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Parathyroid hormone-related protein and primary teeth eruption in stunting children

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Abstract

Stunting is a linear growth failure as an indicator of malnutrition status which is identified by comparing the height of children with normal height according to the same age and sex. Children are categorized as stunting if the child`s height is shorter than the average height of the same age and sex and has a standard deviation of below minus 2 according to the standard who. The cause of stunting is multifactorial, including disruption of hormone function, one of which is a parathyroid hormone. Parathyroid Hormone-related Protein (PTHrP) plays a role in the tooth-eruption process. This literature review aims to study the role of PTHrP on the eruption rate of primary teeth in stunting children. Malfunction of the parathyroid glands in stunted children can cause a deficiency of PTHrP levels. PTHrP and vitamin D play a role in the maintenance and affect calcium levels. Deficiency levels of PTHrP and vitamin d can lead to decreased absorption of calcium in the blood. Calcium deficiency in children can cause osteoclasts and osteoblasts to decrease, which can affect bone growth and tooth eruption patterns. In stunting children, the level of PTHrP will decrease so that tooth eruption will be inhibited.

Keywords: Good Health and Well - Being; Stunting; Parathyroid Hormone-Related Protein; Tooth Eruption

1. Introduction

Tooth eruption is a series of biological processes that happen in the jawbone. These processes are marked by the appearance of the incisal protrusions of the teeth, which push through the gums into the mouth and touch the opposing teeth. The first teeth come in between 4 and 9 months of age, but usually around 6 months. Several things, like genes, gender, race, nutrition, and where you live, can affect when your teeth come in. Nutrition is one of the most important things that affect when teeth come in. A balanced diet is one where you eat foods that have all the nutrients your teeth need to grow in [1]. Some research says that a child's nutritional status affects when their teeth come in, and that children with a higher nutritional status (> 2.0 SD) have faster tooth eruption. When a child has a good nutritional status (-2.0 SD to 2.0 SD), eruptions happen in a normal way, and sometimes eruptions are delayed. Having a low birth weight, being of a certain race, having been hurt, or having ankylosis can all cause this. Children with poor nutrition (-3.0 SD) and poor nutrition (-3.0 SD) had to wait longer for their teeth to come in [2,3].

Stunting, also called shortness, is a lack of linear growth and an indicator of poor nutrition. It is found by comparing a person's height to normal height standards for the same age and gender. It is caused by long-term nutritional problems, such as not getting enough food, especially in the first 1000 days of life. When a child's height is less than -2 SD from the WHO standard, this is called stunting [4]. Stunting is a condition in which a person doesn't grow as much as they should for their age. Stunting in children is caused by a cycle of malnutrition in the mother, which leads to babies being born with low birth weight, slow growth, and long-term malnutrition [5]. Stunting is caused by many things, including genetics, infectious diseases, WASH (Water, Sanitation, and Hygiene), nutritional deficiencies, hormonal factors, and

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risk factors that are affected by the birth history of low-weight babies (LBW), not breastfeeding, and not having enough complementary foods for breastfeeding (MPASI) [6].

One thing that can cause stunting is a problem with how hormones work. One of these problems is a drop in parathyroid hormone levels. Parathyroid hormone is a peptide hormone that is made by the four small glands on the back of the thyroid gland called parathyroid glands. Parathyroid Hormone is made up of PTHrP, which stands for Parathyroid Hormone Related Protein. PTHrP keeps the amount of calcium ions in the plasma steady, controls how much calcium is excreted by the kidneys, affects tubular hormone reabsorption from calcium and phosphorus secretion, speeds up calcium absorption in the intestine, and stimulates bone reabsorption when calcium intake goes down, which raises the amount of calcium in the blood. Along with vitamin D and calcitonin, PTHrP also works to control how calcium is used in the blood and bones [6,7].

Hypoparathyroidism in stunted children is induced by Protein Energy Malnutrition (PEM). WASH and EED can induce systemic inflammation, suppressing growth hormone release. Serum levels will drop, then saliva. Salivary PTHrP levels fell. Calcium levels drop. An integrated hormonal system governs calcium transport in the stomach, kidney, and bone. PTHrP and vitamin D are involved. A decrease in PTHrP and vitamin D can cause a decrease in calcitrol (1, 25-(OH) 2D3) and vitamin D receptors (VDR), which open absorption-related transient receptor potential channels (TRVP 5, 6). Blood calcium. This lowers calcium levels, reducing osteoblasts and osteoclasts and inhibiting primary tooth eruption. Inadequate nutrition and/or poor calcium absorption can also cause a calcium deficiency, which can lead to stunting, rickets, and osteomalacia [8].

