

Human derived and recombinant gonadotropins: an overview

Prof. Marco Filicori

Reproductive Endocrinology Center, University of Bologna, Bologna, Italy

Controversy surrounds the use of different gonadotropin preparations for ovulation induction and controlled ovarian stimulation (COS). Hormone content, serum levels dynamics and mechanism of action are important parameters for the activity of exogenous gonadotropins. Recombinant (r) FSH is devoid of LH activity. Conversely, hMG and highly purified (HP) hMG contain relevant amounts of LH activity in the form of human derived LH and hCG; the hCG contained in HP hMG contributes in a substantial manner to the overall LH activity of this preparation. hCG has a longer plasma half-life than LH and provides a more prolonged and stable occupancy of LH receptors; furthermore, it was suggested that hCG can promote uterine and endometrial angiogenesis, a crucial process involved in embryo implantation. hMG and HP hMG stimulate serum estradiol more effectively than FSH-only products and do not cause premature luteinization.

Other factors may influence treatment and hormone dynamics during different drug regimens. We showed that serum levels of immunoreactive FSH are significantly higher among patients receiving hMG or HP hMG due to the reduced acidity of rFSH isoform composition that affects serum half-life. Conversely, rFSH is more efficient than hFSH (but not hMG/HP hMG) to stimulate the granulosa cell aromatase system and estrogen secretion also because of its isoform composition. Other new gonadotropin preparations such as rLH, rCG and low-dose hCG can be used to optimize treatment outcome or replace currently employed formulations; additional information will be needed to fully assess these new drug regimens.

Most individual studies and meta-analyses have not detected significant differences in clinical outcome between recombinant and human derived gonadotropins. The safety record of human derived gonadotropins has been outstanding over 40 years of clinical use. Because of their endocrine characteristics hMG/HP hMG are particularly suited for the treatment of hypogonadotropic hypogonadism and in ART when endogenous LH is profoundly suppressed by GnRH analogs. Otherwise, both recombinant and human derived gonadotropins are effective and safe and can be applied for human treatment in ART.