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Research Article

A REVIEW ON RARE ENDOCRINE DISORDER –HYPOPARATHYROIDISM

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A R T I C L E I N F O

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A B S T R A C T

Hypoparathyroidism is arare endocrine disorder characterized by low calcium and high phosphate levels. Hypoparathyroidism has been classified as an orphan disease in the United States and by the European Commission. Many clinicians have limited experience or expertise in treating this specialized disorder. Until recently the only treatment options available for chronic hypoparathyroidism included calcium supplements, activated vitamin D and thiazide diuretics. In the last few years recombinant human (rh) PTH has been approved for the treatment of hypoparathyroidism and is a useful therapeutic option for patients with suboptimal calcium levels inspite of high dose calcium and activated vitamin D.Based upon current evidence, a set of guidelinesis proposed to help clinicians to diagnose, evaluate, and manage this disorder. This document should be helpful to all who are or will become interested in hypoparathyroidism.It not only provides a summary of our current knowledge of hypoparathyroidism but also places recent advances in its management into a context that should enhance future advances in our understanding of this disorder.

INTRODUCTION

Parathyroid Hormone

Hypoparathyroidism is the result of decreased secretions of Parathyroid hormone known as Parathormone. Parathormone is secreted by the epithelial cells of Parathyroid glands. There are four parathyroid glands situated as two in each Thyroid gland. This parathormone regulates the levels of calcium, magnesium and phosphates in to the blood. Parathormone also acts on the kidneys, enhances the calcium reabsorption in the renal tubules and increases the loss of phosphate ions through urine. Parathormone promotes the formation of Calcitriol hormone. Calcitriol, also known as 1, 25-dihydroxyvitamin D3 increases the rate of calcium, magnesium and phosphate absorption from the gastrointestinal tract into the blood.

Types of Hypoparathyroidism

Hypoparathyroidism

Based on the etiology of the disease hypoparathyroidism can be classified in to following types.

Post-surgical Hypoparathyroidism

It is the most common type of hypoparathyroidism in adults. Post-surgical hypoparathyroidism is usually due to unavoidable removal of damage to the parathyroid gland and or their blood supply. The parathyroid gland function restarts in most of the patients who have undergone neck surgery.

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Hence at least 6 months of persistence of features of hypoparathyroidism is regulated to conform the hypoparathyroidism. Some patient's remains asymptomatic and their biochemical abnormalities will be found only in routine investigation. Post-operative hypoparathyroidism occurs in mostly in patients who have undergone more than one neck surgery like surgery for sub sterna goitre, head or neck malignancies.

Immune System Hypoparathyroidism

It is the most common type of para thyroidism in adult .
Blizzard etal announced that parathyroid organ antibodies in 35% of 75 patients with idiopathic hypoparathyroidism,26% of 92 patients with idiopathic addition ailment,12% of 49 patients with hashimato thyroiditis and 6% of 245 ordinary controls.
Li et al announced that sera from 5 of 25 patients with immune system hyperparathyroidism, idiopathic hypoparathyroidism or aps type1had immune reactivity with the extra cellular calcium detecting receptor.

Auto immune disease causes the hormonal deficiencies of one or more of the endocrine glands and this reason constitutes the second most common etiology.

Magnesium levels can significantly influences the parathormone secretion and action. Hypermagnesemia supresses the PTH release levels. Severe hypomagnesemia also impairs PTH secretion in patients with low serum calcium and PTH levels.Parathyroid gland can also be destroyed by deposits of iron and copper or by tumour metastasis which results in hypoparathyroidism.

Hereditary Hypoparathyroidism

Genetic disorders are infrequent causes of hypoparathyroidism. Hypoparathyroidism results due to disorders like polyglandular deficiency, Digeorge's syndrome, Bartter's syndrome.

Hypocalcaemia also occurs due to mutations in the genes encoding the caSR (Para thyroid calcium sensing receptor) and g-protein subunit which results in the autosomal dominant hypocalcaemia (ADH).The patients having ADH may have normal PTH levels but hypocalcaemia persists representing abnormally sensitive ca SR.

Germ line mutation therapy will be useful in treating the disease.

Pathophysiology

Generally one normal parathyroid gland is enough to maintain the normal calcium levels in the body. Bone, kidney, intestinal mucosa are the three principal organs that are involved in the regulation of calcium levels. In a normal individual, PTHstimulates bone resorption and the release of calcium ions into the circulation. PTH promotes calcium reabsorption in the kidney. PTH also converts the 25-hydroxy vitamin D3 into active form of vitamin D.vitamin D increases the intestinal absorption of dietary calcium as well as renal absorption of filtered calcium.

Calcium and Phosphate Homeostasis

Hypocalcaemia, hyper phosphatemia are the main biochemical abnormalities of hypoparathyroidism. Hypocalcaemia gives rise most of the neuro muscular symptoms and signs of hypoparathyroidism .hyper phosphatemia cause the abnormal mineralisation in soft tissues. There is negative sigmoidal relationship between serum calcium concentration and Para thromone secretion. Serum phosphate does not directly regulatePTH secretion.in hypo parathyroidism patients, renal tubular reabsorption of calcium is reduced and renal tubular re absorption of phosphate is increased which leads to hypocalcaemia, hyper phosphatemia respectively. Magnesium also plays an important role in controlling PTH secretion and action .Increased Mglevels decreases the PTH synthesis and secretion by activating the caSR. In contrast severe hypomagnesaemia also decreases the level of PTH secretion even though mild hypomagnesaemia increases the PTH synthesis.this is due to intracellular magnesium depletion on the α–subunit of G-protein associated with caSR.

