Prediction of ovarian hyperstimulation syndrome (OHSS)

Estradiol level has an important role in the prediction of OHSS

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The cascade of events that leads to the development of ovarian hyperstimulation syndrome (OHSS) is almost always accompanied by elevated estradiol (E₂) levels. The role of estrogen level in OHSS has not been confirmed; however, it was shown repeatedly in the literature that elevated levels of E₂ constitute a risk for OHSS. Monitoring E₂ was found to be effective in reducing the incidence of OHSS. It was also reported that reducing the E₂ level by coasting helps to prevent OHSS. It is believed that irrespective of the debatable role of estrogen in the pathogenesis of OHSS, there is a general agreement that E₂ assay is an important marker to detect the majority of patients at risk of OHSS.

Key words: coasting/E₂ level/OHSS/prediction

It is well documented that exogenous and endogenous hCG are the triggering factors for the cascade of events which results in the development of ovarian hyperstimulation syndrome (OHSS; Schenker and Weinstein, 1978). These events were almost always accompanied by elevated estradiol (E₂) levels and estrogen has been implicated as a potential aetiologic factor (Haning et al., 1983), although the relevance of E₂ levels has been challenged (Orvieto, 2003). The extraperitonealization of the ovaries has not prevented OHSS and because the syndrome cannot be reproduced in males it is feasible that there exists a mediator of ovarian origin, which allows for the increase in capillary permeability in the presence of elevated E₂ levels (Bassil et al., 1995).

Many investigators have shown that elevated levels of estrogen constitute a risk factor for OHSS (Haning et al., 1983; Navot et al., 1988). In a group of IVF patients, Asch et al. (1991) found that none of the patients with E₂ serum levels <3500 pg/ml developed OHSS, while 1.5% of those with 3500–5999 pg/ml and 38% with E₂ levels >6000 pg/ml developed OHSS. If the values of E₂ more than doubled during 2 or 3 days, the OHSS risk was high (Schenker, 1993). The role of the elevated E₂ level in OHSS has not been confirmed; however, lowering E₂ level helps to prevent OHSS (Sher et al., 1995). Monitoring E₂ was found to be effective in reducing the incidence of OHSS (Haning et al., 1983; Tulandi et al., 1984; Varma and Patel, 1988; Golan et al., 1989). The reasons why coasting is effective in preventing OHSS are speculative. Tortoriello et al. (1998) hypothesized that coasting may diminish the functional granulosa cell cohort, resulting in the gradual decline in circulating levels of E₂, and possibly this will result in the reduction of the chemical mediators or precursors that augment fluid extravasation. The threshold of E₂ level above which there is a considerable risk of OHSS, varies widely among different investigators. Most of the studies selected an E₂ of 3000 pg/ml as a safe value for hCG administration (Sher et al., 1995; Benadiva et al., 1997).

It may be that many players, including possibly E₂, may trigger the chemical mediator responsible for the development of OHSS. This can explain why OHSS may not occur in the presence of high E₂ level and that OHSS rarely develops in the absence of high E₂ levels.

There is also a possible role of ovarian mediators secreted by the corpus luteum in the pathogenesis of OHSS. Biron et al. (1997) suggested that a change in the haemostasis activation at the progesterone plateau may occur during stimulation. Manau et al. (2002) suggested that the corpus luteum plays a major role in the deterioration of circulatory function in IVF. Ujioka et al. (1997) suggested that progesterone may contribute at least in part to the pathophysiology of OHSS in an experimental model.

There are rare case reports on OHSS associated with pregnancy in non-stimulated cycles. The authors had different explanations for these rare cases. Zalel (1992) suggested that the polycystic ovaries may be very sensitive to the circulating FSH hormone. Lipitz et al. (1996) reported a case with minor elevation of liver enzymes resulting from hepatitis B infection. This in turn may have led to an increase in free estrogens as a result of a decrease in sex-hormone binding globulin and ultimately to OHSS. Rotmensch and Scommegna (1989) blamed the presence of hypothyroidism. Edi- Osagie and
Hopkins (1997) reported OHSS in six consecutive spontaneous pregnancies in the same patient and they suggested that this is due to an oversensitive response in women with polycystic ovaries.

It is not difficult to explain the absence of OHSS in the study of Asch et al. (1993) on the role of i.v. albumin for prevention of OHSS. In 36 patients with E<sub>2</sub> levels >6000 pg/ml and >30 retrieved oocytes no severe OHSS developed. The study was not controlled, the sample size was small and embryo transfer rate was very low (15/36), i.e. 60% did not reach embryo transfer stage, and the patients were followed only for 5 days post oocyte retrieval. On the other hand, there is a randomized controlled study (Shoham et al., 1994) which showed that i.v. albumin protects against OHSS. A recently published Cochrane review leads to the same conclusion (Aboulghar et al., 2002).

In conclusion, it is believed that irrespective of the debatable role of E<sub>2</sub> in the pathogenesis of OHSS, there is a general agreement that E<sub>2</sub> assay is an important marker to detect the majority of patients at risk for OHSS.

References


