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Influence of genetic and environmental factors on bone growth during adolescence

Influência dos fatores genéticos e ambientais no crescimento ósseo durante a adolescência

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ABSTRACT

INTRODUCTION: Growth is a dynamic and continuous process that occurs from conception to the end of life and reflects the conditions of life in the past and present. All these factors together influence positively or negatively, accelerating or slowing down this growth process. Eating habits in general have a decisive effect on the bone growth process and their lack has severe implications on child growth and development. During puberty, the secretion of three hormones increases: sex steroids, growth hormone (GH), and IGF-1. The bone remodeling process is controlled by several local factors that act on osteoblastic and osteoclastic cells. This process together influences the proliferation and recruitment of undifferentiated cells, resulting in cell differentiation and bone remodeling. OBJECTIVE: To understand the influence of genetic and environmental factors that determine bone growth during adolescence/puberty. METHODS: A qualitative literature review was carried out from secondary sources with the objective of mapping knowledge about the influence of GH and sex hormones on bone growth. Electronic medical record tools were used in the research, seeking to catalog studies that addressed the GH-IGF-1 axis, endochondral and intramembranous bone growth type, epiphyseal line, influence of genetic and environmental factors on growth, sex hormones correlated with bone growth, puberty spurt, and cartilaginous bone tissue. RESULTS: The sequence of biological events of

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puberty is caused by the activation of the hypothalamic-pituitary-adrenal-gonads axis. However, environmental factors can influence this hormonal chain. Adolescent nutrition needs to be healthy and full of nutrients for proper bone growth to occur. The practice of physical activities plays a crucial role and favors bone growth. DISCUSSION: The review highlights the influence of genetic and environmental factors on the growth process, highlighting the most relevant ones on growth, such as the epidemiological profile of nutritional problems and how they impact on the possible implications on child growth and the current public health policy.

Keywords: Bone growth, Genetic and environmental factors, Puberty hormones and Child development.

INTRODUCTION

Growth is a dynamic and continuous process that occurs from conception to the end of life and reflects the conditions of life in the past and present. Thus, it is vulnerable both by intrinsic (genetic) and extrinsic (environmental) factors, emphasizing the importance of food, health, hygiene and housing. All these factors together influence positively or negatively, that is, accelerating or slowing down this growth process. [1]

It is evident that if a person or population lives in a satisfactory environment, intrinsic factors can express their maximum potential. This line of dialectical reasoning that relates extrinsic and intrinsic factors is in the opposite direction to ideas mechanistic that only the genes that are determinants of the characteristics of individuals. [2]

Eating habits in general, such as intake of fruits, fibers, vegetables, micronutrients (minerals and vitamins) and appropriate diet in iron, zinc, calcium and proteins, have a determining effect on the bone growth process and their deficiency has severe implications on child growth and development, as well as on resistance to infections. [3,4]

Other determinants, such as education, type of housing, sanitation, access to health services, consumer goods and maternal schooling, have contributed to significantly increase the chances of children presenting growth retardation, especially in the case of mothers with low schooling and/or no schooling. [5,6,7,8]

In view of these biological, socioeconomic, environmental, cultural, demographic, and hereditary variables, we emphasize the relevance of understanding on the part of health professionals and students on the subject.

During childhood, growth occurs mainly due to feeding, as in this phase there is a lower growth rate compared to the pubertal phase. It is known that three intrinsic, endocrine events are fundamental to initiate the puberty process, such as increased hormone secretion by the adrenal gland (Adrenarche), increased pituitary gonadotropins (Activation or disinhibition of

hypothalamic neurons secreting LHRH) and increased sex steroids (Gonadarch). In addition, there is a peak in GH production and as a result there is an increase in growth speed, being considered one of the phases in which the individual grows the most during life. This process occurs first in girls and later in boys, as a consequence of stimulation of the GH-IGF axis. [9]

During puberty, the secretion of three hormones increases: sex steroids, growth hormone (GH), and IGF-1. In females, the increase in estradiol secretion is accompanied by an acceleration of growth velocity since the appearance of thelarche, suggesting that moderate levels of this sex steroid are capable of stimulating pubertal growth. Adrenarche begins between 6 and 8 years, with the production of androgens (DHEA and SDHEA) from the adrenal gland. These seem to contribute to the disinhibition of the hypothalamus, providing increasingly frequent nocturnal pulses of LHRH and later of LH. Recent studies reveal that leptin, a hormone secreted by adipose tissue, also contributes to the reduction of hypothalamus inhibition. In males, increased testosterone secretion appears to stimulate increased GH and IGF-1 before promoting growth acceleration.