General Signs and Symptoms

The general abnormalities of hypo parathyroidism are hypocalcaemia, hyper phosphatemia.Hypocalcaemia can alter neurological, cardiac, cognitive functions. During the treatment of hypocalcaemia with calcium supplements might result in the consequences like renal stones. The following are the general signs and symptoms

Organ system	Manifestations ,signs, symptoms
Neuromuscular	Fatigue Generalized muscle weakness Muscle cramping Tetany Laryngospasm and stridor Bronchospasm and wheezing
Cardiovascular	Congestive heart failure Chest pain Arrhythmias Heart block
Dermatological	Alopecia Scaling of the skin Deformities of the nails
Gastrointestinal	Constipation Abdominal cramps Steatorrhea
Dental	Cemental hyperplasia Hypoplastic enamel Short rounded roots Hypodontia and delay or lack of tooth eruption
Neurological or psychiatric	Paraesthesia and numbness especially around the mouth and in the fingers and toes Seizures Poor memory and concentration Parkinsonism and chorea Depression Anxiety Personality disturbances

Current Management of Hypoparathyroidism: Approaches and Associated Complications

Intense Management

In hypoparathyroidism, hypocalcaemia requires intravenous administration of calcium. Frequent monitoring of serum calcium levels is important to maintain the limit of intense administration of calcium. Generally intravenous administration of calcium gluconate is recommended.10 ml of 10% calcium gluconate diluted in 100 ml 5%dextrose is injected intravenously for more than 5-10 minutes.5mg/kg of natural calcium around 10 ampoules diluted in 1L of Dextrose at 50ml/hr. this will raise the serum calcium by roughly 2mg/dl.

Ceaseless Management

The drugs that are administered for the treatment of hypo parathyroidism must keep the following with in normal range.A) Serum calcium level, B) Serum phosphorous level c) 24 hr.calciumdischarge. For intermittent administration current treatment options like oral calcium, nutrient D analogs and thiazide diuretics are used.

Calcium

Calcium carbonate and calcium citrate are the prescribed calcium supplements.Achlorhydria patients are recommended to use these calcium supplements along with protein rich diet.The dose of 1g/day to 9g/day is recommended among different patients.

Calcitriol is a vitD metabolite increases the serum calcium level by increasing the productivity of intestinal calcium absorption. Calcitriol is managed over a wide range (0.25-2.0µg/dl) can build serum calcium.Along with the calcitriol, nutrient D2 ergocalciferolor nutrient D3 cholecalciferol are frequently utilised.

Thiazide Diuretics

Thiazide diuretics like chlorthiazide, hydrochlorthiazide, polythiazide, chlorthalidone lowers urinary calcium discharge .These drugs helps in maintaining the calcium levels in normal range in hypoparathyroidism patients.

Confinements of Currently ApprovedTreatment Options

Hypercalcemia and Hypercalciuria

Higher doses of calcium and vitaminD supplement leads to hyper calcaemia in few patients. Treatment with vitaminD sterols leads to vitaminD poisonous effects such as hypocalcaemia hyper calciuria, and hypophosphatemia. calcitriol has short half-life hence hyper calcemia is inverted to normal.

Hyperphosphatemia

Vitamin D metabolites cause hyper phosphataemia by increasing the intestinal absorption of phosphate ions. Anyway, this can be managed by decreasing the dietary phosphate intake.

Hypokalaemia and Additionally Hyponatremia

Thiazide diuretics are identified with the danger of creating hypokalaemia or potentially hyponatremia. A low-sodium diet is a successful subordinate.

Diet

Rich in Calcium: This includes dairy products, green leafy vegetables, broccoli and foods with added calcium, such as some orange juice and breakfast cereals.

Low in Phosphorus: This means avoiding carbonated soft drinks, which contain phosphorus in the form of phosphoric acid, and limiting meats, hard cheeses and whole grains.

Monitoring

Your doctor will regularly check your blood to monitor levels of calcium and phosphorus. Initially, these tests will probably be weekly to monthly. Eventually, you'll need blood tests just twice a year.

Because hypoparathyroidism is usually a long-lasting (chronic) disorder, treatment generally is lifelong, as are regular blood tests to determine whether calcium in particular is at normallevels. Your doctor will adjust your dose of supplemental calcium if your blood-calcium levels rise or fall.

Drug	Mechanism of action	Side effects
Oral calcium carbonate tablets	Oral calcium supplements can increase calcium levels in your blood.	At high doses, calcium supplements can cause gastrointestinalside effects, such as constipation, in some people.
Vitamin D	High doses of vitamin D, generally in the form of calcitriol, can help your body to absorb calciumand eliminate phosphorus	Dry mouth, increased thirst; metallic taste in your mouth
Parathyroid hormone (Natpara)	The Food and Drug Administrationhas approved this once-daily injection for treatment of low blood calcium due tohypoparathyroidism.	The potential risk of bone cancer (osteosarcoma)
Thiazide Diuretics Ex: chlorothiazide, hydrochlorothiazide, polythiazide, and chlorthalidone	By upgrading distal tubule calcium reabsorption, thiazide diuretics lessen urinary calcium discharge	Confinements of thiazide diuretics are identified with the danger of creating hypokalaemia or potentially hyponatremia.
Intravenous infusion of Calcium	If you need immediate symptom relief, your doctor might recommend hospitalization so that you can receive calcium by intravenous (IV) infusion, as well as oral calcium tablets.	----------

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