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The Treatment of Patients with Polycystic Ovaries Undergoing IVF

INTRODUCTION

Polycystic ovary syndrome (PCOS) is a very common cause of anovulation (1), accounting for nearly 75% of patients with anovulatory infertility (2). The prevalence of polycystic ovarian morphology is even higher; it has been estimated that more than 20% of women in the normal population have polycystic ovaries (PCO) (3). Although the majority of women with PCO are only mildly symptomatic or asymptomatic, the finding of PCO on ultrasound

has considerable implications when considering superovulation for IVF. It has been demonstrated that women with PCO who have regular, ovulatory menses and who present with tubal, male-factor, or unexplained infertility, are much more likely to hyperrespond to gonadotropin therapy than those with normal ovarian morphology. The particular problems associated with superovulation in IVF are premature triggering of the LH surge, reduced quality of eggs and embryos, and, most seriously, ovarian hyperstimulation syndrome (OHSS).

PREMATURE LH SURGE

Patients with PCOS and, to a lesser extent, those with asymptomatic PCO are characterized by tonic hypersecretion of LH (4,5). During superovulation therapy, estradiol concentrations tend to be higher than in women without PCO (a function mainly of the increased number of follicles recruited) and this phenomenon, together with the higher tonic LH levels, encourages activation of surge concentrations of LH which are inappropriate for the stage of follicle development. The use of analogues of gonadotropin-releasing hormone (GnRHa) to suppress endogenous LH is important in this context. The "long protocol" is more appropriate for such patients to ensure adequate inhibition of LH secretion (6,7). Such treatment is also useful in allowing some flexibility in the timing of hCG administration and, indeed, providing an opportunity to withhold hCG if there appears to be a danger of hyperstimulation syndrome (see below).

EGGS, EMBRYOS, AND PREGNANCIES IN PCOS

The general consensus from published studies is that patients with polycystic ovaries (whether or not they have other features of the syndrome) develop more follicles and produce more eggs but have a lower proportion of fertilized eggs than patients with normal ovaries (8,9). These observations appear to hold true irrespective of the method used for superovulation (9). However, the absolute number of fertilized eggs per patient is similar to, if not greater than, that in non-PCO subjects, resulting in similar rates of implantation and ongoing pregnancy between the groups (8–10). Despite the lack of any clear-cut difference in outcome according to choice of superovulation regimen in PCO patients, the number of canceled cycles is likely to be lower if pretreatment with GnRHa is employed (6) (see above).

There is no evidence that purified preparations of FSH (recombinant or urine-derived) are significantly more effective or safer than hMG in PCOS patients. "Poor responders" to gonadotropin treatment are no more common among women with PCO than among those with normal ovaries. Cotreatment with recombinant human growth hormone has been shown to be marginally more effective than GnRHa/gonadotropin alone (11) but it is doubtful whether

growth hormone has a significant therapeutic role in such patients.

HYPERSTIMULATION SYNDROME

There seems to be little doubt that PCO is a major risk factor for OHSS (9,12). MacDougall and colleagues conducted a study in which 76 women with PCO were compared with a similar number of control subjects, matched for age, cause of infertility, and stimulation regimen (9). Despite the fact that women with PCO received significantly less gonadotropin, eight of these patients developed moderate/severe OHSS (10.5%), compared with none in the control group. The occurrence of OHSS was not prevented by pretreatment with GnRHa, but because there is little risk of a spontaneous LH surge in such subjects, hyperstimulation can be avoided if the decision is made to withhold hCG.

CONCLUSIONS AND RECOMMENDATIONS

Women with PCO, whether or not they have other features of polycystic ovary syndrome, are more likely than women with normal ovaries to have canceled stimulation cycles, to have lower than normal rates of fertilization but similar pregnancy rates, and, most importantly, to develop OHSS. These dangers can be limited by the use of GnRHa and, particularly, by careful attention to the dose and monitoring of gonadotropin treatment. It is conventional in many modern IVF programs to use only 1 ampoule (75 IU FSH) of gonadotropin per day, increasing by increments of 37.5 IU when indicated by ultrasound and estradiol measurements (10).

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