HORMONAL THERAPY OF LUTEINISED UNRUPTURED FOLLICLE

Hormones and hormone-derived medications used in the treatment of luteinised unruptured follicle syndrome.

About Hormonal therapy of luteinised unruptured follicle

Hormonal therapy of luteinised unruptured follicle syndrome utilizes hormones and hormonally active medications in the treatment of luteinised unruptured follicle (LUF) syndrome.

In luteinised unruptured follicle syndrome, the dominant ovarian follicle (a small pouch lined with cells that contains an oocyte, Pic. 1) fails to rupture and release the oocyte, resulting in absent ovulation. Despite this, the follicle undergoes luteinisation (change in cell structure and function) induced by LH (luteinising hormone). Therefore, normal amounts of progesterone are produced and the cycle is regular. LUF may be a subtle cause of infertility, as the hormone levels including progesterone appear completely normal. LUF are reported to occur in about 10% of cycles in healthy women. In infertile women, the incidence is higher, however as the diagnosis requires continuous ultrasound monitoring, the real extent of the syndrome remains unclear.

LUF syndrome may be treated with hormonal therapy. This includes naturally occurring gonadotropins (hCG (human chorionic gonadotropin) or and hMG (menotropin; human menopausal gonadotropin). hCG is an analogue to LH which naturally induces ovulation, so it can be used to trigger the ovulation. hMG maintains low levels of FSH (follicle-stimulating hormone) and high levels of LH within post-menopausal women. This state corresponds with similar hormonal balance during natural ovulation and therefore its administration may help to trigger ovulation.

Hormonal therapy may be substituted or combined with specific drug administration. These medications include clomiphene citrate and letrozole, both up-regulating FSH concentration due to negative feedback on oestrogen levels. Clomiphene citrate inhibits oestrogen receptors in the hypothalamus, inhibiting negative feedback of oestrogen on gonadotropin release (Pic. 2), leading to increased FSH levels with consequential maturation of follicle. Letrozole is an aromatase inhibitor that stimulates FSH release by blocking the conversion of androgen to estradiol and increases FSH receptors in the ovarian tissue.

Success or failure factors

As there seems to be a relation between hormonal balance, size of follicles and treatment outcomes, the stimulation of FSH inducing the growth of follicle may prove beneficial to a certain level. The two drugs commonly used for this purpose are clomiphene citrate and letrozole. Both of these drugs utilize the negative feedback mechanism of estrogen levels to increase FSH secretion, although each by a different pathway. Letrozole is a suitable and cost-effective ovarian stimulation agent that is associated with higher ovulation and pregnancy rates compared to clomiphene.

Complications

Ovulation induction by exogenous gonadotropin administration is associated with the risk of several
complications. The most severe ones include:

**Ovarian hyperstimulation syndrome**

Ovarian hyperstimulation syndrome (OHSS, PGC 3) is a clinical symptom complex associated with ovarian enlargement resulting from exogenous gonadotropin therapy.

In severe cases, a critical condition develops with massive ascites (fluid accumulation in the abdominal cavity), marked ovarian enlargement, pleural effusion, electrolyte imbalance, hypovolemia (decreased volume of circulating blood) with hypotension (low blood pressure), oliguria (low production of urine), hemoconcentration (abnormally viscous blood), and thromboembolism (occlusion of arteries by blood clots).

Moderate to severe ovarian hyperstimulation syndrome (OHSS) has been calculated to occur in 0.2% to 2% of all ovarian stimulation cycles. Severe OHSS can be a life-threatening complication. The prognosis is usually worse in patients who get pregnant and have this syndrome.

**Allergic reaction**

The patient may develop an allergic reaction to one or more components of the hCG injection. Signs and symptoms of an allergic reaction include hives, itching, swelling of the tongue, lips or throat, and difficulty breathing. The most severe type of such an allergic reaction is called an anaphylactic shock and can be lethal. Patients presenting with the mentioned symptoms should immediately seek medical care.

**Prognosis**

Due to a lack of extensive studies, the reported incidence of LUF among infertile women varies greatly, from 6% up to 79%. However, LUF cycles are reported to occur even in fertile patients in up to 47% of cases. Anovulatory cycles characterised by LUF development are not necessarily continuous in infertile women, but may alternate with ovulatory cycles. In infertile women where the cause is identified as LUF syndrome, it is crucial to correctly establish the diagnosis, which enables proper treatment of the condition with hormonal therapy.
A microphotograph of a dominant ovarian follicle, called also Graafian follicle. This follicle contains an oocyte (egg cell), which is released during ovulation.

Illustration of how estrogen (4) levels inhibit the secretion of FSH (1) via negative feedback mechanism. When estrogen levels are low, FSH level rises.

An ultrasonography image of a mild OHSS case. Fluid accumulated in the abdominal cavity is seen as the dark mass, and the ovary is enlarged.

Sources


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