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Hyperprolactinemia and infertility in female and male

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Abstract

Hyperprolactinemia is characterized by elevated, often pathologic serum prolactin concentrations affecting the reproductive health of both men and women. Prolactin is a hormone the anterior pituitary gland produces that serves numerous reproductive functions. In elevated amounts, prolactin interferes with the hypothalamic-pituitary-gonadal (HPG) axis, causing reproductive dysfunction. In women, hyperprolactinemia manifests with irregular menstruation, anovulatory cycles, or galactorrhea, while in men, low libido, erectile dysfunction, or oligospermia may ensue. Such effects are often linked to infertility and impaired conception. Diagnosis begins with measuring prolactin levels in the serum to confirm hyperprolactinemia and MRI imaging for suspicion of pituitary adenomas, a common cause. Most cases could be managed by dopaminergic treatment, such as bromocriptine and cabergoline, to help restore gonadal function, while surgical intervention would be resorted to in cases of large or resistant prolactinomas. To effectively frame treatment approaches, one has to understand the pathology behind hyperprolactinemia and infertility. This review discusses the etiology, pathophysiology, clinical presentation, and management of hyperprolactinemia, focusing on its reproductive health and fertility consequences.

Keywords: hyperprolactinemia, prolactin, hypogonadism, prolactinoma, gonadal dysfunction, dopamine agonists

1. Introduction

1.1. Defining Hyperprolactinemia and Infertility

Hyperprolactinemia refers to a condition characterized by excessive release of the hormone prolactin, which also facilitates lactation and other reproductive functions. The prolactin levels are normally controlled by dopamine, which inhibits its release from the lactotrophs of the anterior pituitary gland. Any alteration in the regulation of prolactin secretion would alter the production of gonadal hormones, thus affecting fertility in both males and females. The clinical definition of infertility is 12 months of unprotected sexual intercourse without a conception event.. This rate is pegged around 15% of couples worldwide, hyperprolactinemia being an essential contributory cause behind it. High prolactin levels inhibit gonadotropin-releasing hormone (GnRH) secretion, which drops down follicle-stimulating hormone (FSH) and luteinizing hormone (LH) levels, which are critical for ovulation and spermatogenesis. Thus, hyperprolactinemia is now considered a primary endocrine disorder affecting fertility outcomes.

1.2. Etiology of Hyperprolactinemia

Hyperprolactinemia has both physiological, pathological, and pharmacological causes.

The physiological causes include pregnancy, lactation, stress, and sleep, which are natural elevations of prolactin levels (7). Pathological hyperprolactinemia results mostly from prolactin- secreting pituitary adenomas (prolactinomas), hypothyroidism, chronic kidney disease, or liver cirrhosis (8). Prolactinomas are the most common cause, with microadenomas (<10 mm) or 3 macroadenomas (>10 mm) creating sustained prolactin elevations (9). Others include any pituitary and hypothalamic disorder that might induce prolactin secretion, for example, stalk compression from non-functioning adenomas (10). Hyperprolactinemia could be caused by medications such as antipsychotics (including risperidone and haloperidol), antidepressants (mainly selective serotonin reuptake inhibitors), and antihypertensives (like verapamil) (11). These drugs act by interfering with dopamine signaling, taking off the inhibitory control prolactin release had, thus predisposing to hyperprolactinemia.

1.3. Impact of Hyperprolactinemia on Fertility in Males and Females

1.3.1. Effects on Female Fertility

High prolactin levels disturb ovarian function in females by suppressing GnRH secretion, which results in decreased levels of FSH and LH. This inhibition results in anovulation, menstrual irregularities (e.g., oligomenorrhea or amenorrhea), and reduced estrogen production (12). Galactorrhea, the inappropriate secretion of breast milk, may also be another prominent symptom in hyperprolactinemic women, but it does not always arise (3). Extended hyperprolactinemia hampers

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endometrial receptivity, possibly reducing implantation success (4). Primary tenets of reproductive endocrinology are that hyperprolactinemia is seen in 10-20% of women who are infertile (5). Long-standing hyperprolactinemia can lead to suppression of estrogen, which can affect bone mineral density and postulate the risk of osteoporosis (6).

