Reply: GnRH agonist for triggering final oocyte maturation: time for a critical evaluation of data

Sir,

We read with interest the letter by Kolibianakis et al., concerning our consensus paper by The Copenhagen GnRH agonist Triggering Workshop Group (Humaidan et al., 2011). In their letter, the authors conclude that ovarian hyperstimulation syndrome (OHSS) is reduced only in the OHSS high-risk patient and not in the normal OHSS-risk patient, by further subdividing the population of six recently published studies into normo-ovulatory (normal OHSS-risk patients) (Humaidan et al., 2006, 2010; Pirard et al., 2006; Papanikolaou et al., 2011) and high-risk OHSS patients—mainly polycystic ovary syndrome patients (Babayof et al., 2006; Engmann et al., 2008), using a modified luteal phase support after GnRHa trigger.

Clearly, the authors of the current letter focus on statistical significance. When analyzing the results of the four trials in the normal OHSS-risk patient, using a modified luteal phase support; however, still not 1 patient of a total of 188 patients triggered with GnRHa developed OHSS, compared with 3 of 189 patients (2%) triggered with hCG.

Moreover, the findings of the four studies performed in a donor oocyte population are completely ignored (Acevedo et al., 2006; Galindo et al., 2009; Melo et al., 2009; Sismanoglu et al., 2009). When analyzing the data from these studies, the OHSS incidence is 0% (0/230) after GnRHa trigger versus 8% (19/230) after hCG trigger. Importantly, the oocyte donor is a normo-ovulatory volunteer and special care is, therefore, taken to avoid OHSS. However, as mentioned, 8% of oocyte donors developed early-onset OHSS after hCG trigger. This further supports the OHSS preventive effect of GnRHa trigger even in the normal OHSS-risk patient.

The concept of modified luteal phase support after GnRHa trigger aims at transferring fresh embryos with a reproductive outcome comparable to that seen after hCG trigger. We are still in the process of describing the most optimal luteal phase protocol after GnRHa trigger—a protocol which should secure the reproductive outcome of the patient as well as eliminate the risk of OHSS. On this basis, we founded The Copenhagen GnRH Agonist Triggering Workshop Group—an international network of clinical scientists with a specific interest in GnRHa triggering.

Based on our present knowledge, we disagree with the authors’ statement that after further subdividing the data, ‘the picture is significantly different’. Although low-risk patients by definition will have a lower risk of developing OHSS, when hCG is used for triggering final oocyte maturation, only the use of a GnRHa trigger will completely eliminate that risk. Considering the medical, social and economical consequences of even one single case of OHSS, the clinical implications are not insignificant.

Although we understand that hCG triggering still remains the standard of care for triggering final oocyte maturation for the OHSS low-risk patient, we maintain that based on the available data, GnRHa triggering is a valid alternative to hCG triggering for both the low-risk and the high-risk patients.

Finally, we certainly agree that the time has come for a ‘critical evaluation of data’ as the health and well-being of a patient undergoing controlled ovarian stimulation is beyond the confidence interval of statistical significance.

References