Low PTHrP can affect toddlers' bone growth and tooth eruption. The researcher wants to study the relationship between Parathyroid Hormone related Protein (PTHrP) and primary tooth eruption in stunted children.

2. Literature Reviews

Stunting is caused by persistent malnutrition, especially in the first 1000 days of life. Stunting was diagnosed by comparing a person's height to a WHO normal height standard for the same age and sex. Genetic factors, viral diseases, WASH (Water, Sanitation, and Hygiene), dietary deficits, hormonal variables, and risk factors induce stunting. WASH causes stunting. WASH can cause EED in children, infectious diseases, and nutrient absorption issues. Long-term infections can affect children's bone growth [4–6].

Nutritional deficiencies can be in the form of macronutrient deficiencies or micronutrient deficiencies. Protein Energy Malnutrition (PEM) is caused by a lack of macronutrients, while bone growth problems are caused by a lack of micronutrients, especially vitamin D and calcium. Vitamin D helps keep calcium levels in the blood steady and increases calcium absorption in the intestine, which raises calcium levels in the blood. Bone growth problems can be caused by not getting enough vitamin D and calcium. This can stop osteoblasts and osteoclasts from doing their jobs [4,9].

Low-weight babies at birth (LBW), not drinking breast milk, and not getting enough complementary foods for breast milk are all things that can make a child short (MPASI). Hormone function problems, such as problems with the thyroid hormone or the parathyroid hormone, are another cause of short stature (PTH). Hypothyoid and hypoparathyroidism happen when a person is short for their age [4,6,9].

2.1. Parathyroid Hormone Related Protein in children with stunting.

Parathyroid hormone is secreted by four tiny glands on the rear of the oval-shaped thyroid gland. The parathyroid glands develop from the third and fourth brachial sacs. Third pharyngeal sac parathyroids become inferior parathyroids. Superior parathyroid glands arise in the fourth pharyngeal sac [10]. Parathyroid hormone has 3 exons and 2 introns on chromosome 11. Parathyroid primary cells express it mostly. PreproPTH is a 115-amino-acid PTH gene transcript. PreproPTH connects immature proteins through signal-recognition particles that bind it when it exits the ribosome and direct it to the endoplasmic reticulum, where pro-chain cleavage occurs. PTH matures into granules. PTH's 84 amino acids weigh 9,300 grams. Parathyroid secretory granules contain chromograin. Chromogranin contains 50% parathyroid protein. Hypocalcemia and hypercalcemia increase chromogenin. Chromogenin blocks PTH production and release [11,12].

A decrease in blood calcium levels stimulates parathyroid gland secretion. Blood calcium levels are maintained in very small amounts concurrently with calcitonin secretion. PTH is the most important hormone in regulating blood calcium levels. Meanwhile, calcitonin contributes to the formation of a complementary mechanism for its balance [11].

PTH works to raise serum calcium levels in three ways:

- When calcium intake is reduced, it stimulates bone reabsorption, resulting in an increase in calcium in the blood.
- It acts directly on the kidneys by increasing calcium ion reabsorption in the renal tubules and inhibiting phosphate ion reabsorption from the glomerular filtrate.
- Maintain calcium ion concentration in small intestine and synthesize calcitriol. Calcitriol stimulates calcium and phosphorus absorption in the intestine.

Furthermore, Parathyroid Hormone, along with vitamin D and calcitonin, regulates calcium metabolism in the blood and bones [10].

PTHrP is a parathyroid hormone excreted by the kidneys and bones. Vitamin D and PTHrP aid in the formation and maintenance of bones. PTHrP has the ability to influence calcium and phosphorus levels. PTHrP can raise blood calcium levels by increasing calcium release from the bones [13].