1.3.2. Effects on Male Fertility

By suppressing the secretion of GnRH in men, hyperprolactinemia causes hypogonadotropic hypogonadism, reducing LH and FSH levels and thus decreasing testosterone production and interfering with spermatogenesis (3). Just like in females, reduced libido, erectile dysfunction, and gynecomastia (breast enlargement) are common symptoms in males as well (6).

High prolactin levels are found in 3-11% of men with oligozoospermia (low sperm count), which leads to high oxidative stress in spermatozoa, causing sperm DNA fragmentation and decreased fertilization potential (12). Although many men may not see hyperprolactinemia manifest as overt symptoms so frequently, it exerts profound impacts on sperm morphology, motility, and fertility. Evidence suggests that untreated hyperprolactinemia will lead to irreversible gonadal dysfunction, even after normalization of prolactin levels

2. The Mechanisms of Hyperprolactinemia and Its Impacts on Reproductive Physiology

2.1. Disruption of the Hypothalamic-Pituitary-Gonadal Axis

Hyperprolactinemia mainly disrupts the hypothalamic-pituitary-gonadal (HPG) axis and affects reproductive physiology. The hypothalamus controls reproductive function through the secretion of gonadotropin-releasing hormone (GnRH), acting upon the anterior pituitary for the subsequent release of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) (1).

These hormones are indispensable for ovarian follicle development, ovulation, corpus luteum function in females, and testosterone production and corpus luteum function in females; the primary results are decreased FSH and LH levels and spermatogenesis in males. Excess levels of the hormone prolactin inhibit GnRH secretion, causing low levels of FSH and LH and ultimately thwarting regular reproductive action (2).

The hormonal imbalance in females appears to be responsible for several clinical manifestations relating to reproductive physiology, such as anovulation, irregular menstrual cycles, and decreased estrogen levels, rendering females infertile. On the other hand, hyperprolactinemia inhibits the secretion of estradiol, the hormone responsible for maintaining endometrium thickness necessary for implantation of the fertilized egg. So even if ovulation occurs, the endometrium may not be ideal for implantation, reducing the chances of conception. In males, prolactin excess suppresses testosterone secretion by inhibiting Leydig cell function in the testes, resulting in hypogonadotropic hypogonadism (4). Manifestations include diminished sexual drive, erectile dysfunction, and deficient sperm production. The significance of testosterone to spermatogenesis means that reduced levels are often paired with the manifestation of oligospermia (low sperm count) or azoospermia (absence of sperm in semen), both contributing to male infertility.

2.2. Direct Effects on Reproductive Tissues

Hyperprolactinemia has direct effects as well as direct results beyond endocrine suppression on reproductive tissues. In women, prolonged exposure to high prolactin levels inhibits ovarian follicle maturation. These inhibitory effects primarily affect the granulosa, a cell type essential for follicular maturation and estrogen synthesis (6). High levels of blood prolactin impair oocyte-creating fertilization rates and embryo developmental competence. In addition, it negatively affects the receptivity of the endometrium, affecting implantation failure and increasing the risk of early pregnancy loss. Likewise, hyperprolactinemia disrupts the testicular microenvironment in men. Studies have shown that prolactin interacts with Sertoli cells, supporting sperm development and causing abnormal spermatogenesis (8). Besides producing increased prolactin levels, it has heightened oxidative stress in spermatozoa, resulting in sperm DNA fragmentation, decreased motility, and low fertilizing potential (9). These factors hinder sperm function to such an extent that it becomes difficult to conceive, even when the concentration is otherwise normal. One of the most significant concerns, however, is the long- term impact on reproductive function from hyperprolactinemia. After normalization of serum prolactin levels, long-persisting gonadotropin suppression can succeed in causing irreversible gonadal dysfunction. In females, this condition manifests as premature ovarian insufficiency, while males would have persistent testicular atrophy associated with compromised fertility potential. Early diagnosis and treatment of hyperprolactinemia play a vital role in preventing irreversible reproductive damage.

