Vascular endothelial growth factor production by circulating immune cells is elevated in ovarian hyperstimulation syndrome

Sir,

We read with interest the study by Kosaka et al. (2007), on vascular endothelial growth factor (VEGF) production by circulating immune cells in ovarian hyperstimulation syndrome (OHSS) patients. In this study, they demonstrated an elevated basal VEGF production by peripheral blood mononuclear cells of OHSS patients and concluded that their study provides ‘new evidence’ to suggest that circulating immune cells are involved in the pathogenesis of OHSS.

Surprisingly, our 10 years of research on controlled ovarian hyperstimulation, OHSS and systemic inflammation went unnoticed (Orvieto, 2004). In our studies, we have suggested that the hyperstimulated human ovaries produce and secrete factor/s, which cause OHSS, probably by activating a systemic inflammatory response. This notion was based on the similarity of vascular leak syndrome to the clinical picture of OHSS (Orvieto et al., 1995), the significantly higher cytokines’ concentration in the follicular fluid at the time of oocyte retrieval in patients in whom OHSS subsequently developed (Orvieto and Ben Rafael, 1998), and the neutrophil and endothelial activations following hCG administration (Orvieto et al., 1999, 2000, 2001).

Moreover, due to the observed direct depressive effect of hCG on interleukin (IL)-2 production by human peripheral lymphocyte and mononuclear cells in vitro (Orvieto et al., 2003), we suggested that that hCG probably causes OHSS by stimulating the ovaries to produce and secrete a still unknown intermediate factor which causes the increase in capillary permeability, rather than by directly stimulating the peripheral lymphocytes and mononuclear cells to secrete IL-2.

Furthermore, in accordance with Kosaka et al. (2007), we also could not find any correlation between the inflammatory mediators and estradiol (E2) levels, which to our opinion, reinforces the ongoing debate on the role of E2 in the pathogenesis or prediction of OHSS (Orvieto, 2003).

References


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Reply: Vascular endothelial growth factor production by circulating immune cells is elevated in ovarian hyperstimulation syndrome

Sir,

We would like to thank Dr Orvieto for his interest in our study. Based on the findings that hCG directly decreased interleukin (IL)-2 production by human peripheral lymphocyte and mononuclear cells in vitro (Orvieto et al., 2003), Dr Orvieto speculated that hCG probably causes ovarian hyperstimulation syndrome (OHSS) by stimulating the ovaries to produce and secrete a still unknown intermediate factor which causes the increase in capillary permeability, rather than by directly stimulating the peripheral blood mononuclear cells (PBMCs) to secrete IL-2.

However, as we described in the Introduction section of our paper (Kosaka et al., 2007), we reported that recombinant-hCG (r-hCG) at high concentration stimulates IL-8 production by PBMC (Kosaka et al., 2002). Using anti-hCG antibodies, it was demonstrated that the promotion of IL-8 production by PBMC was specific to r-hCG, and not due to other