PEM causes parathyroid gland dysfunction in stunted children. Increased systemic inflammation in stunted children can suppress growth hormone secretion in serum. A drop in serum levels is followed by a drop in saliva levels. This can result in a drop in parathyroid hormone levels [10]. PTHrP levels in saliva can be affected by low PTH.

2.2. PTHrP (Parathyroid Hormone Related Protein) and tooth eruption.

PTH acts directly on bone to increase bone resorption, and it also stimulates the function of osteoblasts and osteoclasts in the long run. PTHrP is a component of PTH, which is excreted through the bones and kidneys. Vitamin D and PTHrP aid in the formation and maintenance of bones. PTHrP has the ability to influence calcium and phosphorus levels. PTHrP can raise blood calcium levels by increasing calcium release from bones [14].

PTHrP that has been secreted binds to the PTHrP receptor, which is then expressed by the dental follicle. The stellate epithelium also secretes interleukin 1a, which binds to the IL-1a receptor found in dental follicles. As a result, stimulated dental follicular cells secrete monocyte-recruitment factors like colony-stimulating factor-1, monocyte chemotactic protein-1, and vascular endothelial growth factor. These factors then cause monocytes to migrate from the richly vascularized dental follicle region to the coronal region [15].

Periodontal precursor cells (DFCs) are found in the dental follicle. DFCs isolated from the bone differentiated into periodontal ligament cells, alveolar osteoblasts, and cementoblasts. PTHrP is an extracellular protein that is required for endochondral bone growth, bone precursor cell differentiation, and craniofacial tissue growth. PTHrP is involved in tooth eruption [16].

2.3. Stunting children's tooth eruption

Several factors can influence the eruption of mandibular teeth, including heredity (genetic), race, nutrition, and the presence of systemic diseases. Nutrients are required for bone and tooth growth. Maternal nutritional intake during pregnancy has a direct impact on fetal tooth development. As a result, pregnant women's nutritional status will determine their children's dental and oral health. Maternal and child nutrition in the first three years of life is critical because primary teeth begin to develop during the fourth month of pregnancy and continue until the deciduous teeth erupt at the age of three years [2,17].

According to some research, the pattern of tooth eruption based on nutritional status with BW/U indicators reveals that children with higher nutritional status (> 2.0 SD) have quicker tooth eruption. Children with good nutritional status (-2.0 SD to 2.0 SD) have a normal eruption pattern, with some delays. This is caused by a number of circumstances, including low birth weight, ethnicity (race), trauma, and ankylosis. Children with poor nutritional status (-3.0 SD to -2.0 SD) and poor nutrition (-3.0 SD) have delayed tooth eruption [2,3,18].

Toddler stunting is caused not just by an uneven nutritional intake, but also by the state of a toddler's teeth, which might impede with the chewing process. Adequate nutrition is also essential in the eruption of teeth in toddlers, therefore stunted toddlers may experience delays in tooth eruption [3].

Nutritional deficits arise in stunted children in the form of macronutrient and micronutrient deficiencies. Protein Energy Malnutrition results from Macronutrient deficit in stunted children (PEM). PEM can impair the salivary glands' ability to perform blood capillary ultrafiltration, resulting in lower component values in stunted children's saliva than

in normal children. Meanwhile, micronutrient insufficiency impairs bone formation, particularly calcium and vitamin D deficiency, resulting in hypocalcemia due to decreased calcium intake [8,19].

The interaction of osteoblasts, osteoclasts, and dental follicles causes the eruption process (DF). Tooth growth activity is caused by the interaction of growth hormones on coronal dental follicles such as (GH, IGF-1, EGF, IL-1). These hormones stimulate the activity of surrounding cells such as endothelial cells, fibroblasts, myoblasts, and osteoblasts to secrete CSF-1 and cause monocyte migration and osteoclast activation with other molecules such as CSF-1, MCP 1, NF-kB, PTHrP, RANK [20]. Growth hormone disruptions occur in stunted children, causing osteoclast activity to be interrupted and tooth eruption to be impeded.