Thyroid hormone, along with GH, IGFs, glucocorticoids, and in adolescence, estrogens and androgens represent the major systemic factors influencing skeletal growth and maturation. Before adolescence, thyroid hormone is considered the main prerequisite for normal maturation of bone tissue. [10,11]

Growth hormone (GH) is a peptide produced by cells of the anterior pituitary gland, the so-called somatotrophs, whose main function is to stimulate bone growth, especially in the pubertal phase. Its secretion occurs during the night, in phases III and IV of sleep, and occurs between 6 and 10 pulses in 24 hours. [12,13,14]

The bone remodeling process is controlled by several local factors that act on osteoblastic and osteoclastic cells, as well as a variety of systemic hormones. This process together influences the proliferation and recruitment of undifferentiated cells, resulting in cell differentiation and bone remodeling itself. [1]

The endochondral ossification process occurs in the bone growth plate, epiphyseal line, resulting in longitudinal bone growth. This line is identified in long bones and lies between the epiphysis and shaft of the bone. Cartilage cells are formed first and later remodeled into bone tissue. However, with the passage of time and the individual's aging, this mechanism progressively decreases.

The determining mechanisms of this increase are dependent on several biological, socioeconomic, environmental, cultural, demographic and hereditary variables and are not fully

understood. This explains the increasingly evident importance of investigations between growth and external conditions (environmental, social, economic and cultural). [16]

METHODS

The work is based on bibliographic research with a qualitative approach. It consists of a research of secondary sources, with the objective of mapping the knowledge about the influence of GH and sex hormones on bone growth. Information collection and literature analysis were used from texts, journal articles, journal materials, documents and other scientific materials. The research used tools through electronic medical records, with discussion based on scientific articles from PubMed and Scielo, with material from the last 20 years (2000 to 2020) and with languages: "Portuguese" (Brazil) and "English". The descriptors used: "GH therapy in children", "GH and sex hormones", "Effects of growth hormone", "GH", "IGFs and GH", "Treatment with growth hormone in children with short stature", "Short stature and GH" and "Genetics and GH-IGF-1", "Bone growth and Growth Hormone", "GH", "Endochondral bone growth", "Sex hormones and bone growth".

Initially, 18 scientific articles were chosen, the criteria encompassed were to catalog the studies that addressed the GH-IGF-1 axis, type of endochondral and intramembranous bone growth, epiphyseal line, influence of genetic and environmental factors on growth, sex hormones correlated with bone growth, puberty spurt and cartilage bone tissue.

RESULTS

Longitudinal bone growth is strongly controlled by growth hormone (GH), insulin-like growth factors (IGF-1), glucocorticoids, thyroid and sex hormones. GH can stimulate longitudinal bone growth by a local action on the growth plate, as well as being a fundamental regulator of postnatal bone growth and bone remodeling. This action of GH can be mediated by increasing the local production of IGF-I, which acts in a paracrine and autocrine manner to potentiate chondrogenesis. [17,18]

The sequence of biological events of puberty is caused by the activation of the hypothalamic-pituitary-adrenal-gonad axis. However, environmental factors can influence this hormonal chain.

The "double effect" hypothesis states that GH can recruit chondrocytes, induce a proliferative state, and stimulate local IGF-1 production [18,19,20]. High-dose, long-term glucocorticoids often lead to growth failure by inducing apoptosis of chondrocytes in the growth

plate, resulting in blockage and inhibition of longitudinal bone growth. In addition, they are widely used as anti-inflammatory drugs and immunosuppressants in children. For normal bone growth and maturation, thyroid hormone is necessary, which acts directly on the growth plate and indirectly increases the secretion of GH and IGF-1. [21,22]

During puberty, sex steroids, such as estrogen, induce a pubertal growth spurt, directly on the growth plate, and at low doses can accelerate growth in prepubertal boys and girls. However, in precocious puberty, early exposure to estrogen accelerates skeletal maturation, resulting in the fusion of the epiphyseal line and consequently a decrease in the individual's final height. In cases of estrogen absence, such as hypogonadism, fusion of the epiphyseal line occurs late and a final height higher than expected. [16,23,24,25,26]

