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Review Article

Role of growth hormone in orthodontics

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ABSTRACT

Human growth hormone (Somatotropin) is produced by acidophilic growth hormone cells in the anterior pituitary gland, stimulated by hypothalamus. Its production is regulated by several complex feedback mechanisms in response to stress, exercise, diet, sleep and growth hormone itself. Growth hormone plays a major role in linear body growth and craniofacial growth. In Orthodontics, it induces orthodontic tooth movement by activating specific cytokines to regulate osteoclast & osteoblast activity. It mediates STAT signalling in liver & pancreas to produce JAK-IGF-1. IGF-1 has stimulatory effects on osteoblasts and chondrocytes for endochondral ossification to promote bone growth. Growth hormone mediates mitogenic stimulus to odontoblast lineage cells by epidermal growth factor (EGF) to differentiate into odontoblasts. It also stimulates production of alkaline phosphatase and osteocalcin in osteoblasts to improve osteoblast proliferation and differentiation. It also induces osteoclastic activity indirectly by production of IGF-1 and IL- 6 thereby activating RANK-RANKL/OPG phenomenon. It also promotes myofibrillar diameter expansion so it increases muscle mass with strength. Growth Hormone Replacement therapy reduces facial convexity and its main effect appears to be on condylar growth. Since deficiencies of growth hormone can adversely affect orthodontic treatment, effects of growth hormone treatment on craniofacial structures should be considered in order to maximize the effectiveness of orthodontic treatment with appliances and it is more important to understand.

1. Introduction

Human growth hormone (GH), also known as somatotropin, is produced by acidophilic growth hormone cells in the anterior pituitary gland. Its production is tightly regulated by several complex feedback mechanisms in response to stress, exercise, diet, sleep, and growth hormone itself.[1] Its molecular structure is one 191 amino acid polypeptide chain with 2 di-sulphide bridges and a 22kDa1 molecular weight. Plasma half-life of 15 to 20 minutes after intravenous injection or secretion.[2] The functions of the two organs are mediated by a nervous system that activates the endocrine system. The hypothalamus acts as a master orchestra, stimulating the pituitary gland and stimulating the endocrine system. This endocrine system is made up of endocrine glands that facilitate the direct secretion of chemical mediators/hormones into the bloodstream. The word hormone was first used by Ernst Sterling in 1905 and defined as a chemical substance that stimulates cellular activity and promotes growth in various parts of the body.[3]

Various hormones play important roles in the growth and development of various tissues and organs. Growth hormone (GH) plays a major role in linear body growth and craniofacial growth in infants.[4]Evaluating the role of GH in the field of orthodontics, GH acts on specific signaling pathways. It induces orthodontic tooth movement by activating specific cytokines to regulate osteoclast and osteoblast activity for selective formation and remodeling

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of bone. The GH family genes map to chromosome 17q23-q24. It is a 191 amino acid anabolic hormone with a molecular weight of 22,005.[5,6] GH that stimulates the liver and pancreas to secrete insulin-like growth factor I (IGF-1/somatomedin). GH and IGF-1 then act on specific cellular structures in various organs through growth hormone receptor (GHR) and IGF-binding protein (IGFBP)-3, -4, and -5 to Activates and strengthens the second messengers within. Metabolic activity of cells for the secretion of specific proteins.[7,8]

2. Mechanism of Action

GH is a non-lipid soluble hormone. Binding to specific GH-binding domain receptors (GHRs) on target cells, initiating the second messenger activity inosine triphosphate (IP3) and activating MAPK/ERK signaling pathways to enhance metabolic effects on cells.[9] GH mediates STAT signaling in the liver and pancreas to produce JAK-IGF-1. IGF-1 has stimulatory effects on osteoblasts and chondrocytes for the development of secondary ossification centers for endochondral ossification to promote bone growth.[10] Thus, GH and IGF-1working mechanism is cited as GH/IGF-1 axis.

Various theories have been proposed, citing the effects of GH/IGF-1 on target organs. They are:

1. Stomatomedin theory – suggested that GH stimulates skeletal growth by stimulating IGF-1, which endocrinally stimulates longitudinal bone growth.[11]
2. Dual effector theory – suggested that GH and IGF-1 act independently at different stages of maturation and differentiation within the cartilage. GH is known to stimulate young preadipocytes in the early stages of development, whereas IGF-I stimulates mature cells in the later stages of development.[12] It is also affected by various hormones such as thyroid hormone,[13] while glucocorticoids and parathyroid hormone have the effect of suppressing the effects of GH.[14] The overall action of GH mainly affects tissues such as muscle and bone. and have general effects on all parts of the body.[15] However, the independent action of IGF-1 is associated with cartilage growth and the anabolic effects of GH.[16]

