

# Growth hormone in the management of female infertility

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### ABSTRACT

Growth hormone (GH) is involved in the regulation of male and female infertility and has been used in the management of both male and female infertility. GH is also produced by the ovary apart from it being produced from pituitary. GH helps in monofollicular growth. GH therapy is one of the adjuvant treatment used in ovarian stimulation and Assisted Reproductive Technologies Assisted Reproductive Technology (ART). GH supplementation has been shown to improve pregnancy rates in poor responders. Growth hormone cotherapy has a definite role to play in ovarian stimulation and is effective in appropriately selected cases. However, it cannot be recommended indiscriminately in every patient undergoing ovarian stimulation or assisted reproductive technology.

**Key words:** Assisted Reproductive Technology, growth hormone, infertility, *in vitro* fertilization, ovulation induction

Growth hormone (GH) is a pleiotropic, multifunctional hormone with effects ranging far beyond those on linear growth. GH is involved in the regulation of male and female infertility and has been used in the management of both male and female infertility. This brief communication highlights the potential utility of growth hormone in female infertility.

GH is produced not only by the pituitary but also locally by the ovary. It binds to GH receptors on granulosa, thecal, and luteal cells, thus promoting steroidogenesis and gametogenesis. Growth hormone, IGF-1, and GHRH, all increase the sensitivity of ovaries to gonadotropin stimulation and enhance follicular development.<sup>[1]</sup> Growth hormone also enhances aromatase and 3- $\beta$ -hydrogenase activity, thus increasing the conversion of androgen

into oestrogens in females. This effect on the ovarian steroidogenic enzymes occurs through a direct and/or IGF-I mediated mechanism. Growth hormones, IGF-1 and IGF-2, all affect the maturation of the follicle and gamete as well.

GH directly inhibits follicle apoptosis in conjunction with gonadotropins and may enhance follicular survival and cell proliferation by strengthening LH action.

Both GH and IGF-I play a role in the recruitment of the dominant follicle from its cohort, leading to monofollicular growth in women.<sup>[2]</sup> When GH is deficient, low serum levels of IGF-I prevent the dominant follicle from increasing IGF-I levels. This allows equal multifollicular growth. With GH treatment, a differential in sensitivity to follicle stimulating hormone Follicle-stimulating hormone (FSH) between this follicle and its cohort are restored by higher IGF-I levels, leading to monofollicular growth.

Oocytes harvested from follicles with normal antral fluid GH concentration are more fertile than those from follicles with low GH concentrations. Growth hormone enhances oocyte quality by accelerating and coordinating cytoplasmic and nuclear maturation, as seen in bovine oocytes.<sup>[3]</sup>

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Ovarian stimulation is an important treatment technique for female infertility. While ovarian stimulation is traditionally done with gonadotropins, clomiphene, or letrozole, many adjuvant therapies have been tried to improve the outcome of the procedure. Growth hormone is one such therapy.

Cotreatment of GH combined with hMG and hCG for ovulation induction has been suggested as a way to improve follicle growth, and probably pregnancy rate, in patients with hypogonadotropic hypogonadism.<sup>[4]</sup> This reduces gonadotropin dose requirement, reduces duration of hMG treatment, and improves success rates.<sup>[5]</sup>

Growth hormone might have an independent or an estrogen-mediated effect on uterine size,<sup>[6]</sup> which may contribute to its therapeutic effect. GH supplementation has been shown to improve pregnancy rates in poor responders.<sup>[7]</sup> In women with no history of poor response to IVF stimulation protocols, however, the use of growth hormone did not show benefits.<sup>[5]</sup>

Good patient selection has been shown to improve results of GH cotherapy for female infertility. Eugonadotrophic normoprolactinemic patients with long-standing infertility and documented growth hormone deficiency or pan hypopituitarism respond well to this treatment. Workers have, however, used GH in non-GH deficient patients as well.

Recent reviews have listed the doses of growth hormone used by various workers.<sup>[8]</sup> Doses used in recent reports have ranged from 0.9 to 1.8 mg/week, administered until pregnancy is proven. Previously, higher doses have been used.

Growth hormone cotherapy has a definite role to play in ovarian stimulation and is effective in appropriately selected

cases. However, it cannot be recommended indiscriminately in every patient undergoing ovarian stimulation or assisted reproductive technology. Research should be encouraged in this interesting field of gynecological endocrinology to understand appropriate patient selection for growth hormone therapy. Closer collaboration between reproductive and medical endocrinologists is required in order to achieve optimal therapeutic benefits of this hormone.

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