation.

Corticosteroids accelerate tooth movement, and because the formation of new bone in treated individuals is complicated, they generally reduce tooth movement stability and orthodontic therapy.[17] The biggest negative impact when they are used for prolonged periods of time is osteoporosis. The rate of active tooth movement is higher in animal models with such type of osteoporosis, yet the movement of the tooth is less stable because there is less bone present and there are no indications of any bone formation.

Estrogens

Estrogen is the hormone that has the greatest impact on bone metabolism in women. It regulates bone remodeling throughout reproductive life and bone mass maintenance following menarche. The hormone estrogen slows bone resorption. Estrogen decreases the synthesis of cytokines like the tumor necrosis factor-alpha, IL-1, and interleukin-6, which play a role in bone resorption by increasing osteoclastic bone resorption.[18] Estrogen reduces the velocity of the movement of the tooth. Tooth movement rate could be influenced by long-term use of oral contraceptives. Androgens can impact the results and length of orthodontic therapy by inhibiting bone resorption

and modulating muscle growth.

When the force is applied to the teeth, periodontal remodeling of the tissue results in tooth movement. The tension region involves extending periodontal ligament and depositions of the new alveolar bone, while pressure area involves periodontal ligament compression and alveolar bone resorption. Different factors, like estrogen levels, alter periodontal tissue remodeling rate. Estrogen affects the degradation and composition of the collagen fibers in the periodontal ligaments and alveolar bone remodeling.

While estrogen affects collagen fiber deposition and crosslinking, it also boosts alkaline phosphatase (ALP) activity and osteoprotegerin (OPG) and osteocalcin (OCN) production in the periodontal ligament cells (PDLC).[19] The tooth movement rate is linked to osteoclast activity. Estrogen could directly or indirectly inhibit osteoclast activity, influencing bone resorption. Low levels of the estrogen result in the stimulation of synthesis of the bone resorption-related factors like tumor necrosis factor alpha, interleukin-1 and -6, and macrophage colony-stimulating factor (M-CSF), which could cause bone loss through influencing osteoclast differentiation and activity. Estrogen inhibits the movement of the tooth through the increase of bone mineral concentration and mass while also slowing bone resorption. Many researchers have found that low estrogen speeds up tooth movement.[20] Because estrogen enhances osteoblasts' bone-forming activity, it is realistic to predict a slower rate of orthodontic tooth movement.

Insulin

Insulin can be defined as poly-peptide hormone secreted via beta cells of pancreas' Langerhans islets. A healthy, non-obese male secretes about 50 U/day, with basal concentration of the plasma insulin of 10-50microns/ml. Its primary task is to keep blood glucose levels. Insulin deficiency results in DM, whereas insulin excess results in hypoglycemia. In our daily orthodontic practice, DM is identified in 3-4% of the population. The orthodontic practitioner must have a fundamental understanding regarding such condition and its effects on the oral cavity, along with the implications for dental therapy [21].

The dental practitioner must be aware of the oral problems caused via diabetes mellitus while treating a DM patient; adequate medical control is the key to any orthodontic treatment. In a patient who has uncontrolled diabetes, no orthodontic treatment must be conducted. There is no difference in treatment for removable or fixed appliances. Effective oral hygiene is particularly necessary when fixed appliances are utilized since they might increase plaque retention, making periodontal disease and tooth decay more likely. Daily mouthwash rinses using fluoride-rich mouthwash could help in having preventive effects. Candida infections could also occur in the oral cavity and must be closely examined. Microangiopathy caused by diabetes might often arise in periapical vascular supply, causing unexplained odontalgia, pulpitis, percussion sensitivity, or even vitality loss in otherwise fine teeth. The practitioner must assess the vitality regarding the teeth involved in orthodontic procedures, particularly when force is used to move teeth across a significant distance. It is best to use light efforts and avoid overloading the teeth.[22] Before beginning orthodontic treatments, orthodontists must perform a full-mouth (i.e. periodontal) examination and determine whether periodontal therapy is required. Before beginning treatment, the periodontal status must be enhanced and checked regularly.

