



Calcium disturbances in thyroid and parathyroid dysfunctions

Samaneh Khodadadi*

Abstract

Primary hyperparathyroidism (PHPT) results from over secretion of parathyroid hormone (PTH) from parathyroid gland(s) and presents with hypercalcemia. The disorder includes various abnormalities that occur in the rest of the body such as loss of calcium from bones and in some cases neuralgic manifestations. Statistical analysis estimated that 0.3% of the general populations are affected by this third most common endocrine disorder. Most people with PHPT have no family history of the disorder, but some cases can be linked to an inherited problem. The aim of this investigation was to understand the mechanism of neurological disorder result from PHPT.

Keywords: Primary hyperparathyroidism, Neurologic manifestation, Calcium, Multiple endocrine neoplasia

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Introduction

Primary hyperparathyroidism (PHPT) is as a disorder of the parathyroid glands. "Primary" means this disorder originates in the parathyroid glands. In PHPT, one or more of the parathyroid glands are overactive. Thus, the gland releases too much parathyroid hormone (PTH). PTH is the main regulator of calcium homeostasis in the body. PHPT results from incorrect production of PTH from parathyroid gland(s) and presents with hypercalcemia. According to statistical estimations 0.3% of the general populations have been affected by this third most common endocrine disorder. PHPT typically occurs as sporadic parathyroid adenomas or carcinomas but can also be detected in association with multiple endocrine neoplasia and in scarce genetic syndromes and metabolic diseases (1).

Materials and Methods

For this mini-review, we used a diversity of sources by searching through PubMed/Medline, Scopus, EMBASE, EBSCO and directory of open access journals (DOAJ). The search was conducted, using combination of the following key words and or their equivalents; primary hyperparathyroidism, thyrotoxicosis, hyperthyroidism, neurologic manifestation, calcium and multiple endocrine neoplasia. Titles and abstracts of articles were investigated of review articles, clinical trials, cohort studies, case-control studies, and reports related to the intended topic.

Primary hyperparathyroidism

PHPT is not uncommon medical condition in general

population. In addition to the physical symptoms associated with hyperparathyroidism, a heterogeneous group of psychiatric symptoms and syndromes may occur (1,2).

Thyroid and parathyroid disorders have reversible neurologic signs and affecting nervous system, musculature, and mental function. Individuals with thyrotoxicosis may have myopathy, spasticity, seizures, and multiple psychiatric symptoms. The insufficiency of thyroid hormones also causes muscle weakness and may be accompanied by reversible muscle hypertrophy or movement disorders. The chronic hypercalcemia which develops secondary to hyperparathyroidism produces various psychiatric and cognitive symptoms, and also a reversible myopathy. Calcium deficiency leads to neuromuscular irritability, paresthesia, and tetany. Psychiatric disorders are also common in this disorder (3).

Pathophysiology

The dominant effects of hyperthyroidism are most declared in development. Studies on the rat brain mitochondria indicate minimal effects. Measurements from rats suggest well-preserved brain iodothyronine homeostasis in spite of high thyroid hormone levels. Brain T4, T3 concentrations and brain T3 production and turnover rates do not change meaningfully cerebral circulation and oxygen consumption, the levels of glutamate dehydrogenase and pyruvate dehydrogenase activity in the brain are decreased. Beta-adrenergic binding sites in the cerebral cortex are increased and gamma-aminobutyric acid (GABA) binding sites are diminished. Brain levels of serotonin, 5-hydroxyindoleacetic acid, and substance P are changed.

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Nickan Research Institute, Isfahan, Iran

*Corresponding Author: Samaneh Khodadadi; Email: sama_khodadadi@yahoo.com

■ Implication for health policy/practice/research/medical education

Primary hyperparathyroidism (PHPT) results from over secretion of parathyroid hormone (PTH) from parathyroid gland(s) and presents with hypercalcemia. The disorder includes various abnormalities in the rest of the body such as loss of calcium from bones and in some cases neuralgic manifestations.

Native pain sensitivity and proportion of opiate receptors are increased. Thyroid hormones affect myelination, therefore elevated levels result to oxidative injury to the myelin membrane and/or the oligodendroglial cells (4).

In hypothyroidism, muscle contraction and relaxation are reduced while duration is prolonged. The amount of myosin ATPase decreases. Slowing of delivery and re-accumulation of calcium in the endoplasmic reticulum may decrease relaxation. In peripheral nerves, segmental demyelination has been detected with diminished nerve conduction velocities. Patients develop polyneuropathy with loss of reflexes and weakness. Reductions in vibration, joint-position, and touch-pressure sensations also are seen. Thyroid insufficiency can damage hippocampal neurogenesis, differentiation, and maturation in developmental and adult rat brains, proposing a similar mechanism in humans. Hypothyroidism alters synaptic transmission and plasticity in area CA1 of the hippocampus, which, finally, may be the mechanism which results to impairment in learning and memory (2-4).

