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Letters to the Editor

Luteal support post GnRH agonist trigger: do not stop too soon

Sir,

Humaidan *et al*. (2005) compared GnRH agonist (buserelin) and hCG triggers in a GnRH antagonist-based protocol. Luteal support was given for 12 days starting on the day following oocyte retrieval and stopping on the day of pregnancy test. The GnRH agonist group suffered a 79% early pregnancy loss.

Although recruitment for this study was complete by February 2004, recent studies have shown that triggering ovulation with a GnRH agonist causes complete luteolysis (Nevo *et al*., 2003), with the implication that luteal support is needed until week 9 of pregnancy (~2 weeks post luteal-placental shift). Without such support, a high rate of early pregnancy loss is inevitable.

References

Humaidan P, Ejdrup Bredkjaer H, Bungum L, Bungum M, Grondahl ML, Westergaard L and Yding Andersen C (2005) GnRH agonist (buserelin) or hCG for ovulation induction in GnRH antagonist IVF/ICSI cycles: a prospective randomized study. Hum Reprod 20,1213–1220.

Nevo O, Eldar-Geva T, Kol S and Itskovitz-Eldor J (2003) Lower levels of inhibin A and pro-alphaC during the luteal phase after triggering oocyte maturation with a gonadotropin-releasing hormone agonist versus human chorionic gonadotropin. Fertil Steril 79,1123–1128.

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Reply: Luteal support post GnRH agonist trigger: do not stop too soon

Sir,

We wish to thank Dr Kol for his letter regarding the length of the luteal support given in GnRH antagonist IVF/ICSI cycles in which ovulation was induced with a single bolus of a GnRH agonist. In our study (Humaidan *et al*., 2005) we showed that patients who were treated with a GnRH agonist for final oocyte maturation had a significantly lower implantation rate and clinical pregnancy rate as compared to patients treated with hCG for final oocyte maturation. At the same time the rate of early pregnancy loss was significantly higher. This occurred despite luteal support with micronized progesterone vaginally, 90 mg/day, and estradiol, 4 mg/day *per os*, administered from the day following oocyte aspiration and continuing until the day of the pregnancy test, i.e. a total of 13–14 days. We concluded that this protocol is not clinically acceptable in its present design.

Of course we cannot totally exclude that the length of the luteal phase support in the present set up could have an impact on the poor clinical results, as a prospective randomized study regarding this issue, according to our knowledge, has not been performed. But several factors support the results of our study.

First of all, Griesinger *et al*. (2004) in a study with a design similar to ours has obtained equally poor reproductive outcome results, despite luteal support with micronized progesterone and estradiol orally until 7 weeks of gestation.

Secondly, Dr Kol is one of the co-authors of a study by Itskovitz *et al.* (2000), including few patients, in which a low pregnancy rate per transfer (14.3%) was found in a non-randomized group of high-responder IVF/ICSI patients treated with a GnRH agonist to trigger ovulation. The low pregnancy rate was obtained despite luteal support until 9 weeks of gestation.

Thirdly, in the study by Fauser *et al.* (2002) pregnancy rates remained low and rates of early pregnancy loss high despite luteal support for >2 weeks in the two arms of the study in which ovulation was triggered with a GnRH agonist.

Finally, in the present study the mean plasma β-hCG levels on the day of the pregnancy test (day 12 after embryo transfer) were already significantly lower in the GnRH agonist group as compared to the hCG group, indicative of an early malfunction of the trophoblast, irrespective of the length of the luteal support given.

In conclusion, our present knowledge does not support the notion that the length of the luteal support, >12 days, has a major impact on the reproductive outcome when regarding the use of GnRH agonists to trigger ovulation. Other factors seem to play a key role. Given the fact that significantly more metaphase II oocytes (16%) were harvested in the GnRH agonist group, we are currently developing new strategies in an attempt to improve this protocol.

References

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