Children and adolescents who practice sports or physical activity have better bone density than when compared to sedentary young people [27]. In addition, physical activity in the interval between 14 and 21 years was identified as the best phase for a positive response in the bone growth process. [28] The number of centimeters gained during pubertal development represents 16% of adult height. [28]

According to the Brazilian Society of Pediatrics (SBP), annual height gain during puberty goes from 8.0 to 10 cm/year in girls and 10 to 12 cm/year in boys. [29] During peak growth, which occurs around 12 and 14 years of age in females and males, respectively, the average gain during puberty is 25 cm in girls and 27 cm in boys. [28]

In addition to intrinsic factors, there are extrinsic factors that have great relevance in pubertal bone growth. Among the main ones are physical activity and food. With this, in addition to improving quality of life, these two elements combined can help and improve bone mineralization.

Adolescent nutrition needs to be healthy and full of nutrients for proper bone growth to occur. For girls, the average maximum consumption during puberty should be 2350 kcal, while for boys 3100 kcal, varying the amount that should be ingested depending on the stage of puberty in which it is, such as menarche, in females, and at the beginning of the spurt, in males [30]. Osteocalcin, a protein found in the bone matrix, is related to the increase in the serum concentration of IGF-I, calcitriol and phosphorus, which are very important for the spurt. So, it is necessary to ingest calcium due to the increase in calcitriol, which stimulates greater intestinal absorption of the mineral, and phosphorus due to greater reabsorption by the kidneys. [31, 32] Furthermore, proteins are necessary for the increase of the musculature, which is very important since when practicing physical activity the muscle contracts and increases the osteoblastic

activity of the bone in which this musculature is inserted [30,33]. Fats, in addition to being important for the onset of puberty, especially in girls, they provide the energy necessary for the event of the spurt. Its lack can cause short stature and pubertal delay and its excess can advance bone age. With the increase in anabolism, it is necessary to consume vitamins A, B, C, and D mainly due to bone mineralization and cellular metabolism. [30]

The practice of physical activities plays a crucial role during puberty. In addition to promoting more health for adolescents and avoiding a sedentary lifestyle, it favors bone growth. The intensity and frequency of exercise are determining factors in relation to gain of the young person's bone mass. Athletes in competitive sports have higher bone mineralization than those who engage in no or little physical activity [31, 33]. However, excess can cause delayed puberty compromising optimal bone mass [30].

An active life promotes an increase in the blood concentration of GH and IGF-I by contracting the muscles and their afferent nerve fibers that carry this information to the anterior pituitary gland that produces them. However, the exaggeration of sports activities, especially those of a competitive nature and with a high expenditure of energy, can cause the inhibition of this axis, as there is the release of cytokines that could inhibit it. In addition, it can cause the blocking of GnRH release that would impair the production of sex hormones and, consequently, affect bone growth [33].

DISCUSSION

The review highlights the influence of genetic and environmental factors on the growth process, highlighting the most relevant ones on growth. Mainly because they have long-term repercussions. Thus, the complex network of causality involved in the growth process of children and adolescents, such as biological and socioeconomic variables, among others. [1,2,5]

These variables should prioritize longitudinal studies identifying new risk factors, since changes in the epidemiological profile of nutritional problems impact on the possible implications for child growth and the current public health policy. In which the monitoring of the development of children and adolescents can result in a relevant contribution to future interventions with the objective of ensuring a better quality of life and health for this population. [6,40]

Accordingly, in addition to promoting a better quality of life for young people, physical activities are important for adequate bone mineralization to occur. However, just as its lack can be harmful, excessive exercise can disrupt the ideal pubescent height. Thus, along with an

adequate and balanced diet, moderate physical activity is extremely important for the bone growth of young people. [7,8,19]

Furthermore, most of our knowledge about the regulation of physiological epiphyseal fusion is not completely understood. In addition, most of the studies observed are based on studies using rodents. However, the mechanism of fusion of rodent growth plates does not occur at the end of puberty in normal physiological situations. Therefore, there is a need for further studies and models to be carried out to develop new strategies for the treatment of the main disorders of growth and its functioning.

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