Letters to the Editor

Counselling patients undergoing controlled ovarian stimulation about the risks of ovarian hyperstimulation syndrome

Dear Sir,

Iatrogenic death of a patient or morbidity is always shattering for the clinician who has had to balance the risks and benefits of medical intervention when considering treatment options. Iatrogenic morbidity is all the worse when the treatment is of no immediate benefit to the patient in terms of improving their health. Such is the case in ovarian hyperstimulation syndrome (OHSS) which follows controlled ovarian hyperstimulation (COH).

OHSS is the most common complication of ‘controlled’ ovarian stimulation, the most serious consequence of which is death. The mortality associated with OHSS is estimated at 1:45 000–500 000 (Brinsden et al., 1995). It complicates 0.6–8.4% of treatment cycles (Rizk and Smitez, 1992), depending on the criteria used for diagnosis. Thus couples requiring assisted conception should receive a clear explanation of the procedures involved prior to treatment, if they are to give their informed consent to treatment. This must include any complications, including OHSS. It is a truism that OHSS can be avoided by not treating the patient.

There is no consensus opinion as to how to manage OHSS; although everybody would agree that its prevention in patients undergoing COH is the aim. Certain ‘at risk’ groups have been identified (Royal College of Obstetrics and Gynaecology, 1995), but this does not allow the clinician to be complacent in managing COH. Those patients at risk of OHSS may undergo a step-up regime of COH. Pre-treatment of patients with polycystic ovaries using ovarian electrocautery has been shown to significantly reduce the incidence of OHSS in a randomized controlled trial (Rimington et al., 1997).

Early cancellation of high-risk patients based upon clinical condition, serum oestradiol concentrations and ultrasound findings is the safest strategy. Avoiding the human chorionic gonadotrophin (HCG) injection to induce ovulation is also likely to reduce the risk of developing OHSS (Rizk and Abdoughar, 1991). However, these are radical strategies and do not achieve any progress towards the aim of treating the infertile patient.

If the patient is considered at risk of OHSS, but their condition does not warrant cycle cancellation, several options are available. Early follicular aspiration prior to HCG administration (Tomazevic and Meden-Vrtovec, 1996), controlled drift (Sher et al., 1993), oocyte retrieval and freezing of all embryos (Wada et al., 1972) have all been advocated. None of these strategies have been proven to avoid OHSS, and for those patients who become ill, supportive therapy remains the basis of treatment. Patients with OHSS have been subjected to a range of therapies, including systemic steroids (Tan et al., 1992) and i.v. albumin (Shoham et al., 1994). Few of these studies have been validated and demonstrated to show any clear benefit to the recovery of the patient.

The pathophysiology of OHSS remains unclear. Elevated values of circulating and intrafollicular cytokines are thought to play a role in its development, although these high concentrations may simply be a function of COH. Recent studies on ovarian cytokines suggest that vascular endothelial growth factor (VEGF) may be important in the development of OHSS, with increased amounts of VEGF leading to increased ovarian capillary permeability. The ascites from OHSS in the human would appear to be formed by leakage from the ovarian surface (Blumenfeld et al., 1997).

The degree of leakage of fluid through the ovarian surface may be related to the severity of the ensuing OHSS. Any process which reduces this leakage, whether medical or surgical, may therefore be of benefit. It could be postulated that scarring of the ovarian surface may effectively reduce its functional surface area. This would be consistent with the observation that the follicular response to COH in patients with polycystic ovaries pre-treated with ovarian electrocautery (OE) was no different when compared to a control group of patients with PCO who did not receive OE but the incidence of OHSS was significantly reduced (Rimington et al., 1997).

While no strategy for the prevention of OHSS can be guaranteed to work, it should be made clear to the patient that there is a small, but real, risk associated with COH. Infertility treatment may be seen by some as non-essential. The clinician should not take any risk with the patient’s health and there should be a low threshold for cancelling treatment to minimize the risks of OHSS. There is no absolute way of avoiding its development (short of not undergoing treatment) which is of course a valid option for some couples. Should OHSS develop, the clinician must use his or her clinical judgement based upon experience and knowledge gained from the published work, in order to limit its course. There is currently no consensus opinion on how best to manage OHSS, hence the large number of proposed methods. The clinician should do his best for the patient, using the management strategy with which they feel most comfortable. Occasionally, a patient will become critically ill from OHSS despite their best efforts.

The pathophysiology and management of OHSS remains an inexact science. Properly conducted studies including large numbers of patients are required in order to determine the best method of prevention and, if necessary, management. This will, of necessity, require multicentre studies with co-operation between clinicians. COH is not risk free and this fact should be made clear to patients before informed consent for treatment is taken. The decision to undergo treatment by COH is made by balancing the risk of developing OHSS and its consequences against the potential benefits (i.e. pregnancy), and can only be taken by the patient.
References


M.R. Rimington1, E.G. Simons and K.K. Ahuja
Cromwell IVF and Fertility Centre, Cromwell Hospital, Cromwell Road, London SW3 6TW, UK

1To whom correspondence should be addressed