Review Article

Indian Journal of Diabetes and Endocrinology
Volume 5 Number 1, January - June 2023

Hypoparathyroidism and its Management: A Systematic Review

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How to cite this article:
Simrat Kaur, S.P. Subashini, Pooja Jain/Hypoparathyroidism and its Management: A Systematic Review/Indian Journal of Diabetes and Endocrinology, 2023;5(1):13–17.

Abstract

Hypoparathyroidism is a combination of symptoms that occur due to inadequate parathyroid hormone (PTH) production. It is very rare and most commonly occurs because of damage to or removal of parathyroid glands during parathyroid or thyroid surgery. Less commonly, it can be caused by a defect present at birth (congenital) in which a person is born without parathyroid glands. Decreased secretion or activity of parathyroid hormone leads to decreased blood levels of calcium (hypocalcemia) and increased levels of blood phosphorus (hyperphosphatemia).

Keywords: Endocrine; Parathyroid; Hypoparathyroidism; Glands; Hypocalcemia.

INTRODUCTION

The most common cause of hypoparathyroidism is inadequate secretion of parathoromone after interruption of the blood supply or surgical removal of parathyroid gland tissue *during thyroidectomy, parathyroidectomy or radical neck dissection***.**These small glands are easily overlooked and can be removed inadvertently during thyroid surgery. Atrophy of the parathyroid gland of unknown cause is a less common cause of hypoparathyroidism. Deficiency of parathoromone results in increased blood phosphate **(***hyperphosphatemia***)** and decreased blood calcium **(***hypocalcemia***)** levels. In the absence of parathoromone there is decreased intestinal absorption of dietary calcium and decreased resorption of calcium and from bone and through the renal tubules. Decreased renal excretion of phosphate causes hypophosphaturia and low serum calcium levels result in hypocalciuria.

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Received on: 15.03.2023

Accepted on: 10.04.2023

Types and Causes of Hypoparathyroidism

There are two types of hypoparathyroidism:

- Deficient parathyroid hormone (PTH) secretion
- Inability of the kidneys and bones to respond to PTH

Deficient Parathyroid Hormone Secretion

This type of hypoparathyroidism is the easiest to understand. A patient with this condition simply has too little (or a complete absence of) parathyroid tissue; therefore, inadequate PTH is produced.

There are two major causes of this problem

Cause 1: Hypoparathyroidism Following Thyroid or Parathyroid Surgery

The first and by far most common cause of

inadequate parathyroid hormone production is the accidental removal of parathyroid glands during thyroid surgery.

Although the vast majority of thyroid operations are not associated with hypoparathyroidism, this complication can occur in about 1% to 3% of cases following a total thyroidectomy (the removal of the entire thyroid).

Because of the close relationship that the thyroid and parathyroid have to one another (including sharing the same blood supply), the parathyroid glands can be injured or removed accidentally when the much larger thyroid is removed. This is a well known but uncommon complication of thyroid surgery and is one of the primary dangers of thyroid surgery.

Many patients who have a successful thyroid operation can have a transient inadequate secretion of PTH for several days following surgery on the thyroid. It is common for surgeons to give their thyroid patients calcium pills for a few days after surgery to prevent any symptoms from the transient lack of PTH.

The second operation associated with post -operative hypoparathyroidism is parathyroid surgery, or "parathyroidectomy." Parathyroid surgery is performed for patients who have overactive parathyroid glands, which causes a condition called hyperparathyroidism.

Since hyperparathyroidism is typically caused by one or more parathyroid tumors, surgery for hyperparathyroidism is aimed at removing the parathyroid tumor(s) and leaving behind the normal parathyroid glands.

The goal of parathyroid surgery is to remove the parathyroid glands that are overproducing PTH. But occasionally, too much parathyroid tissue is removed during the operation. Like thyroid surgery, the incidence of this complication can be related to the experience of the surgeon and is why endocrinologists typically recommend surgeons with the most experience. Surgeons with little experience can have as many as 5% of their patients develop permanent hypoparathyroidism, while surgeons performing more than 100 parathyroid operations per year typically have hypoparathyroidism complications very rarely.

Cause 2: Idiopathic Hypoparathyroidism

Deficient PTH secretion without a defined cause is called idiopathic hypoparathyroidism. This condition is extremely rare and can be congenital or acquired later in life.

