Subgroup analyses in Orgalutran trials

Dear Sir,

I read with interest the European–Middle East Orgalutran trial (The European Orgalutran Study Group et al., 2000) and I noticed that the study extensively monitored hormonal assays (LH, FSH, oestradiol). It is well known that sufficient stimulation of both theca cells and granulosa cells by LH and FSH is required for adequate oestradiol biosynthesis (Short, 1962; Schoot et al., 1992) and hence endometrial proliferation and receptivity. Recent in-vivo evidence also demonstrates that dominant follicle development and oestriol production are also dependent on late-follicular phase LH concentrations (Zeleznik et al., 1974; Sullivan et al., 1999).

However, in contrast to gonadotrophin-releasing hormone (GnRH) agonists, the suppression of LH secretion by GnRH antagonists is more pronounced than that of FSH (Hall et al., 1988). Whether this more pronounced suppression could have an impact on clinical outcome is still a matter of debate. I was wondering if a subgroup analysis was done in the antagonists-treated group (those who got pregnant and those who did not) based on the difference in ratios between basal FSH and LH and their concentrations on day of HCG administration.

References


Hesham Al-Innay, 8-Moustepha Hassanin St, Manial, Cairo 11451, Egypt

Dear Sir,

In the European Middle East trial of Orgalutran, a subgroup analysis was performed to evaluate the possible impact of LH concentrations during ovarian stimulation on the clinical outcome. Moreover, this retrospective analysis was performed over the pooled data of subjects treated with Orgalutran in three large controlled studies (The European Orgalutran Study Group et al., 2000; The European and Middle East Orgalutran Study Group, 2001; The North American Ganirelix Study Group, 2001), using criteria presented by Westergaard et al. (Westergaard et al., 2000).

Similarly, a threshold value of 0.6 IU/l (detection limit of LH immunoassay performed by central laboratory) on stimulation day 8 was chosen to discriminate between patients with low endogenous LH and normal LH. In total, 795 subjects were included in the analysis and 11.9% of these patients had an LH value <0.6 IU/l on stimulation day 8. The biochemical, clinical and ongoing pregnancy rate per attempt was 37.9 versus 33.0%, 34.7 versus 28.0% and 33.7 versus 24.0%, for those with LH <0.6 IU/l and ≥0.6 IU/l respectively. So, if this would be a clinical significant difference it would be in favour of those with undetectable LH (Mannaerts et al., 2000).

Our findings concur with those of a recently published study on the role of profound suppression of LH during ovarian stimulation, in which no significant differences were found in ovarian response, IVF/intracytoplasmic sperm injection outcome, implantation and early pregnancy loss between women with low day 7 LH levels applying different threshold values (0.5, 0.7 and ≤1.0 IU/l) and normal day 7 LH levels (Balasch et al., 2001).

References


Bernadette Mannaerts, Eric van Hooren and Peter Boerrigter

NV Organon PO Box 20, 5340 BH Oss, The Netherlands