3. Impact of GH on the Growth of Craniofacial Structures

In idiopathic growth hormone deficiency, the depth and length of the face are abnormally small for the child's age, and the face retains a childlike convexity. Various studies have shown that the total length of the mandible (Gn-Cd) is shortened due to the lower branch height (Cd-Go). In addition, the upper jaw may shrink significantly, and the lower jaw may shrink as well. The maxilla is often postgnathic, but less so than the mandible. Regarding skull base size, various studies have found that the length of the posterior skull base is shorter than the length of the anterior skull base (N-S). In contrast, GH replacement therapy reduces facial convexity and its main effect appears to be on condylar growth.[17]

3.1. Impact on dental development

The dentition appears to be in harmony, and all tested components related to tooth development show the same delay. The impact of growth hormone to growth begins after 9 months of birth. Therefore, the impact on the growth on primary teeth is unknown.[18] Similar to bone -forming proteins, growth hormones are known to increase the production of bones and hard tooth tissue.[19] Those tissues have GH receptors, which can mediate local growth responses, which is discovered in future amelodentinal junction's distal cytoplasm.[20] The GH mediates the mitogenic stimulus to the odontoblast lineage cells by epidermal growth factor (EGF) to differentiate into odontoblasts.[21] Differentiation of odontoblast into various tooth structures like dentin, cementum and enamel, is mediated through the action of IGF-1 and BMP 2. GH affects the morphological differentiation and maturity of tooth. However, it has least effect on the eruption of tooth.[22]

3.2. Impact on osteoblasts

This has a strong effect on structures primarily derived from neural crest cells (originally from the outer mesenchyme). GH promotes the differentiation of osteoprogenitor cells and increases the production of cells of the osteoblastic lineage. It also stimulates the production of alkaline phosphatase and osteocalcin in osteoblasts to improve osteoblast proliferation and differentiation.[23]

3.3. Impact on osteoclasts

GH uplifts the bone turnover through upregulation of osteoclast production in osteoblast cells leading to production of mature osteoclasts through osteoclastogenesis.[24] GH also induces osteoclastic activity indirectly by inducing the production of IGF-1 and IL-6, which in turn activates RANK- RANKL/OPG phenomenon. Hence GH plays a dual activity, to regulate both bone modelling aswell as remodelling.[25]

3.4. Impact on odontoblasts

GH mediates the mitogenic stimulation to the odontoblast lineage cells via epidermal growth factor (EGF) to differentiate into odontoblasts.[26] 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

holding a dimunitive role in tooth eruption.[27]

3.5. Impact on muscles fibres

GH is also required for skeletal muscle development, GH binds to GHR in target cells and activates second messengers that activate tyrosine kinase enzymes through phosphorylation mediated by the JAK signaling pathway. This leads to increased protein synthesis by the rough endoplasmic reticulum and increased cellular expression. Thus, GH promotes myofibrillar diameter expansion along with fusion of myoblasts with myotubes, increasing muscle mass with strength.[28]

3.6. Over secretion of GH

Hypersecretion of GH leads to gigantism (before fusion of epiphysis and metaphysis) and acromegaly (apposition overgrowth of bone after fusion of epiphysis and metaphysis). Common clinical features are prominent supraorbital ridges, dehiscence associated with temporal changes in intermaxillary occlusion, anterior and inferior mandibular growth leading to crossbite and cleft jaw.[29] A study by Cohen et al. suggested any surgery to correct the bite and orthodontic surgery to resolve masticatory complaints should be deferred until it is ensured that GH levels remain at normal levels for the next 12 months.[30]

3.7. Deficiency of GH

A study by Cantu et al. GH deficiency has been suggested to significantly retard maturation and body growth.[4] Height is affected slightly more than skeletal maturation.[22] During facial development, facial depth and length remain small for age, and facial convexity[21] increases due to the shorter length of the posterior skull base compared to the anterior skull base.[26]However, the mandible is significantly smaller in size compared to the maxilla. This is due to the reduced height of the temporomandibular joints and the propensity for open bite, crossbite and crowding.[27] The success of GH therapy is based on promoting prepubertal growth, so it is said that the development of the child is similar to that of a normal child. Bone formation is delayed and more severe bone resorption occurs, especially in the early stages of administration of GH therapy, requiring longer intervals of light corrective force. GH does not stimulate bone development until 12-24 months of age, so it is recommended to take GH before starting orthodontic treatment.[31]

4. Conclusion

Growth hormone plays an important role in the growth of skeletal and tooth structures and affects tooth movement during orthodontic treatment due to its function of regulation of cellular proliferation, differentiation and metabolic activity control. Therefore, since deficiencies in these hormones can adversely affect orthodontic treatment, the effects of GH treatment on craniofacial structures should be considered in order to maximize the effectiveness of orthodontic treatment with effective appliances is important to understand.

5. Conflict of Interest

The authors declare that they have no conflict of interest.

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None.

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