Prolactin and prolactinomas

Key points

- The commonest pointers to a high prolactin in women are irregular or absent periods and breast milk production. In men, symptoms include loss of sex drive and erectile dysfunction.
- A high prolactin may be caused by a benign tumour of the pituitary gland called a prolactinoma, but there are a number of other causes including pregnancy and several different drugs.
- Only about 5% of small prolactinomas increase significantly in size with time.
- Large prolactinomas may cause problems because of their size, including peripheral vision problems and low levels of other pituitary gland hormones.
- Treatment is usually with medications such as cabergoline or bromocriptine taken in tablet form.

Prolactin is a hormone made by the pituitary gland, a small gland situated at the base of the brain, and circulates in the blood in all people. It probably has many roles that we don't yet understand, but in women, one of the main ones is to prepare the breast for the job of breastfeeding, by encouraging milk production.

During pregnancy, the level of prolactin in the blood goes up, and remains higher than usual after the baby is born while the mother is breastfeeding. During this time, the woman often remains without a period, this too is a result of the high prolactin levels. Different women may be more or less sensitive to prolactin, which probably accounts for why some women get their period back earlier than others.

Sometimes prolactin levels may rise for reasons other than the natural ones just outlined. In women, this may become noticed as a change in menstrual cycle (missed periods), infertility or developing a milky discharge from the breast. This is known as galactorrhoea. Not all women with galactorrhoea have a high prolactin, just as not all women with a high prolactin have galactorrhoea. Similarly, some women may lose their period with just a slight rise in prolactin, while others still have regular periods despite levels two or three times normal.

In men, there may be no symptoms at all. However, high levels frequently reduce libido (sex drive) and may cause erectile dysfunction and infertility. Where a raised prolactin causes a lowering of sex hormones (oestrogen in women and testosterone in men), there can be important long-term effects on bone and muscle tissues. For these reasons, a specialist assessment of the high prolactin is always warranted.
What else causes high prolactin?

There are many causes of a high prolactin. Stress can cause a brief rise in some cases. A common cause is drug-induced. A number of medications may increase prolactin levels, including those used to treat some psychiatric conditions, painkillers such as morphine, anti-depressants, anti-nausea drugs and some blood pressure medications.

People on a methadone programme commonly have a raised prolactin. Other causes include liver and kidney disease, epileptic seizures, an under-active thyroid (hypothyroidism), polycystic ovary syndrome (mild increase occurs in 20%), injury to the chest or skin conditions on the chest such as shingles.

If the above causes have been excluded, then the possibility that there is an abnormality of the pituitary gland needs further investigation. Sometimes a group of prolactin-producing cells in the pituitary gland start to divide more rapidly and eventually produce a small growth or tumour. These are almost always benign – pituitary cancer is extremely rare. Pituitary tumours that make prolactin are called prolactinomas.

Tell me more about prolactinomas

Prolactinomas account for about a third of pituitary tumours. They are classified according to size, those less than 10 mm are called microprolactinomas, while those 10 mm or greater are called macroprolactinomas. The smaller microadenomas commonly present in women with irregular or absent periods and or breast milk production, problems directly related to the excessive prolactin levels. However, if the tumour becomes large it may press on the important eye nerves causing a loss of peripheral vision and interrupt the function of the rest of the pituitary gland.

Very rarely, a prolactinoma may invade other nearby structures which can cause double vision and other problems. Fortunately very few (about 5%) of microprolactinomas increase in size even if left untreated, but we have no way of telling which tumours are more likely to enlarge. Men tend to have larger tumours than women, and there is some evidence that prolactinomas are more aggressive in men.

Sometimes pituitary tumours other than prolactinomas may cause an increase in prolactin. Prolactin is kept under control by a substance called dopamine which comes from an area called the hypothalamus, just above the pituitary at the base of the brain. If a pituitary gland tumour that is "non-functioning" (not making any hormone) blocks the flow of dopamine, the prolactin level goes up.

Sometimes it can be hard to tell if the tumour is really a prolactinoma or a non-functioning tumour, but the prolactin levels are usually higher in a prolactinoma. Making this distinction is important because the treatment differs.
Treatment

For most people with a raised prolactin not caused by pregnancy, breastfeeding or medications, treatment is recommended. The exception to this would be the woman with a mildly raised prolactin but normal, regular periods.

The standard treatment is with medications known as dopamine agonists. The two most commonly used are cabergoline and bromocriptine. Cabergoline is a newer drug with a lower rate of side effects (see below). Often it can be given only once or twice a week. Treatment with these medications usually restores the prolactin level to normal, brings about the return of normal regular periods and the breast milk disappears. Women trying to get pregnant have a greater chance of doing so and women not desiring pregnancy need adequate contraception (which they may not have needed before).

Larger tumours may be more resistant to these medications, and require a higher dose. Occasionally a surgical operation is needed for the small number of tumours that do not shrink in response to the medication, or where the diagnosis is in doubt. Small tumours in women are usually treated until menopause, while large tumours in both sexes may require life-long treatment.

If a woman is seeking pregnancy, generally the medication is stopped as soon as pregnancy is diagnosed. The woman is followed up at least once every three months, and the medication is only restarted if there are signs that the pituitary gland tumour is increasing significantly in size. Most women do not require treatment during pregnancy and breastfeeding. In fact 25 to 30% will have resolution of the high prolactin after a successful pregnancy.

Side effects of treatments

The medications used, including cabergoline and bromocriptine have the following side effects:

Nausea, light-headedness on standing, stuffy nose, constipation, cold hands and feet. Some people notice an intolerance to alcohol.

These side effects are less common with cabergoline than with bromocriptine. Nausea is reduced by taking the medication with food, and building up the dose gradually.

Because bromocriptine has been available since the 1970s, it is established to be safe during early pregnancy. The experience with cabergoline in pregnancy is more limited, but data so far does not indicate a risk of malformations in a baby whose mother received cabergoline around the time of conception.

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