Congenital hypoparathyroidism. People in this category are born without parathyroid tissues. Most patients with congenital hypoparathyroidism have no family history of the condition. Those who do may have any one of several congenital causes. The inherited forms tend to arise from abnormal genes that may encode abnormal forms of PTH or its receptor, prevent normal conduction of cell signals from the PTH receptor to the nucleus, or prevent normal gland development before birth.

Additionally, if a woman with overactive parathyroid glands and high calcium levels (hyperparathyroidism) becomes pregnant, the excess calcium can enter the fetus and suppress the baby's parathyroid gland development. These babies are at risk of being born with underdeveloped parathyroid glands. This is why it recommended that pregnant women with high blood calcium levels have their parathyroid operation before the middle of the second trimester of pregnancy, to decrease the chance of the child being born with poorly formed parathyroid glands. Usually this will not result in permanent parathyroid gland dysfunction in the child.

Hypoparathyroidism with onset during the first few months of life can be permanent or temporary. The cause is usually unknown if spontaneous resolution occurs. If it does not, it will usually manifest by 24 months of age.

Acquired hypoparathyroidism: The acquired form of this disease typically arises because the immune system has developed antibodies against parathyroid tissues in an attempt to reject what it sees as a foreign tissue (autoimmunity). This condition can affect the parathyroid glands in isolation or can be part of a syndrome that involves many organs.

An antibody that binds to the calcium sensor in the parathyroid gland has been discovered in the blood of patients with autoimmune hypoparathyroidism. It has been proposed that such binding "tricks" the parathyroid gland into believing that the blood level of calcium is high. Responding to this signal, the parathyroid stops making PTH.

Resistance to Parathyroid Hormone (Pseudo-Hypoparathyroidism)

Less commonly, hypocalcemia (too low calcium levels) and hyperphosphatemia (too high phosphorus levels) are caused not by inadequate PTH production but by resistance to this hormone in the body. This is known as pseudo-hypoparathyroidism because it looks like

hypoparathyroidism, but inadequate PTH isn't the issue. People with this condition produce PTH, but their bones and kidneys do not respond to it. Even if PTH is given to them in their veins, they do not respond to it.

CLINICAL MANIFESTATIONS

- Hypocalcemia causes irritability of the neuromuscular system and contributes to the chief symptoms of hypoparathyroidism tetany.
- Tetany is a general muscle hypertonia, with tremor and spasmodic or uncoordinated contractions occurring with or without efforts to make voluntary movements.
- Symptoms of latent tetany are numbness, tingling and cramps in the extremities and the patient complains of stiffness in the hands and feet.
- In overt tetany, the signs include bronchospasm, laryngeal spasm, carpopedal spasm (flexion of the elbows and wrists and extension of the carpophalagengal joints and dorsiflexion of the feet), dysphagia, photophobia, cardiac dysrhythmia and seizures.
- Other symptoms include anxiety, irritability, depression and even delirium.

