Luteinizing Hormone and Folliclestimulating Hormone Synergy

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Abstract:
Proper development and maturation of follicles are encouraged by LH and FSH, both of which are produced in the ovaries. When it comes to ART, the hormone FSH is often injected. More excellent knowledge of the LH-FSH relationship has been gained via recent research. However, questions remain about LH's involvement in stimulating follicles, the appropriate amount of LH used in stimulation, and its value for older individuals. Although individuals with hypogonadotropic hypogonadism need the injection of exogenous LH with FSH for controlled ovarian stimulation, nothing is known about its use in other patient groups. In order to better understand the LH requirement in ART patients, we examined the multiple activities that LH fulfills in addition to FSH.

Keywords: *Assisted reproductive techniques, follicle-stimulating hormone, luteinizing hormone*

1. Introduction

Male infertility and subfertility are public health issues since they affect about 15% of all couples [1] and account for nearly 50% of all cases [2]. In addition, the amount and quality of sperm have declined worldwide [3]. Understanding the processes governing spermatogenesis's start and maintenance is critical to developing effective treatments for a condition that has been poorly understood for a long time. Sertoli, Leydig, peritubular, and germ cell contacts all play a role in controlling spermatogenesis, which includes the differentiation and proliferation of spermatogenic cells [4–7].

One of the essential hormones in human reproduction is LH, Follicle-stimulating hormone (FSH), and follicular growth hormone (LH) promotes ovulation and follicular development FSH and LH work in concert to promote healthy follicular development.

In assisted reproductive technologies, FSH is often employed (ART). Recombinant human FSH (r-FSH, also known as a recombinant human follicle-stimulating hormone) injections are the most regularly used artificial insemination (ART) method. "Gonadotropin-releasing hormone (GnRH) agonist or blocker is administered daily to avoid early LH surge and premature ovulation. Endogenous pituitary suppression, accomplished with GnRH analogs, generates an environment in which the LH level is insufficient or very low, which may be deleterious to the growth of normal healthy follicles".' Studies have demonstrated that the presence of LH affects the growth of developing follicles, making it more critical [8]. Patients with low LH concentrations after GnRH analog medication for pituitary suppression had worse outcomes, as documented data show [9-10].

IVF cycles may benefit from LH supplementation since recombinant human LH is now available (r-hLH) Studies on R-LH in women who underwent IVF with GnRH analogs and r-hFSH have mixed results According to one study, r-hLH supplementation decreased cumulus cell apoptosis less than FSH treatment alone, implying higher oocyte quality in LH-supplemented cycles R-hLH decreased cumulus cell mortality, which might be owing to a growth factor generated by granulosa/theca cells in response to LH/FSH and other proliferative/apoptotic factors termed follicular fluid vascular endothelial growth factor (FVEG) (FF VEGF-marker of maturation and quality of oocytes) [11-12] According to these

studies, LH may have a significant role in COH An advanced age (over 35 years), an insufficient ovarian reserve, an ineffective response to past IVF cycles, and genetic variations are all factors that contribute to a poor outcome for patients with COH (AMH) [13] It seems that LH supplementation may be advantageous to a specific group of patients, particularly older or who are less responsive to treatment This may be attributed to the higher oocyte quality in these ART patients owing to the restored follicle quality after the conclusion of stimulation [14] As our data show, a patient's need should be the driving cause for r-hLH usage in ART.

Supplementing LH with FSH hormone is now well understood, although research into its use in ART patients remains scarce despite recent advances in scientific knowledge. When it comes to ART patients, LH plays a variety of functions that FSH does not, and this review aims to provide light on why.

2. Follicle-Stimulating Hormone

The pituitary secretes and exports Follicle Stimulating Hormone, which mostly affects Sertoli cells, although it is also possible that interstitial testicular macrophages react to Follicle Stimulating Hormone. Each of the two components of FSH is a glycoprotein hormone. Gonadotropin-releasing hormone (GnRH) stimulates its pulsatile release in response to luteinizing hormone-releasing hormone (LHRH). Sertoli cell-secreted inhibin is part of a feedback loop from the pituitary to the testis to suppress FSH production. The bulk of the actions of FSH are thought to be mediated through the conventional cAMP second messenger pathway. FSH has a drastically different effect on adult and immature animals. When FSH levels rise, the testicles expand, spermatogenesis begins, and the somniferous tubules expand. This is why FSH is sometimes referred to as the "puberty hormone." Sertoli cells move from responding to FSH to testosterone once this occurs, and many of the juvenile animal's FSH-regulated tasks are taken over by testosterone as an adult. FSH's mechanism of action in the adult is unclear, however its relevance seems to differ across species. In the adult rat, FSH suppression has little effect on spermatogenesis, however in nonhuman primates it has a significant impact on sperm production and spermatogenesis. However, FSH seems to have only a little impact on the mitotic growth of the undifferentiated and differentiating population when administered to rats. It seems that FSH regulates the growth of spermatogonia stem cells in primates.

Seasonal breeding animals seem to be regulated by follicle stimulating hormone, which increases the number of Leydig cells and reactivates spermatogenesis in response to a stimulating photoperiod in the animals. Additionally, it is likely that prolactin plays a significant role in these species by modulating LH receptor numbers and so influencing the Leydig cell's response to LH" [15].

