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LETTER

GnRH agonist administration in the luteal phase of IVF cycles: still an experimental approach

To the Editor

This letter concerns the study 'Single-dose GnRH agonist administration in the luteal phase of GnRH antagonist cycles: a prospective study' by Isik et al. (2009) that was published in a recent issue of Reproductive BioMedicine Online. The administration of gonadotrophin-releasing hormone (GnRH) agonists during luteal phases is a promising method for improving the outcome in IVF cycles hence we read this article with great interest.

The published results from the authors are very encouraging and confirm previous reports on the advantages of luteal administration of GnRH agonists in IVF cycles (Tesarik et al., 2004, 2006). However, we would like to add some thoughts on the discussion regarding the role of GnRH and GnRH agonists in luteal phase.

It seems that GnRH, as well as GnRH agonists, exerts its actions on both embryos and endometrium. It is well known that human embryos and luteal-phase endometrium express GnRH receptors (for a review, see Metallinou et al., 2007). GnRH seems to be a primary regulator of human chorionic gonadotrophin synthesis and secretion both in preimplantation embryos and in the placenta (Prager et al., 1992; Seshagiri et al., 1994). It has been also shown that incubation with GnRH agonist improves preimplantation development in murine embryos (Raga et al., 1999a). It is also known that GnRH agonists decrease, whereas GnRH antagonist increase, the expression of tissue inhibitors of matrix metalloproteinases in stromal cells, thus improving the implantation of embryos (Raga et al., 1999b). These points are in favour of the use of GnRH agonists as a luteal support, especially in GnRH antagonist cycles.

On the other hand, it is well documented that both isoforms of GnRH directly inhibits progesterone production in human granulosa luteal cells and at the same time increases the numbers of apoptotic granulosa luteal cells (Metallinou et al., 2007). Moreover, it has been shown that GnRH agonists suppress vascular endothelial growth factor (VEGF) and VEGF receptor expression in corpora lutea of rats (Kitajima et al., 1998). GnRH and, subsequently, GnRH agonists have been suggested as luteolytic factors. Based on its luteolytic properties, luteal GnRH administration has been used successfully to prevent ovarian hyperstimulation syndrome (Endo et al., 2002; Nikolettos et al., 2003).

Inhibition of progesterone production, decrease of VEGF and VEGF receptor expression and increase of apoptosis in granulosa luteal cells are unfavourable for the IVF outcome. Thus, we come to the point: is GnRH administration during luteal phase useful or not? The clinical studies of Isik et al. (2009) and Tesarik et al. (2004, 2006) provide encouraging data but, in our opinion, are not enough to establish this method of luteal support. As long as the direct ovarian and endometrial actions of GnRH and GnRH agonists remain obscure and at the same time there are no many large relevant clinical studies, the administration of GnRH agonists during the luteal phase should be considered as an experimental approach.

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