Reply: HCG supplementation of controlled ovarian stimulation cycles

Sir,

We would like to thank Dr Manno for the comments regarding pre-ovulatory progesterone levels in our paper on controlled ovarian stimulation with hCG supplementation (Thuesen et al., 2012).

Dr Manno concluded that our study was another study denying a prognostic value to pre-triggering P4 levels. We think that our study should not be used to clarify a possible role of elevated progesterone levels on the day of hCG in relation to pregnancy. The reason for this is simply because the study sample was limited to 60 patients divided into four groups, and hence not powered to allow conclusions on pregnancy or delivery rates. The key importance of our study was to show that within the hCG dose range of 0–150 IU/day, supplementation with hCG did not seem to reduce but rather to increase late follicular phase progesterone levels.

Concerns have been published regarding the capacity of commercially available assays to measure progesterone in the follicular phase (values <1.5 ng/ml). The minor changes during the follicular phase are detectable only with assays validated in the lower measurement range (Bosch et al., 2010). Coucke et al. (2007) showed in a nationwide quality control study done on samples from single bleeds, which were measured by ID-GCMS to define target values, that methods for progesterone on automated systems are not uniformly well calibrated. Some assays lack the sensitivity and precision for the low pre-ovulatory progesterone concentration ranges. The chemiluminescence assay used in our study was found suitable to measure progesterone concentrations in the follicular phase. Furthermore, to reduce variability all samples were quantified in the same run.

We agree on the critical importance of the assays used to quantify small increases in P4 values and look forward to reading further data from Manno et al. regarding their observations of the discrepancy between the prognostic value of P4 pre-triggering levels in two different clinical settings using different immuno-metric methods for P4 determination.

The meta-analysis of Venetis et al. (2007) failed to show a significant association between raised late follicular-phase progesterone concentration and the probability of clinical pregnancy. This may be due to different cut-off values and different methods of analysis in the studies (Coucke et al., 2007). We thus agree it is time for a new meta-analysis. At the ESHRE 2012 Annual Meeting, unpublished data from a new meta-analysis by Venetis were presented. This updated version of the meta-analysis showed that elevated progesterone during mid-to-late follicular phase was associated with a decreased probability of pregnancy.

References


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