Parathyroid Hormone (PTH)

By regulating renal excretion, intestinal reabsorption, and ion exchange between extra-cellular fluid and bone, PTH is a potent mechanism for modulating extracellular calcium and phosphate concentrations. Excess parathyroid gland activity induces rapid absorption of the calcium salts from bones, resulting in hypercalcemia in extra-cellular fluid; hypofunction of parathyroid glands leads to hypocalcemia, frequently with the tetany as a result.[23] The parathyroid glands generate PTH to keep serum calcium levels.

PTH influences gene transcription, cellular metabolic activity, and various protease secretion in osteoblasts. It affects osteoclasts by causing them to produce RANK-L, a protein that is essential for osteoclast activity and formation. The paradoxical effects of parathyroid hormone on the metabolism of the bones have drawn attention as one of the major regulators of calcium and phosphate homeostasis. According to research, parathyroid hormone can increase both osteoblast-mediated bone formation and osteoclast-mediated resorption of the bones, speeding up the bone turnover rate. In clinical osteoporosis treatment, intermittent low-dosage parathyroid hormone analogs were majorly used. Previous research has looked into the effects of various parathyroid hormone administration patterns, and findings proposed that continuous systemic infusions or the local chronic applications of the parathyroid hormone can speed up tooth movement by increasing alveolar bone resorption. In contrast, long-term intermittent injection regarding parathyroid hormone facilitated periodontal bone or root resorption following orthodontic tooth movements by activating the osteoblastic cells.[24]

The "anabolic window," where bone formation is higher than bone resorption over first 6 to 18 months, is responsible for the ultimate rise in bone density. In fact, a few researchers believe that active osteoclastic resorption is required for parathyroid hormone's effect on the formation of the bone in a remodeling system. Intermittent administration of parathyroid hormone causes an increase in osteoclastic resorption activity. As a result, resorptive activity stimulates bone remodeling by increasing the osteogenic growth factors' release from the bone matrix and the osteoclasts.[25]

Vitamin D

Vitamin D has a powerful impact on calcium absorption from the intestinal tract and substantial impacts on bone deposition and absorption. Yet, vitamin D isn't the active substance which results in this side effects. However, vitamin

D should first be converted into final active product, 1, 25-di-hydroxycholecalciferol, by a series of reactions in the kidneys and liver. The sequence of processes that result in synthesizing such substance from vitamin D.[26] The amount of phosphorus and calcium in the human organism is regulated by vitamin D3, parathyroid hormone, and calcitonin. In osteoporosis patients, vitamin D3 enhances bone mass and hence reduces fractures. It's reasonable to suppose that its favorable effects on bone tissue prevents tooth movement.[27]

BIPHOSPHONATES

The high affinity for calcified tissues distinguishes such class of pharmacological agents. Biphosphonates are powerful bone resorption blockers successfully utilized for treating osteoporosis, hypercalcemia, and other metabolic bone disorders characterized by excessive bone resorption. Reducing the number of osteoclasts inhibits the osteoclastic metabolism, which could be beneficial for anchoring and maintaining teeth during orthodontic therapy. Yet, more research is needed prior to any practical application in orthodontics to rule out any systemic effects.[28]

GH Deficiency

Studies by Cantu *et al*. suggest that GH deficiency causes significant delay in maturation and somatic body growth.[4] Height is somewhat more affected than skeletal maturation.[12] During facial development depth and length of face remains small for the age, with increased facial convexity 11 due to decreased posterior cranial base length versus anterior cranial base.[29] However, size of mandible is greatly reduced compared to maxilla due to decreased ramal height with tendency of open bite, cross bite and crowding.[30] The success of GH therapy relies upon promoting the growth before puberty, so that the child's development shall be similar to that of a normal child. On the other hand, individuals getting orthodontic treatment with GH require longer intervals with light orthodontic forces because the formation of new bone is delayed, as well as more intense bone resorption, especially in early stages of GH therapy administration. It's best to start orthodontic treatment after taking GH because it only stimulates bone development following 12 to 24 months.[31]

CONCLUSION

Growth hormones have a great importance in the growth of the face and craniofacial structures, also they affect tooth movement during orthodontic treatment, so orthodontists must have a background of knowledge about these hormones and their impact on the movement of the teeth before starting treatment because any defect in these hormones may negatively affect orthodontic treatment.

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