HIGH LEVEL OF PROLACTIN

Hyperprolactinaemia, Hyperprolactinemia

The presence of abnormally high levels of prolactin in the blood.

⚠ Risk factor ♂ Male & Female

About High level of prolactin

Hyperprolactinaemia or hyperprolactinemia is the presence of abnormally high levels of prolactin in the blood. Normal levels are less than 500 mIU/L [20 ng/mL or μg/L] for women, and less than 450 mIU/L for men (Pic. 1). Levels above this volume are considered as hyperprolactinaemia.

Prolactin (PRL) is one of several hormones that are produced by the pituitary gland. PRL has many different roles throughout the body, and most of those are clearly shown as clinical symptom. Perhaps the most important classical role of prolactin is to stimulate milk production in women after the delivery of a baby. Prolactin levels increase during pregnancy causing the mammary glands to enlarge in preparation for breastfeeding and ready to secrete colostrums (a form of milk produced by the mammary glands during pregnancy, colostrum contains higher amount of antibodies to protect the newborn against disease) closely after delivery. Later on the elevated prolactin levels help with the sustained production of milk during nursing.

During the first several months of breastfeeding, the higher basal prolactin levels also serve to suppress ovarian cyclicity, through the inhibition of pituitary hormones, mainly via LH (luteinizing hormone) suppression (to put an end to the activities of LH hormone). This is the reason why women who are breastfeeding do not get their periods and therefore do not often become pregnant. In actively breastfeeding mothers the related hyperprolactinaemia persisting even over a year.

Menstruation and ovulation may only occasionally occur before the drop of elevated basal PRL levels. As time goes on with less frequent breastfeeding, e.g., during weaning however, the PRL levels do not stay as high and the woman may start to ovulate. In cases of nonlactating/ nonbreastfeeding mothers, that may happen between 2-3 month after delivery.

The function of prolactin in men is not well-known. High levels of prolactine can causes a lower sex drive and loss of body hair.

Hyperprolactinaemia may be caused by either disinhibition (e.g., compression of the pituitary stalk or reduced dopamine levels) or excess production from a prolactinoma (a type of pituitary tumour) (Pic. 2).

If serum prolactin levels are above 200 μg/L, prolactinoma is the underlying cause, but if levels are lower, differential diagnoses include:

Physiological causes

Physiological (i.e., non-pathological) causes include: pregnancy, breastfeeding, and mental stress.

Medications

Prolactin secretion in the pituitary is normally suppressed by the brain chemical dopamine (Pic. 3). Drugs that block the effects of dopamine at the pituitary or deplete dopamine stores in the brain may cause the pituitary to secrete prolactin. These drugs include the major tranquilizers, antipsychotic medications, drugs used to treat gastro-oesophageal reflux (a long-term condition where stomach contents come back up into the esophagus
resulting in either symptoms or complications); medication-induced nausea (such as cancer drugs); and, less often drugs used to control hypertension (a high blood pressure). The sleep drug also increases the risk of hyperprolactinaemia.

**Specific diseases**

Prolactinoma or other tumours arising in or near the pituitary may block the flow of dopamine from the brain to the prolactin-secreting cells, likewise division of the pituitary stalk or hypothalamic disease. Other causes include chronic renal failure, hypothyroidism (a disorder in which the thyroid gland does not produce enough thyroid hormone), bronchogenic carcinoma (a malignant lung tumor of the lungs) and sarcoidosis (a disease involving abnormal collections of inflammatory cells that form lumps). Some women with polycystic ovary syndrome may have mildly-elevated prolactin levels.

Nonpuerperal mastitis (inflammatory lesions of the breast that occur unrelated to pregnancy and breastfeeding) may induce temporary hyperprolactinemia (neurogenic hyperprolactinemia) of about three weeks' duration.

Apart from diagnosing hyperprolactinaemia and hypopituitarism (the decreased secretion of one or more of the eight hormones normally produced by the pituitary gland), prolactin levels are often checked by physicians in patients that have suffered a seizure, when there is doubt as to whether they have had an epileptic seizure or a non-epileptic seizure. Shortly after epileptic seizures, prolactin levels often rise, whereas they are normal in non-epileptic seizures.

In many people, elevated prolactin levels remain unexplained and may represent a form of hypothalamic–pituitary–adrenal axis (a complex set of direct influences and feedback interactions among three endocrine glands: the hypothalamus, the pituitary gland and the suprarenal glands) dysregulation.

**Symptoms**

When a pituitary tumour is present, patients often have pressure symptoms in addition to endocrine dysfunction, such as headaches, visual field defects, or cranial nerve deficits.

Hyperprolactinemia is commonly found in both female and male patients with abnormal sexual and/or reproductive function.

In women, a high blood level of prolactin often causes hypoestrogenism (a lower than normal level of estrogen) with anovulatory infertility (when the ovaries do not release an oocyte during a menstrual cycle) and a decrease in menstruation. In some women, menstruation may disappear altogether (amenorrhea). In others, menstruation may become irregular or menstrual flow may change. Women who are not pregnant or nursing may begin producing breast milk. Some women may experience a loss of libido (interest in sex) and breast pain, especially when prolactin levels begin to rise for the first time, as the hormone promotes tissue changes in the breast. Intercourse may become difficult or painful because of vaginal dryness.