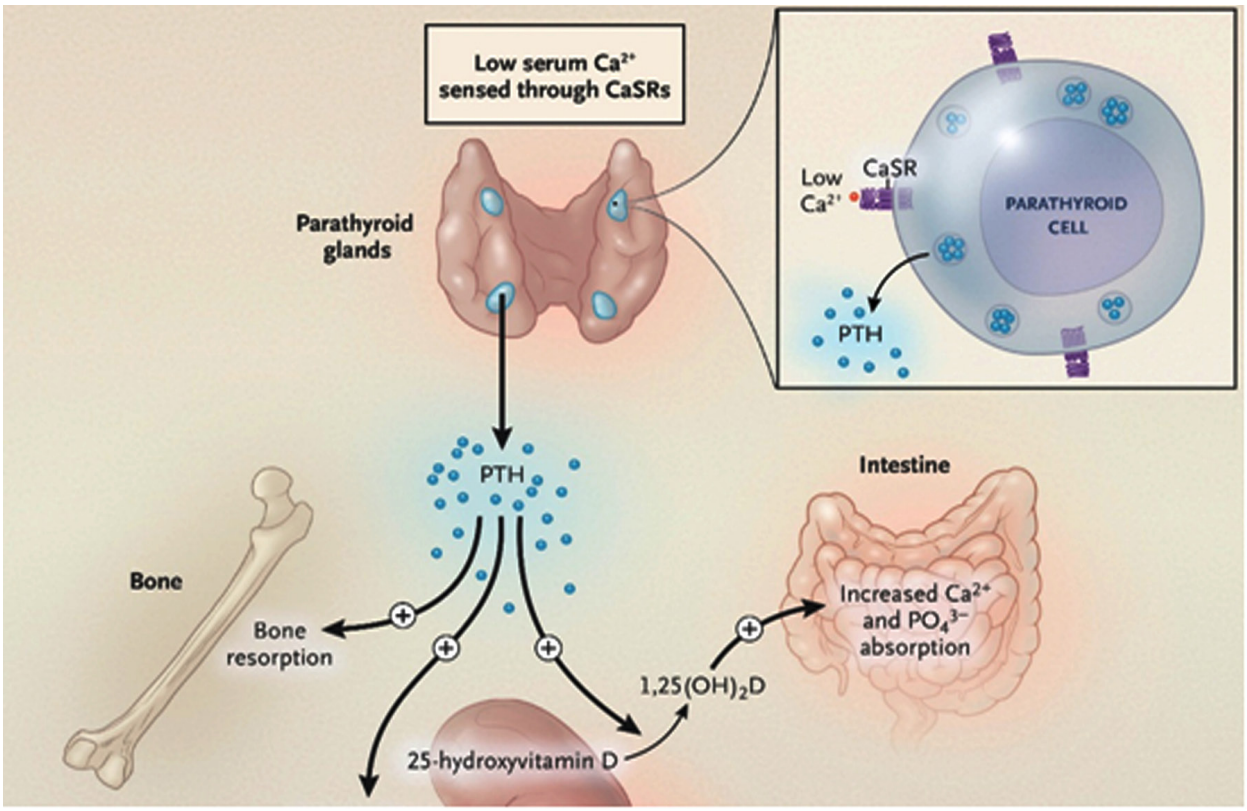

Fig. 1: Showing mechanism of release of parathoromone

- ECG changes and hypotension also may occur.

ASSESSMENT & DIAGNOTIC FINDINGS

A positive Trousseau's sign or a positive Chvostek's sign suggests latent tetany. Trousseau's sign is positive when carpopedal spasm is induced by occluding the blood flow to the arm for 3 minutes with a blood pressure cuff. Chvostek's sign is positive when a sharp tapping over the facial nerve just in front of the parotid gland and anterior to the ear causes spasm or twitching of the mouth, nose and eye. The diagnosis of hypoparathyroidism often is difficult because of the vague symptoms such as aches, and pains. Therefore, lab studies are especially helpful. Tetany develops at serum calcium levels of 5-6mg/dl (1.2-1.5mmol/L) or