2.3. Psychological and Systemic Manifestations

Hyperprolactinemia has effects on the system and psyche, as well as the reproductive function. High prolactin levels indicate mood disorders like depression and anxiety that may further reduce sexual desire and fertility (11). The continual estrogen deficiency in these women poses an even higher risk for the development of osteoporosis and fractures, whereas chronic suppression of testosterone in men results in loss of body mass and increased fatigue (12). This makes a case for holistic management to address issues of fertility and general well-being due to hyperprolactinemia.

3. Clinical Manifestations and Diagnostic Approaches

Hyperprolactinemia is an endocrinological condition involving an increased serum level of blood prolactin and is mainly mediated through the inhibition of hypothalamic-pituitary-

gonadal axis function. Given that multiple aspects of the reproductive and systemic physiology are impacted by GnRH pulsatility, the increase in prolactin levels can lead to severe consequences. The signs and symptoms of hyperprolactinemia are not always obvious, are influenced by sex and age, and may be accompanied by endocrine or metabolic disorders. It is crucial to be mindful of these manifestations to ensure timely diagnosis and management.

3.1. Clinical Presentation in Females

In women, hyperprolactinemia is most commonly manifested by menstrual irregularities. This encompasses the following: oligomenorrhea, which is the infrequent occurrence of enstruation; amenorrhea, which is the complete lack of menstruation; and anovulatory cycles due to the suppression of GnRH and the subsequent suppression of LH and FSH by prolactin. This leads to all their fructose-dependent physiology, including ovulation and follicular development, being severely impacted by the resulting hypoestrogenic state (6). Another intriguing feature that is present, although not in all patients, is galactorrhea, the spontaneous production of breast milk in females who are not pregnant or breastfeeding. They may also demonstrate other features of chronic estrogen deprivation, like vaginal atrophy, painful intercourse, and low sexual desire. Hypoestrogenemia contributes to osteopenia and osteoporosis, particularly in prospective menopausal females, resulting in an enhanced fracture rate and long-term skeletal unreliability (7). These endocrine pathophysiologic changes happen insidiously, and many patients do not seek medical advice until fertility issues arise or other more generalized symptoms manifest.

3.2. Clinical Presentation in Males

Unlike the more severe symptoms seen in females, male symptom patterns are less apparent and sometimes overlooked. The typical clinical manifestations of hyperprolactinemia include decreased libido, erectile dysfunction, gynecomastia, and, rarely, galactorrhea in men. As with hyperprolactinemia, the mechanism is hypogonadotropic hypogonadism due to the suppression of the secretion of gonadotropins by prolactin. It results in lower testosterone levels in the serum, thus impacting sexuality, mood, skeletal muscle mass, and bone density. First of all, it should be mentioned that hyperprolactinemia influences spermatogenesis significantly.

Because the intratesticular microenvironment is especially vulnerable to changes in gonadotropin stimuli, raised prolactin levels are thought to adversely affect sperm concentration, motility, and morphology (9). Thus, conditions such as oligospermia or azoospermia may be present in effected individuals after an appropriate workup to identify contributing factors to subfertility or infertility.

3.3. Neuropsychiatric and Metabolic Consequences

In addition to its effects on reproduction, hyperprolactinemia has been associated with neuropsychiatric and metabolic alterations. Dopamine antagonism in the hypothalamic area due to endogenous or exogenous factors can facilitate mood disorders like depression, anxiety, irritability, and cognitive deterioration. These effects are most apparent in people with prolactinomas or cases of prolonged disease without treatment (19). It is believed that the neuropsychiatric alterations of hyperprolactinemia are due to changes in dopaminergic modulatory tone in mesolimbic and mesocortical circuits. Additionally, other studies conducted in the past years have correlated chronic hyperprolactinemia with metabolic syndrome, which includes central obesity, insulin resistance, and dyslipidemia (11). The prolactin receptors in the adipose tissue indicate that prolactin might regulate adipose tissue formation and lipid homeostasis. This broadens the suggested use of prolactin in fertility, endocrinology, and prospects in cardiovascular diseases.

