

Ovarian hyperstimulation syndrome

Fact Sheet

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updated October 2011

What is it?

Ovarian Hyperstimulation Syndrome (OHSS) is an uncommon but very important problem associated with attempts to stimulate ovulation. It is encountered in its most clinically significant forms in 'controlled' ovarian hyperstimulation used in high technology Assisted Conception, notably IVF, although it can be seen associated with any form of ovulation stimulation. The reported incidence varies between 1 in 250 IVF cycles up to 1 in 20 but this wide range might well be related to recording and to differing thresholds for concern. In its mildest form it causes little more than mild lower abdominal discomfort but severe forms can be life threatening and as such necessitate vigorous therapy. The methods of classifying the stages of OHSS are still controversial as is the exact pathophysiology (i.e. the underlying mechanism).

An important point to clarify is that the syndrome is not directly caused by the drugs but by the hormones produced by the ovaries in response to them. To add to the difficulties we find that whilst one person may develop significant problems at a certain oestrogen level others may suffer no ill effects – the disorder is complex biochemically and appears to involve, among others, a compound known as Vascular Endothelial Growth Factor (VEGF). Large numbers of cases need to be studied to help solve the inadequacies in our knowledge. Nevertheless, we are very keen to avoid the problem and will therefore need to rely on multicentre trials, themselves difficult to organise. Despite these difficulties we can limit the incidence by identifying the population at risk and modifying treatment.

Who is at risk?

Most particularly at risk is the young (less than 35), lean woman with previously diagnosed polycystic ovarian syndrome (PCOS; see fact sheet no. 24) who, with stimulation, rapidly develops very high serum oestrogen levels and shows excessive ovarian response on ultrasound. The introduction of the GnRH analogues (Lucrin and Syneral) into the Assisted Conception treatment protocols allows prolonged stimulation and as such increases the risk of OHSS. Less ovarian stimulation and more use of GnRh antagonists, to suppress premature LH surges, can decrease the occurrence so we can expect 'gentler' stimulation in the future particularly with advances in embryology meaning we have

more high quality embryos and less need for large egg numbers (quality over-riding quantity). 'Support' of the luteal phase with hCG was used routinely in the past but should now only be given with great care, and progesterone (vaginal or by injection), being safer, is preferred. HCG, whether exogenous (given by injection) or endogenous (from an early pregnancy) is a significant factor in the development of the syndrome.

In those at particular risk we have now developed a number of strategies some of which remain controversial. Reducing the ovulatory (trigger) dose of hCG from 10,000 IU to 5,000 IU has some small theoretical advantage. Withholding completely the ovulatory dose of hCG was a mainstay of prevention but a variation

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known as 'coasting' where the hCG is still given but only when the oestrogen levels have fallen back to an 'appropriate' level is now preferred by many clinicians.

Should the ultrasound appearances (i.e. excessive follicular development) be grounds for concern during the oocyte retrieval some advocate the immediate use of intravenous albumen (a protein rich blood product). However, initially encouraging reports have been questioned and albumen carries its own risks. The more established approach is to completely empty all the ultrasonically visible follicles and then to use subsequent embryo cryopreservation (freezing) to avoid the possibility of pregnancy in that cycle (and hence endogenous hCG). The embryos, after freezing then later thawing, can be replaced in a subsequent 'natural' cycle. Following this curtailed cycle some clinicians like to continue the GnRH analogues for one to two weeks, others

using high dose progesterone and some use Danazol. All these approaches are of unproven value.

Treatment

Treatment of the established case of OHSS will depend very much upon the severity of symptoms and whether the problem arises early after embryo replacement or later as a sign of endogenous hCG production indicative of an early pregnancy. Mild to moderate lower abdominal discomfort and nausea can be treated by reduction in activities and attention to an adequate fluid intake (some advocating electrolyte-rich solutions such as Gatorade). Increasing abdominal discomfort often associated with vomiting will require hospitalisation with meticulous monitoring of changes in abdominal girth, blood electrolytes, haemodynamic stability (blood pressure

etc.) and signs of haemoconcentration and most importantly signs of impending coagulation (clotting), liver and kidney failure. Treatment will be directed towards maintenance or restoration of normality in these areas usually achieved by intravenous solutions (albumen is currently preferred) coupled with paracentesis (drainage of the abdominal fluid). There is some support for the early use of this procedure in recent medical literature. Rarely 'intensive care' will be required (beyond the scope of this review) and rarely consideration given to termination of an early pregnancy.

OHSS is a potentially life-threatening disorder. Although we remain uncertain of its exact pathophysiology there are steps that can be taken to predict those at risk and minimise the occurrence and effects.

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