GnRH agonist versus antagonist therapy

Dear Sir,

I read with interest the article titled ‘Human ovarian steroid secretion in vivo: effects of GnRH agonist versus antagonist (cetrorelix)’ (Garcia-Velasco et al., 2001) and I got a little confused. The addition of four patients (two at the beginning of the study and two at the end) in order to have matching groups suggests that the study was a retrospective one. This is further supported by the fact that the subjects selected for this study were a subset of women enrolled in another phase III clinical study. There is no mention of this being a retrospective study, either in the Abstract or the text. Being retrospective can explain why two different regimens of FSH were used in both groups: step-down and fixed dose with gradual increments as needed. If it is really a retrospective study—using material obtained from subjects enrolled in another trial—then the conclusion reached by the authors would be markedly questionable (in view of the very limited sample size).

Moreover, leuprolide acetate was given as 1 mg per day s.c. and the dose was adjusted according to the length of patient’s cycle in order to start the analogue 7 days prior to menstruation. In Table I it is confusing; the mean number of days of GnRH agonist was 12.2 while the mean total dose of GnRH agonist was 18.6 mg. The authors stated that, ‘if serum estradiol concentrations were beyond the cut-off point, the patient was excluded from the study’ and there is no mention of how many cases were excluded. Whether IVF was performed more than ICSI in the GnRH agonist-treated group is unclear from the data presented by the authors.

Finally, the authors claimed a higher fertilization rate in the antagonist-treated group and this was the cornerstone of their conclusions. It is interesting that this was not the case in previous well designed, well conducted, randomized controlled trials comparing agonist versus antagonist (The European Orgalutran Study Group, 2000; the European Middle East Orgalutran Study Group, 2001).

References


Dear Sir,

We thank the interest of Dr Al-Inany in our recent publication (Garcia-Velasco et al., 2001), but most of his concerns are clearly expressed in our manuscript. As stated in the title and discussed throughout the manuscript, the study of main interest was to test if there is any difference in human ovarian steroid secretion in vivo in IVF patients treated either with GnRH agonist or antagonist. Thus, we are dealing with an experimental setting where the main endpoint is to compare steroid concentration in follicular fluids and sera from IVF patients who have been previously treated with these two drugs, but not their clinical outcome. As stated in the Abstract and in the last paragraph of the Discussion, we reached a clear-cut conclusion, as a significant effect on ovarian follicular steroidogenesis was observed in women undergoing GnRH antagonist therapy. Secondary endpoints were several parameters of the ovarian stimulation, but the study was not designed to compare clinical outcome, as it was experimental data obtained from clinical patients undergoing a phase III, prospective, non-randomized clinical trial (Pocock, 1975).

There are already several well-designed, properly conducted clinical trials where their primary endpoint was the clinical outcome using the same GnRH antagonist we used (cetrotide) (Albano et al., 2000; Olivennes et al., 2000), but this was not our purpose, as explained in the Introduction section of the manuscript. Individual variation in the duration of the down-regulation period as well as different length of the stimulation period explains the differences between GnRH agonist mean total dose and mean number of days.

References


Hesham Al-Inany
8-Moustapha Hassanin St,
Manial, Cairo, 11451, Egypt
E-mail: kaainih@idsc.net.eg

Dear Sir,
Letters to the Editor


J.A.Garcia-Velasco1 and A.Pellicer
IVI–Madrid
C/ Santiago de Compostela 88,
28035 Madrid, Spain

1To whom correspondence should be addressed.
E-mail: jgvelasco@ivi.es