3.4. Diagnostic Framework

Thus, properly diagnosing hyperprolactinemia implies systematically identifying biochemical, radiological, and clinical findings. The primary diagnostic test is a prolactin-level blood test. Prolactin levels increase during sleep, exercise, and in response to stress, whereas they decrease in response to food intake; therefore, blood samples should be collected before 10 am after denying the patients food and ensuring they have sat for 30 mins (12). PRL reference values differ from the lab, but >25 ng/mL in women and >20 ng/mL in men are considered high. In those patients with mild elevation of PRL, it is recommended to repeat the test for confirmation of hyperprolactinemia. Moderate hyperprolactinemia (widespread >200 ng/mL) indicates a chance for a prolactinoma, specifically prolactin-secreting pituitary macroadenoma. On the other hand, actual moderate elevation can have a secondary cause, such as steroids, thyroid medication, kidney diseases, or stress. Consequently, a comprehensive review of the patient's medication list is imperative. Prolactin can be raised by various medications, including dopamine receptor antagonists like antipsychotics, risperidone, and haloperidol; SSRIs; and several antihypertensives, including verapamil, due to tuberoinfundibular dopamine (18).

3.5. Neuroimaging and Hormonal Assessments

MRI is the imaging study of choice when hyperprolactinemia is present and involves imaging the sella turcica for the detection of pituitary microadenomas (less than 10 mm) and macroadenomas (greater than 10 mm) and evaluation of the extent of the tumor and the possibility of chiasmal compression by tumor. Patients with macroadenomas should be tested for bitemporal hemianopsia and visual fields, and perimetry should be tested (14). Further endocrinological assessment by systematic blood examination, specifically TSH and free T4, to rule out hypothyroid-induced hyperprolactinemia, which results from stimulation by TRH. It also is necessary to perform renal and hepatic function tests to exclude systemic causes. In women, precisely, the serum levels of estradiol, LH, and FSH help determine the extent of reproductive depression. In men, assessing testosterone, LH, and FSH helps describe the

hypothalamic- pituitary-testicular axis. Under some circumstances, macroprolactin level assays may be relevant. Macroprolactin is a biologically inactive, high molecular weight prolactin complex that, when present in circulation, can lead to raised serum prolactin levels without clinical manifestations.

The PEG precipitation test can distinguish macroprolactin from the biologically active monomeric prolactin (15).

4. Treatment Strategies and Fertility Management in Hyperprolactinemia

The management of hyperprolactinemia needs to be rational and individualized to achieve normalization of serum prolactin levels, the amelioration of hypogonadism and fertility if impaired, and the identification and treatment of the causative factor, which may be a functional pituitary tumor, the use of a drug with hyperprolactinemic effects, or a systemic disorder. Therapeutic management depends on the degree of hyperprolactinemia, tumor size, symptomatology, and the patient's childbearing plan.

4.1. Pharmacologic Therapy

4.1.1. Dopamine Agonists as First-Line Treatment

Dopamine agonists are at present considered the first-line treatment option for hyperprolactinemia. They work on D2 receptors in the pituitary to inhibit prolactin release and to cause tumor regression in prolactinomas. Cabergoline and bromocriptine are the two most commonly used ergot derivatives, but cabergoline is recommended because of its higher efficacy, longer duration of action, and better side effect profile (1). Cabergoline reverses hyperprolactinemia in more than 85% and causes tumor shrinkage in many micro- and macroprolactinomas (19). It is taken twice a week, increases compliance, and diminishes the gastrointestinal side effects seen with bromocriptine. Although adverse effects have been reported in studies, bromocriptine still has its uses, especially for pregnant women, because of its efficacy and fewer side effects than other dopamine agonists. Therapeutic targets are aimed at achieving normoprolactinemia, symptom control (such as galactorrhea or amenorrhea), and recovery of regular menses or testosterone levels. The frequency of monitoring hormonal reassessment is usually 1 to 3 months in the first year, and the intervals between subsequent evaluations are longer if biochemical remission is attained.

