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Successful pregnancy following a novel endometrial preparation in a PCOS patient undergoing IVM: a case report

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Introduction

In-vitro fertilization (IVF) relies heavily on controlled ovarian stimulation to increase the number of available oocytes and embryos, and therefore the pregnancy rate. However, the side effects, such as nausea, mood swings, menopausal symptoms, ovarian hyperstimulation syndrome (OHSS), and potential cancer risk of ovarian stimulation may not be avoided. Therefore, the recovery of immature oocytes followed by in-vitro maturation (IVM) and fertilization is an attractive alternative to avoid the side effects of using gonadotrophin stimulation. In IVM, immature oocytes are retrieved from unstimulated or minimally stimulated cycles, then cultured using IVM culture media for maturation in vitro [1]. In comparison with conventional IVF, IVM technology is generally associated with the absence of OHSS, lower cost, and fewer complications. However, the efficiency of existing IVM technique is suboptimal because embryos generated from IVM exhibit frequent cleavage blocks and low implantation rate [2]. Women with polycystic ovarian syndrome (PCOS) are considered as the target population for this approach. This group of patients is extremely sensitive to ovarian stimulation and have a high potential for developing of OHSS [3].

Capsule We believe that delayed FSH priming until endometrial thickness reaches 7 mm by endogenous estrogen may be an appropriate intervention for endometrial preparation in PCOS cases undergoing IVM.

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In recent years, many improvements have been made in clinical and laboratory aspects of IVM treatment which have resulted in better pregnancy outcomes [4]. It was shown that pretreatment with FSH in the early days of folliculogenesis phase may increase the number of retrieved immature oocytes and/or maturation potential [5, 6]. In addition, hCG priming promotes some GV oocytes to reach the MI stage and increases the maturation rate of immature oocytes in vitro setting. Despite increased pregnancy rates following IVM in recent years, implantation rates are still lower than conventional IVF cycles. One possible explanation may be related to insufficient endometrial preparation during IVM cycles before ET [4, 7]. Here, we aim to report a novel endometrial preparation method in a PCOS case undergoing IVM.

Case report

A 33 years old patient with history of primary infertility for 3 years was referred to our program for infertility treatment. She was diagnosed as PCOS according to Rotterdam criteria [8] with history of acne, hirsutism and oligomenorrhea. The clinical profile showed that she had BMI=28, LH=4, FSH=1.5, LH/FSH>2. The patient had history of both clomiphen failure and metformin administration for more than 6 months. She also underwent laparoscopy and ovarian cauterization approximately 1 year before. Infertility work up for the husband showed abnormal sperm analysis including a count of 28 millions/ml, <20% progressive motility and <14% normal morphology according to WHO criteria. A recent varicocelectomy did not improve semen quality for her husband.

In her first treatment cycle and due to a high response to the antagonist protocol and to avoid the risk of severe OHSS, it was decided to cancel the cycle, and to continue the treatment using IVM techniques. After progesterone withdrawal bleeding, FSH priming was delayed until 13th

day of the cycle when endometrial thickness reached 7 mm. At that time, FSH priming started, 75 IU/day of FSH (Serono, Aubnne, Switzerland) was injected for 3 days, followed by an injection of 10,000 IU hCG (Pregnyl, Organon, Netherlands). Follicular diameters were less than 10 mm at the time of hCG injection. On the day of hCG injection, both endometrial thickness and level of estradiol were measured. Oocytes were retrieved 36 h after hCG injection using a 19-gauge aspiration needle under transvaginal ultrasound guidance. A total of 10 immature oocytes were retrieved, including 3 at GV stage, 5 at MI stage, and 2 were degenerated. Immature oocytes were transferred to IVM culture media (SAGE Co., CT) for 28 h, when 5 oocytes reached MII stage. The rest of oocytes were arrested. The mature oocytes were microinjected with husbands' sperm and normal fertilization was confirmed when two polar bodies with two pronuclei were observed 18–20 h after insemination. A total of 3 oocytes were fertilized and 3 four cells embryos (grade B) were transferred 2 days after microinjection using ET catheter (Labotect, Gottingen, Germany). Lutheal phase support was done with 100 mg progesterone in oil (Aburaihan Co, Tehran, Iran) injected daily. Estradiol valerate (Aburaihan C,Tehran, Iran) was taken orally at the dose of 6 mg/day from day of oocytes retrieval, and continued until confirmation of fetal heart by sonography. βhCG was measured 14 days after ET, which was reported positive (>180 IU/L). A healthy baby girl was born at 39 weeks of pregnancy by cesarean section. The baby weigh at the time of birth was 3,500 g with the apgar of 9/10.

Discussion

Several studies have reported pregnancies after IVM in PCOS with unstimulated cycles, also in cycles with FSH and hCG priming [2–5]. We believe that this is the first case report in which FSH priming was delayed until 13th day of the cycle, when endometrial thickness reached 7 mm by endogenous estrogen. In our previous experience with IVM in PCOS patients, despite use of FSH/hCG priming, and transfer of good quality embryos, the pregnancy rate was discouraging [9]. Our hypothesis was that due to thin endometrium, the endometrial lining was not prepared for embryo implantation. Therefore, it seems that delayed FSH priming until increasing endometrial thickness by endogenous estrogen in PCOS may prepare the endometrium with better potential for embryo implantation [10].

Endometrial preparation is an important factor for IVM success rates. It has been demonstrated that endometrial thickness is an important predictor of IVM outcomes [2, 10]. Recently, Reinblatt et al. (2011) reported a better implantation rate, when endometrial thickness was more than 7 mm in their IVM cases [11]. Others recommended embryo cryopreservation, when endometrial thickness is below 7 mm on the day of ET [2]. Various doses of estradiol valerate, ranging from 4 to 8 mg/day were given to the women for endometrial preparation. It was adjusting according to the endometrial thickness on the day of oocyte retrieval. In addition, Elizur et al. (2009) improved their IVM results with treatment of either low dose hMG or micronized 17β-estradiol initiated several days before oocyte retrieval [12]. Although, both treatments resulted in a significant improvement in the endometrial thickness, but in addition, hMG treatment resulted in significantly larger follicles and a higher number of in-vivo matured oocytes. This may lead to higher embryo implantation without any risk of OHSS.

In conclusion, this case report demonstrates a successful pregnancy following a modified endometrial preparation in a patient with PCOS following IVM treatment cycle. Further investigations are needed to prove whether this successful technique of endometrial preparation can open a new dimension in IVM technology.

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