Role of calcium homeostasis

Accurate regulation of extra and intracellular calcium is necessary for natural physiological activities such as cell signaling, neural function, muscular function (including cardiac contractility), hormone release and regulation, and bone metabolism. PTH with effects on kidney can raise receptor mediated tubular reabsorption of calcium, stimulates release of skeletal calcium stores, upregulates 1- α -hydroxylase leading to increased 1, 25-dihydroxy-vitamin D creation and enhanced calcium reabsorption from the gastrointestinal tract.

Significant to calcium regulation is the calcium-sensing receptor (CaSR) found primarily in the main cells of the parathyroid glands. The CaSR reacts to the level of ionized calcium in the extracellular space and can upregulate or downregulate the exertion of PTH. Latest evidence indicates that the CaSR plays an independent role than PTH in the renal tubules to stimulate calcium secretion in the face of hypercalcemia (5).

All signs of hypercalcemia such as lethargy, weakness, polyuria, thirst, constipation, and gastrointestinal symptoms are seen only in the severe forms of disease. Slight hypercalcemia is often identified during a regular biochemical assessment when patients may not have any symptom, while hypercalcemic patients have considerably more psychiatric signs than controls. Hyper and hypocalcemia may exhibit with psychiatric symptoms that can be insidious and may simulate a bipolar or schizophreniform

disorder (1,2,5). Diagnosis is difficult because there may be no other associated symptoms or signs. Additionally even the biochemical alterations of calcium may be mild (2).

Neurologic manifestations of hyperthyroidism

Common systemic characteristics of hyperthyroidism involve palpitations, heat intolerance, and weight loss. A number of central and peripheral nervous system appearances could also happen in hyperthyroidism patients. In many situations, the neurologic symptoms are associated with systemic features of the disease, but these can be the reporting sign in some patients (6). These contain anxiety, cognitive difficulties, psychotic symptoms, and even major depression. As with hypothyroidism, therapy of underlying endocrine disorder commonly results to resolution of psychiatric symptoms, even though more psychotropic intervention is required rarely (1,4).

In 80% of patients with hyperthyroidism, neuromuscular complaints have been reported and more than 50% have marked muscle weakness. Women in the mean age of fifth decade predominate at 3:1 to 4:1. Weakness is primarily proximal and is generally out of proportion to the amount of worsening process in muscle; distal weakness develops later and is less acute than the proximal myopathy. Myalgia, fatigue, and exercise intolerance are common. Breathlessness is common, and respiratory insufficiency, requiring ventilatory support may happen. Bulbar muscles and the esophagus may be implicated, however sphincters are spared (2-5).

Seizure is one of common neural consequence of hyper and hypocalcemia. Intracranial calcifications are common and are symmetrical, involving the basal ganglia and dentate nuclei of the cerebellum. The calcium deposition is outside the neurons and thus despite of the serious abnormalities on neuroimaging, neurological signs may be few. Movement disorders of different kinds like the chorea, athetosis, and dystonia may be seen in such patients and at times, they can be the leading consequences of the parathyroid disease. Sometimes, the patients present with rise of intracranial pressure with papilledema without localizing signs, like benign intracranial hypertension. Hypocalcemia and hypomagnesemia produce hyper-excitability of nerve fibers with spontaneous and repetitive discharges in them. Consequently, patients have perioral and distal numbness and paresthesia, carpopedal spasm and diffuse muscle cramps (3-7).

Psychiatric symptoms may ensue in up to 23% of individuals with PHPT, of which 78% have depression and anxiety. Other manifestations found are irritability, somatization, fatigue, memory loss, difficulty concentrating, mood and sleep disorders. The prevalence of these abnormalities is not well-defined due to the absence of rigorous assessment of these symptoms in most studies, a small number of studies, and wide variation in the instruments used to consider the psycho-cognitive manifestations (8).

Also hypoparathyroidism has been observed in several cases of Kearns-Sayre syndrome – a non-hereditary mul-

tisystem disease.

In PHPT, patients have symmetrical muscle weakness and atrophy. Muscle cramps also can be seen. Patient with increased PTH may present with muscle weakness and atrophy with hyper-reflexia and spasticity. Untreated patients tend not to do well and progress much like patients with motor neuron disease (2,3,8).

Conclusion

PHPT is a disease caused by overactive parathyroid glands with consequent hypercalcemia. Lots of neurologic processes can be affected by hyperparathyroidism such as increase in cerebral circulation and O₂ consumption, reduction of glutamate and pyruvate dehydrogenase activity in the brain also some studies have been indicated rising in β -adrenergic binding site and falling in GABA binding site. Additionally calcium homeostasis will have role in neural manifestation of PHPT. However, hypercalcemia has been shown in patients who have no sign, however in patients with hypercalcemic psychiatric signs has been proved than controls. Furthermore other neurologic symptoms such as anxiety, cognitive difficulties, psychotic symptoms, and even major depression have been revealed. Debate continues about the best strategies for the management of PHPT and neuralgic and psychotic outcomes. Finally neuro-cognitive or psychiatric manifestations of PHPT are not to be neglected and further clinical investigation on this subject and finding a new approach is needed.

Author's contribution

SK was the single author of the manuscript.

Conflicts of interest

The author declared no competing interests.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the author.

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