4.1.2. Management of Drug-Induced Hyperprolactinemia

The treatment of choice for patients with medication-induced hyperprolactinemia is usually changing or ceasing the causative drug. If cessation is not possible (for instance, in psychotic illnesses), the use of a dopamine agonist or switching to a non-prolactinogenic medication like aripiprazole should be considered (4). However, this should be done under close consultation with the prescriber to prevent risks of psychiatric decompensation.

4.1.3. Addressing Underlying Conditions

Other violations include hypothyroidism, which requires levothyroxine as it inhibits TRH-stimulated prolactin secretion. Hyperprolactinemia due to chronic diseases such as kidney diseases or cirrhosis may resolve with treatment of the underlying condition, but dopamine agonists may be necessary if galactorrhea persists after treatment.

4.2. Surgical and Radiation Options

4.2.1. Transsphenoidal Surgery

Surgical intervention is required in patients for whom dopamine agonist treatment is contraindicated or could be discontinued or in patients who experience compressive symptoms from the macroprolactinoma, such as visual field compromise from optic chiasm compression. The best procedure is adenomectomy through the transsphenoidal approach, which involves direct resection of the lesion with minimal damage to other pituitary gland tissues. Surgical success has been reported to depend on tumor size, its stage or extent of growth, and whether the tumor is well-defined or invasive. Microprolactinomas are reported to have more than 70% remission rates, while macroadenomas have lower remission rates and a high potential for recurrence (18). Hence, there is a general preference for surgical intervention in severe conditions or when all the available medical therapies have been exhausted.

4.2.2. Radiation Therapy

Radiation therapy is not used initially but may be indicated in large prolactinomas that are aggressive or resistant to both medical and surgical management. Stereotactic radiosurgery (Gamma Knife) is preferred as it is less invasive and causes less hypopituitarism as compared to conventional radiotherapy/fractionated radiotherapy.

4.3. Fertility Restoration Strategies

4.4.1. Ovulation Induction in Women

Ovulation is an important biological phenomenon, and hyperprolactinemia poses a massive threat to women's fertility through anovulation. The restoration of ovulatory function is usually accomplished with dopamine agonist therapy only. It has also been found that once the prolactin levels are brought back to normal, as many as eighty percent of women can get back their periods and can conceive again (8). In case it does not return, ovulation can be induced through the use of drugs like clomiphene citrate or letrozole. However, since many couples do not obtain pregnancy even after prolactin levels return to normal, ART, such as in vitro fertilization (IVF), may be used when other infertility factors are present (9).

4.4.2. Male Fertility Management

In men, dopamine agonist therapy raises testosterone concentration and helps to increase the chances of conception by improving sperm production and sexual function. Some studies show that the elevation of prolactin levels is associated

with poor sperm concentration, movement, and morphology (10). In the case of chronic idiopathic oligozoospermia, additional treatments like gonadotropin therapy, including human chorionic gonadotropin (hCG) or follitropin injections to promote spermatogenesis, might be used. It is therefore advocated that a complete workup to rule out other causes of infertility, such as varicocele, testicular failure, and genetic issues, should be done (20). Fertility preservation strategies can also be used in patients with an increased testosterone level that is >20 ng/mL or in those patients receiving pharmacological management for prolactinomas or undergoing surgery or radiotherapy.

4.4. Monitoring and Long-Term Follow-Up

Patients with hyperprolactinemia, especially those with prolactinomas, are usually followed up endocrinologically to monitor executive functioning and the return of tumor activity. It is recommended that prolactin measurements be taken serially and pituitary imaging be performed every 1-2 years in macroadenomas or recurrent microadenomas (17). The selective endocrine evaluation comprises pituitary hormone axes, especially in patients who undergo surgery or radiotherapy for pituitary tumors, as hypopituitarism may be experienced. Screening bone density is recommended if the initiation of treatment with gonadotropin is delayed or if chronic hypogonadism is present.

