Prediction of ovarian hyperstimulation syndrome: why predict if we can prevent!

Dear Sir,

Ovarian hyperstimulation syndrome (OHSS) continues to be a serious and potentially life-threatening complication of ovarian stimulation. A World Health Organization report states that the world-wide incidence of severe OHSS is 0.2–1% of all assisted reproduction cycles, with a 1:45 000–1:50 000 mortality per infertile women receiving gonadotrophins. Following IVF, the overall incidence of OHSS is estimated at 0.6–14% (Hugues, 2002).

Not surprisingly, continuous efforts have been invested in tools that will enable prediction and ultimately prevention of OHSS. In his recent debate article, Orvieto (2003) discusses the chaotic problem of OHSS prediction. In short, current prediction strategies appear to be unreliable, and additional studies are needed to establish new prediction guidelines.

The frustration with this current situation intensifies in light of the fact that for more than a decade the fertility community had in its arsenal a most reliable strategy that totally prevents OHSS (Itskovitz *et al.*, 1991). Since then, numerous publica-

tions have described the astonishing phenomenon of total luteolysis and OHSS prevention following GnRH agonist-triggered ovulation (even in extreme responses to ovarian stimulation). The recent introduction of GnRH antagonists was predicted to increase the interest in this approach (Itskovitz-Eldor *et al.*, 2000; Kol and Itskovitz-Eldor, 2000).

Those who object to this winning strategy for OHSS prevention keep citing a paper by van der Meer *et al.* (1993). Indeed, this unfortunate publication was the focus of a previous debate (Kol *et al.*, 1996). In short, three patients prepared for intrauterine insemination were incompletely triggered with a nasal GnRH agonist preparation (Suprefact), and developed mild to moderate OHSS. Although of marginal significance in the context of OHSS prevention, given its impressive title, this paper has been cited (see WHO publication above) time and again to show that there is no magic bullet to OHSS prevention (do I hear a deep sigh of relief?...). After all, it is inconceivable that the fertility community puts so many patients (for so many years) in danger of OHSS, while a simple treatment exists that prevents it altogether.

Sorry, there is a magic bullet! If ovulation is triggered with indictable preparations (we use 0.2 mg of triptorelin), it is guaranteed that OHSS with be totally avoided with good clinical outcome (pregnancy rate) if adequate luteal support is given.

I urge the fertility community to put this approach to the test. This may help to prevent countless hospitalizations and even deaths.

References

- Hugues, J.N. (2002) Ovarian stimulation for assisted reproductive technologies. In Vayena, E., Rowe, P.J. and Griffin, P.D. (eds). Current Practices and Controversies in Assisted Reproduction. World Health Organization, Geneva, Switzerland, pp 102–125.
- Itskovitz, J., Boldes, R., Levron, J., Erlik, Y., Kahana, L. and Braudes, J.M.(1991) Induction of preovulatory luteinizing hormone surge and prevention of ovarian hyperstimulation syndrome by gonadotropin-releasing hormone agonist. *Fertil. Steril.*, **56**, 213–220.
- Itskovitz-Eldor, J., Kol, S. and Mannaerts, B. (2000) Use of a single bolus of GnRH agonist triptorelin to trigger ovulation after GnRH antagonist ganirelix treatment in women undergoing ovarian stimulation for assisted reproduction, with special reference to the prevention of ovarian hyperstimulation syndrome: preliminary report: short communication. *Hum. Reprod.*, **15**, 1965–1968.
- Kol, S. and Itskovitz- Eldor, J. (2000) Severe OHSS: Yes, there is a strategy to prevent it! *Hum. Reprod.*, 15, 2266–2267.
- Kol, S., Lewit, N. and Itskovitz-Eldor, J. (1996) Ovarian hyperstimulation syndrome after using gonadotrophin-releasing hormone agonist as a trigger of ovulation: Causes and implications. *Hum. Reprod.*, 11, 1143–1144.
- Orvieto, R. (2003) Prediction of ovarian hyperstimulation syndrome. *Hum. Reprod.*. **18**, 665–667.
- van der Meer, S., Gerris, J., Joosten, M. and Tas, B. (1993) Triggering of ovulation using a gonadotrophin-releasing hormone agonist does not prevent ovarian hyperstimulation syndrome. *Hum. Reprod.*, **8**, 1628–1631.

Shahar Kol

IVF Unit, Department of Obstetrics and Gynecology, Rambam Medical Center, POB 9602, Haifa, Israel 31096 E mail: skol@rambam.health.gov.il

DOI: 10.1093/humrep/deg302