THE ROLE OF HYPERPROLACTINEMIA IN REPRODUCTIVE AND METABOLIC ENDOCRINE DISORDERS

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Abstract: Hyperprolactinemia is an endocrine disorder characterized by persistently elevated serum prolactin concentrations and may result from physiological conditions, medications, hypothalamic-pituitary disease, or systemic disorders. The condition has important effects on reproductive, gonadal, metabolic, and neuroendocrine function. The aim of this study was to analyze the major pathophysiological mechanisms, clinical manifestations, diagnostic principles, and treatment strategies associated with hyperprolactinemia. A literature-based analytical approach was used to evaluate prolactin synthesis, dopamine-mediated inhibition, gonadotropin-releasing hormone suppression, pituitary adenomas, medication-induced hyperprolactinemia, and associated reproductive dysfunction. The analysis indicates that excessive prolactin inhibits hypothalamic GnRH secretion, leading to reduced luteinizing hormone and follicle-stimulating hormone release and subsequent hypogonadism. In women, this may cause menstrual disturbances, infertility, and galactorrhea, whereas men may develop reduced libido, erectile dysfunction, infertility, and decreased testosterone levels. Prolactinomas represent an important pathological cause, while dopamine antagonist medications are among the most common pharmacological causes. Accurate diagnosis requires confirmation of persistent prolactin elevation, exclusion of physiological and secondary causes, evaluation of thyroid and renal function, and pituitary imaging when indicated. Dopamine agonists remain the principal treatment in most symptomatic prolactinomas and can normalize prolactin secretion and reduce tumor size. Hyperprolactinemia should therefore be considered an important endocrine disorder with both reproductive and systemic consequences.
Keywords: hyperprolactinemia, prolactin, prolactinoma, dopamine, infertility, hypogonadism, pituitary gland, endocrine disorder.

Introduction

Prolactin is a peptide hormone synthesized and secreted by lactotroph cells of the anterior pituitary gland. Its best-known physiological role is the stimulation and maintenance of lactation, but prolactin also participates in reproductive regulation, immune function, metabolism, and behavioral responses. Unlike many other anterior pituitary hormones, prolactin secretion is primarily under tonic inhibitory control by hypothalamic dopamine. Dopamine reaches the anterior pituitary through the hypophyseal portal circulation and binds to D2 receptors on lactotroph cells, thereby suppressing prolactin synthesis and release.

Any disruption of dopaminergic inhibition can increase circulating prolactin concentrations. This may occur because of pituitary tumors, hypothalamic disease, compression of the pituitary stalk, or the use of medications that block dopamine receptors.

Hyperprolactinemia can also occur under physiological conditions. Pregnancy and lactation are the most important physiological causes. Stress, sleep, nipple stimulation, and physical exercise can produce transient elevations.

Persistent hyperprolactinemia has important reproductive consequences because prolactin interacts directly with the hypothalamic-pituitary-gonadal axis.

The aim of this study was to analyze the mechanisms by which hyperprolactinemia affects endocrine and reproductive function and to review its major causes, clinical manifestations, diagnosis, and management.

Materials and Methods

This study was prepared as a qualitative analytical review of scientific and clinical literature concerning prolactin physiology, hyperprolactinemia, prolactin-secreting pituitary adenomas, reproductive endocrinology, dopamine signaling, and pituitary disease.

The analysis focused on physiological regulation of prolactin secretion, mechanisms of GnRH suppression, gonadotropin abnormalities, prolactinoma pathophysiology, medication-induced hyperprolactinemia, and endocrine consequences in both women and men.

The diagnostic approach was evaluated with particular attention to repeat prolactin measurement, pregnancy testing, thyroid function assessment, renal and hepatic dysfunction, medication history, macroprolactin, and pituitary magnetic resonance imaging.

Therapeutic principles were analyzed according to the use of dopamine agonists, surgical intervention, and monitoring.

Results

The analysis showed that prolactin secretion is mainly controlled by hypothalamic dopamine.

Dopamine released from tuberoinfundibular neurons binds to D2 receptors on pituitary lactotrophs and inhibits prolactin synthesis and secretion.

When this inhibitory influence is reduced, prolactin levels increase.

One of the most important pathological causes is prolactinoma, a pituitary adenoma composed of prolactin-secreting lactotroph cells.

Prolactinomas are generally classified as microadenomas when their diameter is less than 10 mm and macroadenomas when they are 10 mm or larger.

Large tumors may produce both endocrine and mass-related symptoms.

The most important endocrine mechanism involves suppression of the reproductive axis.

Elevated prolactin inhibits hypothalamic GnRH secretion and disrupts normal pulsatile GnRH release.

As a result, pituitary secretion of LH and FSH decreases.

In women, reduced gonadotropin stimulation can impair follicular development, ovulation, and ovarian estrogen production.

This can result in oligomenorrhea, amenorrhea, anovulation, infertility, and reduced bone mineral density when estrogen deficiency is prolonged.

Galactorrhea may occur, although its absence does not exclude hyperprolactinemia.

In men, suppression of the hypothalamic-pituitary-gonadal axis results in decreased testosterone production.

Clinical manifestations may include reduced libido, erectile dysfunction, infertility, decreased muscle mass, fatigue, and, in chronic cases, reduced bone density.