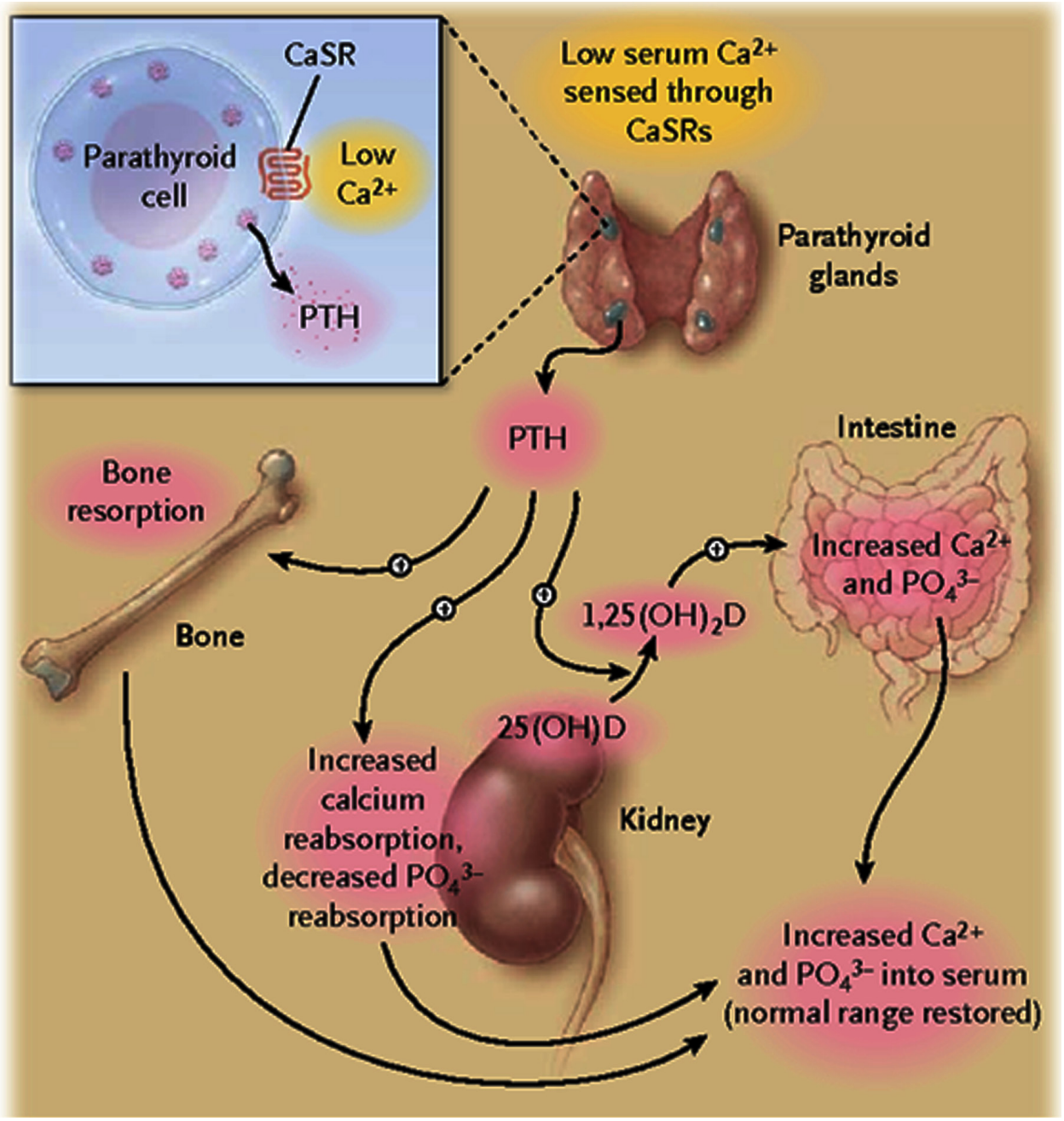

Fig. 2: Showing control of mineral metabolism by parathyroid hormone

lower. Serum phosphate levels are increased and x-rays of bone show increased density.

MEDICAL MANAGEMENT

The goal of the therapy is to increase the serum calcium levels to 9 to 10 mg/dl (2.2 to 2.5 mmol/L) and to eliminate the symptoms of hypoparathyroidism and hypocalcemia. When hypocalcemia and tetany occur after a thyroidectomy the immediate treatment is administration of IV calcium gluconate. If this does not decrease neuromuscular irritability and seizure activity immediately, sedative agents such as phenobarbital may be administered. Parenteral parathoromone can be administered to treat acute hypoparathyroidism with tetany. However, the high incidence of allergic reactions to injections of parathoromone limits its use to acute episodes of hypocalcemia. The patient receiving parathoromone is monitored closely for allergic reactions and changes in serum calcium

levels. Because of neuromuscular irritability, the patient with hypocalcemia and tetany requires an environment that is free of noises, drafts, bright lights or sudden movement. Tracheostomy or mechanical ventilation may become necessary along with bronchodilating medications, if patient develops respiratory distress. Therapy for chronic hypoparathyroidism is determined after serum calcium levels are obtained. A diet high in calcium and low in phosphorus is prescribed. Although milk, milk products and egg yolk are high in calcium, they are restricted because they also contain high levels of phosphorous. Spinach also is avoided because it contains oxalate which would form insoluble calcium substances. Oral tablets of calcium salts such as calcium gluconate may be used to supplement the diet. Aluminum hydroxide gel or aluminum carbonate also administered after meals to bind phosphate and promote its excretion through the GI tract. Variable dosages of a Vitamin D preparation dihydrotachysterol, ergocalciferol (vitamin D) or cholecalciferol (Vitamin D) are usually required and enhance calcium absorption from the GI tract.

CONCLUSION

Hypoparathyroidism is decreased function of the parathyroid glands with underproduction of parathyroid hormone (PTH). This can lead to low levels of calcium in the blood, often causing cramping and twitching of muscles or tetany (involuntary muscle contraction), and several other symptoms. It is a very rare disease. The condition can be inherited, but it is also encountered after thyroid or parathyroid gland surgery, and it can be caused by immune system related damage as well as a number of rarer causes. The diagnosis is made with blood tests, and other investigations such as genetic testing depending on the results. The primary treatment of hypoparathyroidism is calcium and vitamin D supplementation. Calcium replacement or vitamin D can ameliorate the symptoms but can increase the risk of kidney stones and chronic kidney disease. Additionally, medications such as recombinant human parathyroid hormone or teriparatide may be given by injection to replace the missing hormone.

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