Severe OHSS

Decreasing the risk of severe ovarian hyperstimulation syndrome

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Ovarian hyperstimulation syndrome (OHSS) is the most serious complication of ovulation induction. The frequency of OHSS has increased with the introduction of menotrophins used for controlled ovarian stimulation in assisted reproductive technologies (ART) as an active strategy for the management of different causes of infertility. With the introduction of gonadotrophin-releasing hormone (GnRH) agonists and the use of higher doses of menotrophins to retrieve a higher number of mature oocytes to maximize ART pregnancy rates, the incidence of severe OHSS has been increased. After in-vitro fertilization (IVF) and embryo transfer, the overall incidence of OHSS is reported to be 0.6–14% (Rizk, 1992); however, the incidence of severe OHSS is ~1–2% (Smitz et al., 1993). The pathogenesis of OHSS is still unclear. It is believed that overstimulation of the ovarian renin–angiotensin system (OVRAS) may play a part (Ong et al., 1991). It has been suggested that, in the presence of high concentrations of oestrogen, the ovary secretes an angiotensin II-like substance, which leads to vasodilatation and increased capillary permeability (Asch et al., 1993). The increase in capillary permeability leads to a shift of fluid to the extravascular compartments (mainly the peritoneal cavity) with the formation of ascites. Recently, it has been suggested that marked peripheral arteriolar dilatation is a constant and major finding in severe OHSS. Peripheral arteriolar dilatation leads to the stimulation of the renin–angiotensin–aldosterone and sympathetic nervous systems and the secretion of the antidiuretic hormone (ADH). These vasoactive systems promote sodium and water retention, contributing to ascites formation in patients with severe OHSS (Balasch et al., 1998).

Mild cases of OHSS are characterized by the formation of multiple ovarian cysts associated with excess steroid production and ovarian enlargement. Moderate OHSS is associated with abdominal distention, nausea, diarrhoea or vomiting. In severe OHSS, ascites, hydrothorax, electrolyte imbalance, haemococoncentration, hypovolaemia, oliguria or thromboemboli have been reported. The management of mild and moderate OHSS is expectant, while the management of severe forms of OHSS includes hospitalization for fluid and electrolyte management, paracentesis or continuous drainage of the ascitic fluid if necessary (Al-Ramahi et al., 1997) and mini-dose heparin prophylaxis to prevent thromboembolic complications (Hignett et al., 1995).

Several reports have suggested different modalities for the prevention of OHSS. Individualizing ovulation induction protocols for each patient according to different variables may lead to a better control of ovarian hyperstimulation. Those factors may include the age of the patient, weight, day 3 concentrations of follicle stimulating hormone (FSH) and oestradiol, and a history of poor or exaggerated response in previous induction of ovulation cycles. Furthermore, patients with polycystic ovary syndrome (PCOS) or who have a sonographic appearance of multicystic ovaries at baseline ultrasound evaluation, are at more risk for developing OHSS and should be treated less aggressively with menotrophins.

OHSS can be avoided by not administering human chorionic gonadotrophin (HCG), and so cancelling the cycle in patients who have a serum oestradiol concentration of >10 000 pmol/l or who have >20 follicles seen on ultrasound before oocyte retrieval, especially if most of the follicles have the mean follicular diameter <12 mm. Although this is a good preventive measure for avoiding OHSS, it is frustrating for both the patient and the treating physician. Hence, some authors have suggested reducing the dose of HCG instead of avoiding it (Abdalla et al., 1983). Others have suggested triggering ovulation by GnRH agonists instead of HCG in cycles where OHSS is suspected (Balasch et al., 1994).

Using progesterone rather than HCG for luteal phase support has also been suggested in patients who are at risk of developing OHSS (Claman et al., 1992). Withholding HCG and menotrophins for a number of days, while continuing GnRH agonists until serum oestradiol concentrations return to a reasonable value (<10 000 pmol/l), has been widely used and is successful in preventing OHSS (coasting). This strategy shows no deleterious effect on the oocyte quality or on pregnancy rate (Sher et al., 1995).

Cryopreserving all embryos and transferring them later in another cycle has been used as another way of avoiding OHSS (Tiitinen et al., 1995). Furthermore, early timed follicular aspiration (ETFA) for the ovary (10–12 h after HCG administration) has been reported to prevent OHSS (Tomazevic and Meden-Vrtovec, 1996).

Some authors have reported that the administration of i.v. albumin during or after oocyte retrieval prevents OHSS (Shoham et al., 1994). However, most of the later reports have shown that i.v. administration of albumin does not help in preventing OHSS (Orvieto and Ben-Rafael, 1998).

Laparoscopic ovarian diathermy for both ovaries has been
described as preventing OHSS (Rimington et al., 1997). This procedure was carried out after pituitary desensitization and before menotrophin administration in a group of patients at high risk of developing OHSS.

In conclusion, with increasing use of GnRH agonists and high doses of menotrophins for induction of ovulation in assisted reproductive technologies, the incidence of OHSS has increased. By individualizing the induction of ovulation protocols, by avoiding HCG administration when the serum oestradiol value >10 000 pmol/l (especially when many small follicles are seen on ultrasound evaluation) and by using some of the preventive measures mentioned above, the incidence of OHSS may be minimized.

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References