5. Emerging Research and Future Directions

Concerning hyperprolactinemia, the diagnostic tools and approaches to treatment have significantly changed during the last decades, but new information in the field still comes to light regularly. In this chapter, the current topics of hyperprolactinemia molecular pathophysiology, precision medicine, new drugs, and pharmacology, as well as future perspectives on fertility and systemic effects, have been discussed.

5.1. Advancements in Molecular and Genetic Understanding

Some molecular evidence, such as gene and protein expression maps, has revealed that prolactinomas are heterogeneously characterized tumors. MEN1, the MEN type 1 gene, has been linked to familial and sporadic pituitary tumors, which points to hereditary causes in some patients (18). Such pathways may enable risk assessment of individuals and early diagnosis in high-risk populations. New studies on gene variations of dopaminergic receptors also reveal why certain patients do not respond to dopamine agonists. Further, research has pointed to carriers of the D2 receptor gene (DRD2) with treatment-resistant prolactinomas, leading to receptor- selective drugs that bypass such resistance mechanisms (20). Moreover, other molecular changes, including histone methylation and DNA methylation of particular genes, have also been identified in prolactinoma tissues with concerning indications for breast cancer aggressiveness and recurrence.

5.2. Innovations in Pharmacologic Treatment

Even though this medication is deemed the most effective, certain drawbacks have been observed. Chemotherapy-induced toxicities, drug resistance mechanisms, and incomplete eradication of tumors, in some instances, require tweaking of the approach. One of these is the extended-release dopamine agonists, which increase receptor occupancy and reduce dosing frequency, thus enhancing patient compliance and decreasing side effects (4). There are new classes of agents under study. SERMs and SPRMs are under consideration for their ability to intervene in prolactin secretion indirectly, based on hormonal regulation (5). In addition, other early-phase trials with non-selective and selective GnRH kisspeptin agonists, presumed to enhance secretion of GnRH, appear to have the potential to eradicate hyperprolactinemia- induced anovulation without necessarily suppressing prolactin.

5.3. Precision Medicine and Targeted Therapies

The advancement of the concept of precision medicine is also bringing significant changes in the field of endocrine oncology. Practical significance: Using biomarkers such as genetic, hormonal, and imaging, new and existing treatments can be adjusted to be the most effective in treating clients while avoiding potential harm. For instance, when patients presented with tumors with high Ki-67 scores, he could recommend surgery earlier or additional treatment (7). It may also help clinicians select a specific DA or predict patients likely to need a higher dose or a combination therapy. With these approaches becoming more widespread, they are expected to increase long-term remission rates significantly.

5.4. Emerging Technologies in Fertility Preservation

In the field of reproductive medicine, hyperprolactinemia continues to be an essential, although fully reversible, factor behind infertility. Still, distinct possibilities are emerging for new techniques for patients with potential infertility due to long-term gonadal failure. Oocyte vitrification, egg freezing, and testicular sperm extraction, or TESE, are being used more commonly in patients who are to be subjected to invasive cancer treatments or are to receive long -term medical therapies that may affect their vision (8). Stem cell-based ovarian/testicular regeneration is still in the experimental stage but has the potential to restore fertility in hypogonadal patients with secondary hypogonadism attributed to hyperprolactinemia (9). Moreover, machine learning algorithms use multiple parameter data sets to predict ovulatory response and IVF success in hyperprolactinemia (10).

5.5. Future Directions and Research Gaps

There are still some gaps in knowledge despite these accomplishments. One of the reasons is that the long-term effects of untreated or chronic hyperprolactinemia on cardiovascular and neurocognitive health have not been explored adequately. Thus, considering the role of prolactin in endothelial function and dopaminergic signaling, longer-term prospective studies must evaluate the cardiovascular risks of

atherosclerosis and hypertension, as well as cognitive impairment and mood disorders, among patient populations (11). Second, more research is needed to find biomarkers to help distinguish between diseases such as FH and prolactinomas, specifically when prolactin levels are low. Circulating microRNA and prolactin isoform ratios are currently being explored (18). In addition, limited research on hyperprolactinemia among transgender, intersex, and non-binary patients indicates that hormone therapy may have more complex effects in these populations.

