Effects of in vivo and in vitro gonadotropin supplementation in PCOS patients undergoing oocyte in vitro maturation

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Oocyte in vitro maturation (IVM) has been developed to prevent the risk of ovarian hyperstimulation syndrome (OHSS) and other drawbacks derived from conventional ovarian hyperstimulation with gonadotropins. In its original scheme, IVM involves the retrieval of immature germinal vesicle (GV) stage oocytes enclosed in their vestment of cumulus cells from small- and mid-sized antral follicles. These oocytes are placed in culture for 24-36 hours to permit the resumption of meiosis and achievement of meiotic maturation, signified by the emission of the polar body I. In vitro maturation is routinely performed in the presence of follicle stimulating hormone (FSH) and human chorionic gonadotropin (HCG), but in fact experiments in animal models suggest that paracrine factors of the EGF-like family could assist oocyte maturation in a more specific fashion. IVM is particularly suited for the treatment of infertile patients presenting with polycystic ovaries (PCO) or polycystic ovary syndrome (PCOS), because of an elevated risk of OHSS and the high number of antral follicles occurring spontaneously in these subject. More recently, it has been proposed that regularly cycling women may benefit from IVM, despite the reduced number of antral follicles available for recovery.

Because collective experience has shown that the efficiency of IVM performed in total absence of gonadotropin supplementation is reduced in comparison to conventional ovarian stimulation, it has been suggested that mild FSH priming during the early follicular phase and/or induction of final maturation with HCG could improve quantity and quality of immature oocytes. In effect, after HCG administration a proportion of oocytes (15-20%) is found already mature at retrieval. This contributes to increase the overall fraction of mature oocytes available for treatment and could improve the clinical outcome. However, current evidence is conflicting. In PCO patients, initially it was reported by Mikkelsen and Lindenberg (2001) that FSH priming was able to improve the clinical outcome, but more recent studies (Son et al., 2006) have not confirmed a beneficial effect of FSH. In the same category of patients, Chian et al. (2000) have found that HCG induction leads to a higher rate of mature oocytes and determines a trend towards higher pregnancy rates. In recent years, our group has extended the experience of oocyte maturation to normo-ovulatory women. In a prospective randomized study (Fadini et al., 2009), we allocated 400 women to four different treatments: no stimulation, HCG priming, FSH priming, combined FSH and HCG priming. The maturation and overall rates of mature oocytes available for treatment were higher in the FSH/HGC group (77.4 and 82.1%, respectively). These percentages were around 60% after HGC priming alone and dropped to 48-50% in the absence of HCG, irrespective of FSH administration. The clinical pregnancy rate per transfer was significantly higher (29.9%) in the FSH/HGC group in comparison to all other regimens (15.3%, 17.3% and 7.6% in the no supplementation, FSH, and HCG categories, respectively). Therefore, it appears that a combined supplementation of FSH and HCG can improve the IVM outcome while FSH or HGC alone do not seem to be beneficial. Studies
are in progress in our centre to establish whether these conclusions can be extended to PCO and PCOS patients.

References