In men, the most common symptoms of hyperprolactinaemia are decreased libido, sexual dysfunction (in both men and women), erectile dysfunction, infertility, and gynecomastia (enlargement of breasts in men). Because men have no reliable indicator such as menstruation to signal a problem, many men with hyperprolactinaemia being caused by a pituitary adenoma may delay going to the doctor until they have headaches or eye problems caused by the enlarged pituitary pressing against the adjacent optic nerve. They may not recognize a gradual loss of sexual function or libido. Only after treatment do some men realize they had a problem with sexual function.

Because of hypoestrogenism and hypoandrogenism (a medical condition characterized by not enough androgenic activity in the body), hyperprolactinaemia can lead to osteoporosis (a disease where increased bone weakness increases the risk of a broken bone).

**Associated diseases**

- pituitary tumors
- hypothyroidism
- polycystic ovary syndrome (PCOS)
- renal failure
- cirrhosis (the replacement of normal liver tissue by scar tissue)
Complications

- infertility

Risk factors

- medication
- stress
- obesity

Prevention

Hyperprolactinemia caused by prolactinoma or other associated diseases can not be prevented. On the other hand stress and obesity are factors, which can be eliminated by individuals. Healthy lifestyle and plenty of rest are necessary not only as prevention of high levels of prolactin, but it can also prevent the other diseases which are strictly associated with unhealthy lifestyle such as stroke, infarction, high blood pressure and high levels of cholesterol.

How it can affect fertility

High levels of prolactin is considered as the most frequent cause of anovulatory sterility, although spontaneous pregnancy may occur occasionally. In young women, hyperprolactinemia is probably one of the most common endocrine disorders related to pituitary function.

Clinically significant elevation of PRL levels may cause infertility in several different ways. First, prolactin may stop a woman from ovulating. Without ovulation it is not possible to conceive a child. If this occurs, a woman’s menstrual cycles will stop.

In less severe cases, high prolactin levels may only disrupt ovulation once in a while. This would result in intermittent ovulation or ovulation that takes a long time to occur. Women in this category may experience infrequent or irregular periods.

Women with the mildest cases involving high prolactin levels may ovulate regularly but not produce enough of the hormone progesterone after ovulation. This is known as a luteal phase (the latter phase of the menstrual cycle which begins with the formation of the corpus luteum - a temporary endocrine structure in female ovaries that is involved in the production of relatively high levels of progesterone) defect. Deficiency in the amount of progesterone produced after ovulation may result in a uterine lining that is less able to have an embryo implant. Some women with this problem may see their period come a short time after ovulation.

There is no study which can prove the association of male infertility with high levels of prolactin. The only thing that is known, is that hyperprolactinemia is associated with lower sex drive.

Prognosis

Treatment goal is normalize the prolactin level, to restore gonadal function and galactorrhea (the spontaneous flow of milk from the breast, unassociated with childbirth or nursing) termination. Treatment often includes administration of dopamine agonists (a chemical that binds to a receptor and activates the receptor to produce a biological response) such as bromocriptine or cabergoline, or the use of herbal medicines with dopaminergic action.

In the case of prolactinoma the goal is to reduce the tumor mass and local compression effects. People with prolactinoma generally have an excellent prognosis. In 95% of cases the tumor will not show any signs of growth after a 4 to 6-year period. Pharmacotherapy is available to reduce the tumour size and consequently decrease PRL levels.

Surgical resection of the prolactinoma is the option for patients who may refuse or do not respond to long-term pharmacological therapy. Radiotherapy and/or estrogens are also reasonable choices if surgery fails.
In patients with asymptomatic prolactinoma no treatment needs to be given and a regular follow-up with serial prolactin measurements and pituitary imaging should be organized.

In cases when the only cause of infertility is chronic anovulation due to hyperprolactinemia, a 60-80% pregnancy rate can be achieved after treatment.

Find more about related issues

Diagnoses

Anovulation
Failure of the ovaries to release an oocyte over a period of time generally exceeding 3 months. Learn more at: www.fertilitypedia.org/therapy.diag/anovulation

Hyperprolactinemia
The presence of abnormally high levels of prolactin in the blood. Learn more at: www.fertilitypedia.org/therapy.diag/hyperprolactinemia

Non-obstructive azoospermia
Complete absence of sperm in the ejaculate due to testicular failure. Learn more at: www.fertilitypedia.org/therapy.diag/non-obstructive-azoospermia

Thyroid disorders
A medical condition impairing the function of the thyroid. Learn more at: www.fertilitypedia.org/therapy.diag/thyroid-disorders

Gallery

Pic
A table of reference ranges of prolactine.

<table>
<thead>
<tr>
<th>Prolactine</th>
<th>µg/L</th>
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<tbody>
<tr>
<td>Female</td>
<td></td>
</tr>
<tr>
<td>follicular phase (n = 803)</td>
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<tr>
<td>luteal phase (n = 699)</td>
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<tr>
<td>mid-cycle (n = 53)</td>
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<td>whole cycle (n = 1555)</td>
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<tr>
<td>pregnant, 3rd trimester (n = 54)</td>
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<tr>
<td>Male</td>
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<tr>
<td>21–30 (n = 80)</td>
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</tr>
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<td>61–70 (n = 50)</td>
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Pic
A pituitary gland tumour on the left and on the right after seven years of treatment.

Pic
Regulation of prolactin secretion by hypothalamus with feed back mechanisms.