High dose gonadotrophin-releasing hormone antagonist (ganirelix) may prevent ovarian hyperstimulation syndrome caused by ovarian stimulation for in-vitro fertilization

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Case report

A 33 year old regularly menstruating woman (body mass index 23 kg/m²) with an infertility duration of 4.5 years due to tubal pathology underwent IVF in our unit. Before initiation of treatment, endocrine screening and sonographic examination appeared to be normal. As part of a multicentre phase II clinical trial (approved by the local ethics review committee), 150 IU recombinant follicle-stimulating hormone (recFSH) (Puregon®; NV Organon) daily subcutaneous injections were administered, starting on cycle day 2. From cycle day 7 onwards she was co-treated daily with a GnRH antagonist (ganirelix, Org 37 462; NV Organon) (0.125 mg subcutaneously). Initially normal follicular growth was observed and although oestradiol concentrations rose steadily, they remained within the limits normally associated with controlled ovarian hyperstimulation for IVF. The moderate starting dose of 150 IU recFSH was therefore continued. However, on cycle day 11 the patient presented with a serum oestradiol level of 16 500 pmol/l, a level associated with an increased risk of OHSS (Rizk and Aboulghar, 1991). Transvaginal ultrasound showed four preovulatory (≥16 mm) follicles, and nine intermediate sized (10–16 mm) follicles. It was decided to cancel the cycle by withholding HCG injection and discontinuing daily recFSH administration. On cycle day 12 ultrasound showed an increase in the number of follicles (six preovulatory and 27 intermediate sized follicles). The patient complained of abdominal discomfort and a pocket of ascites in the pouch of Douglas was demonstrated on ultrasound. The oestradiol concentration was 22 315 pmol/l and the right and left ovaries were enlarged, with respective mean diameters of 72 mm and 54 mm. The ganirelix dose was increased to 2 mg/d to prevent a possible OHSS.

Introduction

Ovarian hyperstimulation syndrome (OHSS) is a potentially life-threatening complication of assisted reproduction (Schenker and Weinstein, 1978). OHSS does not occur in the absence of either the endogenous luteinizing hormone (LH) surge, or surrogate human chorionic gonadotrophin (HCG). Conditions which may indicate imminent OHSS include late follicular phase serum oestradiol concentrations ≥12 675 pmol/l (3500 pg/ml), and the occurrence of ≥25 small and intermediate sized follicles (Rizk and Aboulghar, 1991). Under these circumstances ovarian stimulation for in-vitro fertilization (IVF) is usually cancelled by cessation of exogenous gonadotrophins, withholding HCG, and continuation of pituitary down regulation by gonadotrophin-releasing hormone (GnRH) agonists in order to prevent unpredictable changes in release of endogenous gonadotrophins. However, it has been reported that the continued administration of GnRH agonists does not affect subsequent ovarian quiescence (Wada et al., 1992). This may be related to prolonged suppression of pituitary function due to slow recovery from down-regulation (Donderwinkel et al., 1993). Some residual gonadotrophin release may remain during GnRH agonist suppression, whereas pituitary release of LH and follicle-stimulating hormone (FSH) may be virtually abolished with the sustained use of a high dose of GnRH antagonist. In this case report we describe an alternative method, using a high dose of a GnRH antagonist which may decrease the risk of a severe OHSS.

Key words: GnRH antagonists/imminent ovarian hyperstimulation syndrome/in-vitro fertilization/ovarian hyperstimulation syndrome


The present case confirms the previously reported efficacy of high dose GnRH antagonist in achieving rapid suppression of endogenous gonadotrophin release even when LH levels have started to rise (Dubourdieu et al., 1994), and in eliciting subsequent ovarian quiescence. It is yet to be determined whether GnRH antagonists act solely through suppression of pituitary function, or whether direct actions at the ovarian level may also be involved. The clinical role played by GnRH antagonist in this case remains uncertain since progression to OHSS may have been prevented by discontinuation of recFSH and withholding HCG. Controlled studies are required to assess the extent to which GnRH antagonist contributes to the early resolution of ovarian hyperstimulation syndrome.

References


Ganirelix may prevent OHSS


Received on August 22, 1997; accepted on December 1, 1997