2.4. PTHrP and stunted children's teeth eruption.

Tooth eruptions in stunted children were typically delayed. This was because of the stunting condition, which was accompanied by PEM. PEM impairs parathyroid gland function, resulting in a reduction in parathyroid hormone levels. WASH and EED can cause systemic inflammation, which can reduce serum growth hormone production. A drop in serum levels is followed by a drop in saliva levels. As a result, salivary PTHrP levels fell. Calcium levels will fall as a result of this. Calcium homeostasis is primarily controlled by an integrated hormonal system that regulates calcium transport in the stomach, kidney, and bone. PTHrP and vitamin D are involved in this mechanism. A drop in PTHrP levels combined with a drop in vitamin D can result in a drop in calcitrol (1,25-OH)2D3 and a drop in vitamin D receptors (VDR), which play a role in opening transient receptor potential channels (TRVP). 5,6), which aids in calcium absorption in the blood. This produces a drop in calcium levels, which inhibits the formation of osteoblasts and osteoclasts and the eruption of primary teeth [8].

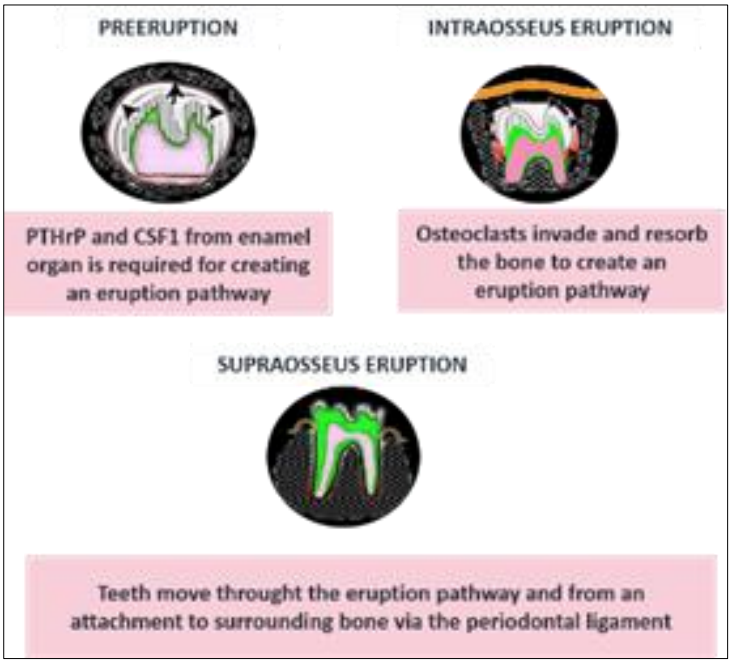

Figure 1 The role of Parathyroid Hormone Related Protein (PTHrP) in primary tooth eruption

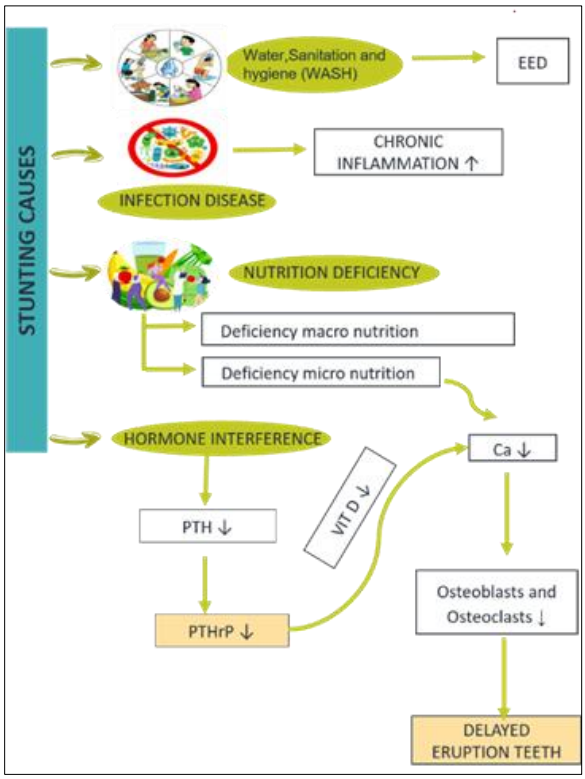

Figure 2 PTHrP, tooth eruption, and stunting

3. Conclusion

In stunted children, low PTHrP levels affect deciduous tooth eruption. A decrease in PTHrP levels and vitamin D causes a delay in the eruption of primary teeth by reducing blood calcium, osteoblasts, and osteoclasts.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this document.

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