Letters to the Editor

HMG is possibly superior to recombinant FSH for IVF

Dear Sir,

I read with interest the manuscript by Ng et al. (Ng et al., 2001). After a series of studies suggesting that recombinant human FSH (rhFSH) may produce superior pregnancy and implantation rates compared with human menopausal gonadotrophin (HMG), as summarized by the meta-analysis of Daya et al., more recent studies, as suggested by the meta-analysis of Agarwal et al., no longer support this contention (Daya et al., 1995; Agarwal et al., 2000). In fact, there have been two other recent studies (Gordon et al., 2001; Strehler et al., 2001) not only concluding that rhFSH is not superior to HMG, but that under certain circumstances, e.g. when using long gonadotrophin-releasing hormone (GnRH) agonist protocols, HMG may result in superior implantation rates compared with rhFSH (Gordon et al., 2001).

Since the study by Ng et al. was conducted from January to September 1999, a time when most data favoured higher pregnancy and implantation rates with rhFSH versus HMG, I suspect that the original objective of the study was to determine if the advantage of rhFSH was in improving embryo quality or not; if the embryo quality was equal one might assume the benefits of rhFSH were related to improving the uterine environment. With recent data no longer corroborating higher pregnancy rates with rhFSH, it is not surprising that embryo quality would be similar with either stimulation protocol.

I think the most interesting finding in the study was the trend for increased pregnancy and implantation rates with HMG. With similar embryo quality from both protocols, the assumption one would make is that the higher implantation rate from HMG is not significant and is related to the small sample size for the study. However, we presented data at the American Society for Reproductive Medicine meeting in 2000 showing statistically higher pregnancy and implantation rates with HMG plus rhFSH versus rhFSH alone in the 50% of patients whose early follicular phase LH is greater than our normal median level of 4 IU/ml (Check et al., 2000). In the discussion by Ng et al. they refer to the Agarwal et al. study which indicated that FSH and HMG were equally effective whenever pituitary down-regulation was used, yet FSH did have higher pregnancy rates when no down-regulation was used (Agarwal et al., 2000; Ng et al., 2001). Thus, I think that the authors were suggesting that the intrinsic superiority of rhFSH over HMG is sometimes negated by over suppression of LH (which is needed for ideal oocyte maturation in some minimal critical level) by the GnRH agonist. However, this mechanism does not make sense in view of our findings that if LH is <=4 mIU/ml, no differences in pregnancy or implantation rates are seen with HMG versus rhFSH, but significantly higher rates are found with HMG when LH is above the median. I was wondering if the authors may have measured the serum LH in the early follicular phase and if so could analyse their data according to their median LH concentrations to see if the trend for higher pregnancy and implantation rates with HMG may have also been in the group with higher, not lower, basal LH concentrations. If the authors’ results are similar to ours, then with similar embryo quality, it would appear that more LH in the gonadotrophin preparation somehow leads to a better uterine environment which facilitates embryo implantation, but only in women who have higher endogenous LH concentrations. If the authors confirm our results with their patient group, or if they cannot give us this information because early follicular LH levels had not been obtained, I would be interested if the authors could hypothesize a mechanism as to why more LH content in the gonadotrophin preparation may improve the uterine environment in women with higher endogenous LH.

References


Check, J.H., Nazari, P., Choe, J.K. et al. (2000) Evaluation of pregnancy and implantation rates following controlled ovarian hyperstimulation (COH) using all follicle stimulating hormone (FSH) versus FSH/luteinizing hormone (LH) combination according to the serum LH obtained in the early follicular phase. Fertil. Steril., 74, 522.


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