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Letters to the Editor

'GnRH agonist trigger: looking for the coin under the lamp post?'

S.Kol
IVF Unit, Department of Obstetrics and Gynaecology, Rambam Medical Center, POB 9602, Haifa 31096, Israel

E-mail: skol@rambam.health.gov.il

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Sir,

The main advantage of GnRH agonist trigger is its ability to totally prevent ovarian hyperstimulation syndrome (OHSS). Ethical considerations cast a serious doubt on our ability to conduct a randomized controlled trial (RCT) to assess agonist versus HCG trigger in the context of OHSS prevention. Similar considerations prevent us from conducting an RCT on the benefit of a parachute when jumping from an airplane in mid-air (Smith and Pell, 2004). Since evidence-based medicine and RCTs are the current gods of medical research, it leaves no alternative but to compare the two triggers in normal responder. Why look for an alternative to HCG in the normal responder is not clear; however, an RCT can be easily performed under these circumstances. Consequently, Kolibianakis *et al*. (2005) chose to repeat previous work (Fauser *et al*., 2002) to conclude that agonist trigger results in lower pregnancy rate compared to HCG.

Unfortunately, these publications may undermine efforts to curb OHSS occurrence, as practitioners are left with the impression that agonist trigger should be abandoned altogether. OHSS is still there. A reliable method for its prevention is urgently needed, if not for the leading centres in Western Europe (in which OHSS is extremely rare, apparently), then for the rest of the world. Is the true occurrence of OHSS higher than reported (Delvigne, 2005)? Agonist trigger prevents OHSS by inducing irreversible luteolysis (Kol, 2004). The scientific community must find a way to bring this gift to OHSS high-risk patients. Agonist trigger can save patients lives.

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Reply: 'GnRH agonist trigger: looking for the coin under the lamp post?'

Sir,

We would like to thank Dr Kol for his interest in the study by Kolibianakis *et al*. (2005), published in *Human Reproduction*. It is clear that Dr Kol does not express any criticism regarding the way the study was designed and performed, the way the data were analysed or regarding the conclusions drawn.

Dr Kol suggests that the GnRH agonist trigger totally prevents ovarian hyperstimulation syndrome (OHSS); however, it has been suggested that this is not always true (van der Meer *et al*., 1993). Moreover, he questions the rationale of performing a randomized controlled trial (RCT) comparing agonist versus HCG for triggering final oocyte maturation in normal responders, although he acknowledges that this is the only population in which such a comparison can be performed for ethical reasons. In addition, although Dr Kol appears to criticize the standard knowledge approach of testing hypotheses by RCTs, he does not suggest a more efficient way of approaching the truth.

Dr Kol appears to be concerned that the recently published studies (Humaidan *et al*., 2005; Kolibianakis *et al*., 2005) comparing GnRH agonists versus HCG for triggering final oocyte maturation could undermine efforts to curb OHSS occurrence. We, in contrast, are in favour of any properly conducted study that leads to valid conclusions regarding the hypothesis tested and thus is enhancing our knowledge in IVF. It was important to know if an intervention (administration of GnRH agonist for triggering final oocyte maturation), proposed with the aim to prevent a serious complication of IVF treatment (OHSS), was not affecting adversely at the same time the goal of IVF treatment (achievement of pregnancy). The study by Kolibianakis *et al*. (2005) has shown that the replacement of HCG by GnRH agonist is not feasible in IVF, as it results in a significantly decreased probability of ongoing pregnancy.

Dr Kol appears to make a distinction between the leading centres in Western Europe in which, as he mentions, 'OHSS is extremely rare, apparently', and the rest of the world (in which, OHSS occurrence is apparently higher). We do not have comparative data to agree or disagree with this statement. However, OHSS occurrence is related to the way patients are stimulated,

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