6. Conclusion and Recommendations

6.1. Conclusion

The current paper focuses on the clinical and endocrine consequences of hyperprolactinemia, a multifaceted affliction with impacts on the reproductive system, psychological functions, and overall body functioning. It results in hypothalamic-pituitary- gonadal (HPG) axis dysfunction due to the suppression of GnRH by prolactin with hypogonadotropic hypogonadism in both sexes. The outcome is not uncomplex: it may run from menstrual disorders, galactorrhea, and infertility in women to erectile dysfunction, decreased libido, and oligospermia in men. Moreover, hyperprolactinemia is no longer only associated with neuropsychiatric disorders but also metabolic syndrome and future cardiovascular disease. The diagnosis depends on biochemical evaluation, imaging of the sellar region, and exclusion of other pathophysiologic conditions that can cause a similar presentation, like hypothyroidism, renal failure, or drug side effects. Including pituitary MRI and hormone assays, which help differentiate prolactinomas and manage patients.

Currently, dopaminergic agents, especially cabergoline, are therapeutically most effective and represent the gold standard in prolactinoma treatment, tumor shrinkage, and recovery of reproductive function. Surgery and radiation therapy are reserved for patients with persistent or progressive tumors that are also rapidly growing; hence, risk stratification is crucial. Although there have been significant achievements in the treatment of cancer, it remains an intervening issue in non-responsive cases, drug allergies, and maintenance of complicated diseases. Luckily, information regarding molecular genetics, receptor pharmacology, and the molecular basis for personalized medicine is gradually improving. Incremental improvements are anticipated to not only advance the outcomes of reproduction but also ameliorate the permanent threats arising from excessive prolactin concentrations.

6.2. Recommendations

6.2.1. Enhance Early Detection and Screening

In women, reproductive endocrinologists and primary care or internal medicine physicians should have a heightened awareness of hyperprolactinemia in women with irregular or oligo menstrual cycles, infertility, galactorrhea, or sexual dysfunction. By including prolactin in the tests associated with infertility and amenorrhea, doctors could make the diagnosis and start treatment on time. Promote interdisciplinary management. Due to the interaction of hyperprolactinemia with various systems, patients should be managed by several specialists, such as endocrinologists, reproductive specialists, neurologists, and psychiatrists, as required. This way is integrated to systematically take care of hormonal and psychological consequences.

6.2.2. Personalize Pharmacologic Therapy

Clinicians should, therefore, adjust the dopamine agonist treatment based on the patient's tolerance level, pharmacogenomic testing, and tumor activity. Monitoring the side effects and prolactin levels regularly is vital to effectively address the symptoms and noise while preventing negative consequences.

6.2.3. Integrate Fertility Preservation Strategies

As previously stated, ALL adult patients and women of childbearing age, including those requiring surgery or taking long-term medications, should discuss fertility preservation with their clinician. Methods like oocyte vitrification, sperm cryopreservation, or embryo banking help to protect future reproductive self-determination.

6.2.4. Continuity, Long-Term Commitment, and Follow-Up

Patients should be followed up longitudinally for tumor recurrence, hypopituitarism, and potential complications like osteoporosis or newly developed metabolic syndrome. Correspondingly, bone density scans, cardiovascular risk, and psychosocial assessment should be integrated into the post-treatment follow-up regimens. Expand research into understudied populations. More studies should be conducted regarding hyperprolactinemia risk and its effects on various population groups like adolescents, the elderly population, transgender people, and those with other endocrine disorders. Awareness of differences in risk-protective factors and treatment intervention in these groups will improve the clinician's effectiveness and sensitivity to cultural differences.

6.2.5. Advanced Public and Provider Education

Informative public health campaigns targeting healthcare professionals and the general populace may help spread knowledge concerning hyperprolactinemia's signs, consequences, and management. It is a powerful strategy to educate patients and engage them in their care to better follow through with therapy regimens.

Conflict of interest
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Ethical Statement

This study is not required ethics approval.

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