Severe OHSS

An ‘epidemic’ of severe OHSS: a price we have to pay?

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This debate was published on Webtrack 87, September 21, 1999

We read with interest the article on severe ovarian hyperstimulation syndrome (OHSS) and fully agree with the authors (Abramov et al., 1999) that overuse of high dose gonadotrophin stimulation protocols, i.e. of those practising pituitary suppression with gonadotrophin-releasing hormone (GnRH) analogues has led to a rise in moderate and severe OHSS, and that a more liberal use of ovulation induction regimes and an increased use in extracorporeal fertilization techniques seem to be responsible for this trend. In the Israeli multicentre study (Abramov et al., 1999), which was carried out between 1987 and 1996, the incidence of severe OHSS during in-vitro fertilization (IVF) cycles increased four-fold from 0.06 to 0.24%, with the greatest number of cases in 1994. In 1993, Asch was the first to introduce i.v. administration of human albumin for the prevention of severe OHSS (Asch et al., 1993). It is of interest that, after a steep increase in number of cases during 1992–1994, the situation appears to be stable or even showing a small decline between 1994 and 1996. During that period, application of i.v. human albumin in patients at high risk became generally accepted in IVF treatment.

Although the safety of human albumin has been questioned (Cochrane Injuries Group Albumin Reviewers, 1998), with regard to an increase in mortality of 6% in critically ill patients who had been treated with human albumin, the patient population is different for OHSS patients. The article by the Cochrane Injuries Group deals with critically ill patients, suffering from burns, hypovolaemia and hypoproteinaemia, while IVF patients at risk of severe OHSS are primarily healthy and, usually, younger. The use of human albumin in these cases is for protection. One possible explanation for the preventative effect of human albumin in imminent OHSS is the avoidance of vascular hyperpermeability by binding vasoactive substances. This differs from the situation in critically ill patients where human albumin was given as fluid replacement and capillary damage had already occurred. We believe that the increase in mortality following human albumin treatment is not an issue in the case of OHSS prevention and, therefore, that we should not alter our treatment (CSM Expert Working Party, 1999).

We have also shown a reduction of moderate and severe OHSS in IVF cycles by hydroxyethyl starch solution (HAES) (Graf et al., 1997). Over the last few years, we have routinely used HAES or human albumin, partly combined with prolonged coasting (Sher et al., 1995) in high risk patients, i.e. those with serum oestradiol concentrations of $\geq 11,010$ pmol/l on the day of human chorionic gonadotrophin (HCG) injection and/or 20 or more oocytes retrieved and/or previous severe OHSS. Between January 1995 and December 1998, a total of 9648 IVF cycles were performed in our group with only 0.2% moderate and severe OHSS (grade II and III, unpublished data), whereas a total of 2.3% OHSS grade III cases were reported in all IVF groups on the German register. In two cases, cycles had to be cancelled because of severe threatened OHSS. We agree with Hillensjö et al., that a combined approach should be taken to avoid severe OHSS (Hillensjö et al., 1999). This begins by recognizing predisposing factors, such as young age, low body weight and hyperandrogenaemic chronic anovulation, to adapt stimulation protocols. It ends in prophylactic measures such as coasting, i.e. infusion of human albumin or HAES and strictly avoidance of HCG for luteal support. Accurate application of all those measures can alleviate the price we have to pay for modern assisted reproduction.

Other authors (Edwards et al., 1996; Olivennes and Frydman, 1998) have suggested milder forms of ovarian stimulation protocols, applied in ‘tailor made’ modes for each patient. This could result in higher-grade embryos and in better implantation rates. A drug-free IVF procedure, e.g. spontaneous cycles or in-vitro maturation, as already practised by some teams in the world would present enormous progress in definitely preventing OHSS, but will probably take some years to become a successful procedure which could then be proposed routinely.

References


Graf, M.A., Fischer, R., Naether, O.G.J. et al. (1997) Reduced incidence of ovarian hyperstimulation syndrome by prophylactic infusion of...