Gynecomastia may occur in some patients but is not always present.

Large pituitary macroadenomas can cause headaches and visual disturbances.

Compression of the optic chiasm may produce bitemporal hemianopia.

Pituitary stalk compression can itself increase prolactin by preventing dopamine delivery to lactotroph cells, a phenomenon commonly referred to as the stalk effect.

Medication-induced hyperprolactinemia represents another important cause.

Dopamine D2 receptor antagonists, particularly several antipsychotic medications, can increase prolactin concentrations.
Some antiemetic and gastrointestinal prokinetic drugs may have similar effects.
The degree of elevation depends on the specific medication, dose, and individual susceptibility.
Primary hypothyroidism is another important endocrine cause.
Reduced thyroid hormone levels increase hypothalamic thyrotropin-releasing hormone secretion.
TRH stimulates both TSH and prolactin secretion, so untreated hypothyroidism may produce moderate hyperprolactinemia.
Chronic renal disease can also increase prolactin because of impaired clearance and altered regulation.
Macroprolactin is another important diagnostic consideration.
Macroprolactin consists mainly of prolactin bound to immunoglobulins.
It may be detected by laboratory immunoassays but usually has reduced biological activity.
Some patients therefore demonstrate elevated measured prolactin without the typical clinical manifestations of true hyperprolactinemia.
The diagnostic process should begin with confirmation of elevated prolactin under appropriate sampling conditions.
Physiological causes, medications, pregnancy, hypothyroidism, and renal dysfunction should be assessed.
If persistent unexplained hyperprolactinemia is confirmed, pituitary MRI may be required.

Discussion

The findings demonstrate that hyperprolactinemia has a particularly important influence on reproductive endocrine function.
Its effects are mediated largely through suppression of GnRH secretion.
This mechanism explains why menstrual abnormalities and infertility are common in women and why testosterone deficiency and sexual dysfunction are common in men.
The reproductive manifestations may occur even when prolactin elevation is moderate.
The clinical severity does not depend entirely on the absolute prolactin concentration. Duration of exposure, sex, gonadal sensitivity, and underlying cause also influence the phenotype.
Prolactinomas are especially important because they combine hormonal hypersecretion with the possibility of pituitary mass effects.
In microprolactinomas, reproductive symptoms may dominate the clinical picture.
In macroprolactinomas, headache, visual impairment, and compression of other pituitary structures may become increasingly important.
The relationship between prolactin level and tumor size can be useful but should not be interpreted rigidly.
Laboratory artifacts can occasionally produce misleading results.
For example, the high-dose hook effect may cause falsely low prolactin values in patients with very large prolactinomas when immunoassays are overwhelmed by extremely high hormone concentrations.
Dilution studies can resolve this problem.
Macroprolactin can cause the opposite problem, producing apparently high prolactin concentrations in patients with limited biological manifestations.
Treatment depends on the underlying cause.

When hyperprolactinemia is caused by medication, the possibility of discontinuing, reducing, or substituting the drug should be considered in coordination with the clinician responsible for the original treatment.
This is particularly important in psychiatric patients, in whom sudden withdrawal of antipsychotic therapy can be harmful.
In prolactinomas, dopamine agonists are the main pharmacological treatment.
Cabergoline is frequently preferred because of its effectiveness, relatively long half-life, and generally favorable tolerability.
Brmocriptine remains another established option.
Dopamine agonist therapy usually reduces prolactin secretion and can substantially decrease tumor size.
Improvement in reproductive function often follows normalization of prolactin.
Surgery is considered when dopamine agonists are ineffective, poorly tolerated, or inappropriate, or when specific tumor-related complications are present.
Long-term follow-up is important because recurrence can occur after treatment withdrawal.
Bone health should also be considered.
Chronic hypogonadism caused by hyperprolactinemia may reduce bone mineral density, particularly when diagnosis and treatment are delayed.
Hyperprolactinemia also demonstrates a broader endocrine principle: pituitary hormones can affect peripheral endocrine organs indirectly through hypothalamic and pituitary regulatory pathways.
Therefore, evaluation should not be limited to prolactin alone but should include the entire hypothalamic-pituitary-gonadal and thyroid axes when clinically indicated.

Conclusion

Hyperprolactinemia is an important endocrine disorder with significant reproductive, gonadal, metabolic, and neurological consequences.
Its principal pathophysiological effect is suppression of hypothalamic GnRH secretion, leading to reduced LH and FSH release and subsequent hypogonadism.
Women may develop menstrual irregularities, anovulation, infertility, galactorrhea, and estrogen deficiency, while men may develop reduced testosterone, sexual dysfunction, and infertility.
Prolactinomas are among the most important pathological causes, whereas dopamine antagonist medications, primary hypothyroidism, renal disease, and pituitary stalk lesions represent other significant causes.
Accurate diagnosis requires confirmation of persistent prolactin elevation and systematic exclusion of physiological, pharmacological, and secondary endocrine causes.
Dopamine agonists remain the cornerstone of treatment for most symptomatic prolactinomas and can normalize prolactin levels while reducing tumor size.Recognition of the underlying mechanism is essential for selecting appropriate therapy and avoiding unnecessary interventions.

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