Clinical relevance for the fact that GnRH antagonists do not down-regulate the GnRH receptor

Sir,

It has been more than 10 years since safe and effective gonadotrophin-releasing hormone (GnRH) antagonists became available for use in controlled ovarian stimulation (COS) cycles. In 2000, we noted that there was an inconsistency with how researchers in this field describe the mechanism of action of GnRH antagonists (Mannaerts and Gordon, 2000). Unfortunately, there is continued misuse of terminology describing the differences in the mechanism of action of the two classes of GnRH analogs in articles published in Human Reproduction and Fertility and Sterility (Huang et al., 2012; Youssef et al., 2012). References to ‘GnRH antagonist down-regulated cycles’ or ‘pituitaries desensitized to GnRH antagonists’ are inaccurate and lead to confusion.

GnRH agonists have been used clinically since the mid-1980s to prevent the occurrence of a surge in LH, which may occur prematurely before the leading follicle reaches the optimum diameter for triggering ovulation with human chorionic gonadotrophin (Gordon and Hodgen, 1991). GnRH agonists reduce the incidence of a premature LH surge by suppressing gonadotrophin levels via pituitary desensitization and down-regulation following an initial short period of gonadotrophin hypersecretion (Conn and Crowley, 1991). Unlike GnRH agonists, GnRH antagonists cause an immediate and rapid inhibition of LH release by competitively blocking GnRH receptors in the anterior pituitary gland and thereby preventing endogenous GnRH secretion. Induction of ovulation after GnRH antagonists (Gordon and Hodgen, 1991). GnRH antagonists have the formal regulatory indication of prevention (inhibition in the USA) of premature LH surges in women undergoing COS prior to IVF/ICSI in most countries.

The fundamental mechanistic difference between GnRH agonists and antagonists has gained clinical significance as it has become apparent that ovarian hyperstimulation syndrome can largely be avoided by using a GnRH agonist bolus to trigger an endogenous LH/FSH surge to produce final oocyte maturation (Ron-El et al., 2000; Humaidan et al., 2010; Devroey et al., 2011). Importantly, this can only be achieved in a GnRH antagonist protocol as an LH/FSH surge cannot be induced with a GnRH agonist if the pituitary is down-regulated and/or desensitized.

Hence, in an attempt to simplify things moving forward we propose that the terms ‘pituitary inhibition’ or ‘pituitary suppression’ are used to signify the actions of GnRH antagonists and the terms ‘down-regulation’ and ‘desensitization’ are used to define the actions of GnRH agonists.

Elective single-embryo transfer in older women

Sir,

We thank Dr Gleicher for his commentary concerning our article ‘Elective single-embryo transfer in women aged 40–44 years’ (Niinimäki et al., 2012; Gleicher, 2012). We understand that in many countries the reimbursement system makes the implementation of the elective single-embryo transfer (eSET) into clinical practice very difficult. However, in the opinion article there are some misinterpretations of our findings, which we would like to correct.

The aim of our retrospective study was to look at the effect of eSET on pregnancy and live birth rates in women 40 years or older, as this embryo transfer strategy has not yet been studied in older patient population (Niinimäki et al., 2012). To evaluate the usefulness of eSET, it is essential to calculate the cumulative pregnancy rate including both fresh and frozen embryo transfers of one oocyte collection.

References


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