3. Result

3.1 Optimizing follicle-stimulating hormone dosing

The chance of developing multiple follicles is linked to four factors, according to several studies: (a) the first dosage of FSH to be administered, (b) the length of the first dosage before increasing or decreasing it, the rate at which the FSH dosage is increased at each increment [16] and (d) the amount of FSH that is reduced after the selection of one of the chosen follicles [17].

Preventing overstimulation and multiple pregnancies may be prevented by beginning with a modest dose of FSH [26] and gradually increasing the daily dosage [17].

3.2 Exogenous luteinizing hormone supplementation

LH plays a crucial role in controlling steroidogenesis; sufficient LH is especially crucial for oocyte maturation [39]. Many Asian assisted reproduction practitioners employ both lengthy agonist and antagonist regimens to stimulate the ovaries. More prolonged agonist procedures have produced additional data on the positive benefits of exogenous LH in individuals who had previously had unsatisfactory responses or low baseline blood LH concentrations [28]. After therapy with GnRH

agonists, and documented data show that patients with low LH concentrations have a worse prognosis [18].

It was highly recommended by the Asia-Pacific Fertility Advisory Group [13] in 2011 to treat individuals who had a history of poor response to therapy with r-hLH and r-hFSH:
1.In extended agonist cycles, the day 6 response is less than optimum.

- If there are no more than six-millimeter-thick endometrial cells,
- then there are no more
- than six-millimeter-thick follicles.

2.The use of r-hLH in women over 35 undergoing ovarian stimulation using long-term agonist or antagonist regimens may also be advantageous [13].

4. Discussion

4.1 The origin of hCG in hMG

High purity hMG (HP-HMG) is usually manufactured entirely from postmenopausal women's urine, and no exogenous hCG is employed in treatment. This is not correct, sadly, "Because more LH molecules are lost during the purification process of a hMG preparation [19]. The quantity of exogenous hCG needed to restore the appropriate FSH:LH ratio of 1:1 increases Purer urinary hMG products (e.g., Pergonal) comprised less exogenous hCG and more endogenous LH in a review of commercially available products [10].

In contrast, the bulk of the LH bioactivity was produced in HP-hMG by hCG supplementation. Prior to this investigation, Giudice [20] showed that the LH concentration was ten times higher than that of hCG, while van de Weijer and colleagues (2003) found that the immunoreactive hCG concentration was three times larger than LH concentration. In a subsequent investigation, it was revealed that hCG greatly influenced the bioactivity of HP-LH hMG To explain the enormous number of corehCG fragments in HP-hMG, it is required to presume that the hormone has been added from outside sources, which has been well established in hMG fabrication for standardization HCG has a longer half-life than hMG, making it more challenging to manage the given product when hCG is injected More exact dosing. Physiological activity is offered by r-hLH, which may be delivered alone or in tandem with r-hFSH, for controlling follicular development.

4.2 The production of progesterone

Activation of the LH/hCG receptors in the granulosa cells of the intrafollicular compartment is the principal driver of progesterone production HCG in hMG is thought to assist the conversion of progesterone to estradiol by providing LH-like activity Because there is no LH component, it is considered that this process is impossible if just r-FSH is employed This may be because women treated with GnRH analogs still have low levels of endogenous LH in their bodies. However, several studies show that ART only works when r-FSH is given [21].

"When the final follicular maturation triggers intrafollicular progesterone conversion to oestradiol, the endometrium becomes more receptive to embryo implantation" "The combination of r-hFSH with the conversion of progesterone to oestradiol by the hCG contained in hMG may result in better outcomes than using just hCG alone Pregnancy rates were elevated in a subset of the MERIT study because of an insufficient post-hoc examination of blood hCG levels [22]. "However, cytochrome 17a-hydroxylase-C17,20 lyase (P450-17) and 3-hydroxysteroid dehydrogenase [3HSD] (which converts pregnenolone to progesterone) are hormone-converting enzymes that can only be found in ovarian thecal/interstitial cells [23]. According to the findings of this research, progesterone does not seem to be converted into estrogen in the follicular compartment hMG-induced progesterone levels were 2–3 times higher than those induced by urinary FSH or r-hFSH, according to Wolfenson et al. [21] in vitro follicle bioassay data [22-27].

5. Conclusion

Ovulation is dependent on the complicated interplay between FSH and LH, as well as their complementing functions. Poor ART outcomes may be caused by low endogenous LH production. Assisted reproduction results may be enhanced in people with hypogonadotropic hypogonadism and those over 35 years of age if they receive exogenous LH; [28-30]. However, the amount of LH is crucial since high levels of LH may harm ART treatment. As a result, optimizing the FSH dosage in different patient populations and supplementing LH in specific subgroups may enhance ART outcomes. Identifying women who need exogenous LH requires the use of biomarkers [31-32]. With the growing evidence of pharmacogenetic techniques, it is anticipated that the patient's genetic composition will also drive the choice of an ART regimen. "Prior to deciding on exogenous LH, we recommend identifying patients who would benefit the most from LH supplementation and evaluating the cost-benefit ratio of exogenous LH usage" For the time being, further study is required to get an agreement on the optimal dose, timing, and patient group for LH supplementation.

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