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Comparison of In-Vitro Maturation and In-Vitro Fertilization in Infertile Females with Polycystic Ovary Syndrome

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Abstract

Background: Both in-vitro maturation and in-vitro fertilization have been used successfully to treat females with polycystic ovarian syndrome, who plan to have child. This study compared outcome of these two approaches to fertilize females with polycystic ovary side effects.

Methods: This prospective study was conducted at Vali-Asr reproductive health research center and included all females with polycystic ovarian syndrome, who underwent in-vitro maturation or in-vitro fertilization from January 2005 to January 2008. Measurements included demographic data, total cost (including drug and laboratory procedures), outcome (chemical and clinical pregnancy), and systemic complication (ovarian hyper-stimulation syndrome), obtained from the patients' clinical files. Patients were informed about the procedures, side effects and goals, and the signed consent form for surgical approaches and use of their data in medical research. Finally, these variables were compared between the two groups.

Results: The in-vitro maturation and in-vitro fertilization groups included 20 and 22 patients, respectively. The range of body mass index was between 17.4 and 28.3 kg/m2 and the mean age of the patients was 29.35 $\pm$ 4.94 and 28.95 $\pm$ 3.84 years, respectively ($P > 0.05$). The total cost was significantly lower in in-vitro maturation group compared to in-vitro fertilization (201.6 $\pm$ 60.1 USD versus 380.5 $\pm$ 143.8 USD, respectively, $P < 0.001$). Positive outcomes were achieved significantly more frequently with the in-vitro fertilization method (1 chemical and no clinical pregnancy in in-vitro maturation versus 7 and 6 in in-vitro fertilization group, respectively, $P < 0.001$). Although, the rate of ovarian hyper-stimulation syndrome was higher in in-vitro fertilization than in in-vitro maturation approach, yet, it was not statistically significant ($P = 0.233$).

Conclusions: Our findings showed the superiority of execution of the in-vitro fertilization approach compared with the in-vitro maturation method in infertile females with polycystic ovary syndrome, who planned to have a child. However, in-vitro maturation approach is cheaper than in-vitro fertilization and is also associated with lower risk of ovarian hyper-stimulation syndrome.

Keywords: Polycystic Ovary Syndrome, Infertility, In-Vitro Fertilization

1. Background

Polycystic ovary syndrome (PCOS) is one of the most frequent endocrine disorders that affect 5% to 10% of females at the reproductive age (1). It is also the most common cause of hyperandrogenism and oligo-anovulation (2, 3).

Anovulatory cycles may lead to dysfunctional uterine bleeding and decreased fertility (3). Thus, females with PCOS often have difficulty becoming pregnant, which necessitate the use of different fertilizer approaches (4). In-Vitro Fertilization (IVF) is one of the anticipatory successful methods for females with PCOS, who have anovulatory cycles when a further infertility causing factor is not involved or when other non-invasive methods of ovulation induction have failed (5). However, IVF also increases the risk of ovarian hyper-stimulation (6). Females with PCOS are very sensitive to ovarian stimulation, and severe ovarian hyper-stimulation syndrome (OHSS) more frequently occurs in this population (7). In-Vitro maturation (IVM) of oocytes was primarily developed in order to make a simpler and safer approach than IVF for females with PCOS or those at higher risk of OHSS (8). IVM permits the use of immature oocytes in the procedure. As in IVM, stimulation of ovaries is not required, it is highly recommended for patients, who are at risk of OHSS (7). The first successful pregnancy using IVM was reported by Cha et al. in 1991 (9), which was followed by subsequent reports (10, 11). Based on our search, current studies that specifically compare the outcome of IVF and IVM in females with PCOS and infertility are not adequate. In this article, we aimed at comparing the outcome of IVF and IVM approaches among females with PCOS, planning to become pregnant at our research center.

2. Methods

This prospective study was carried out at the Vali-Asr reproductive health research center, Tehran University of Medical Sciences, and investigated all infertile females with PCOS, who had undergone IVF or IVM from January 2005 to January 2008. All data were obtained from the patients' clinical reports. The patients were primarily informed about the procedures, side effects and goals, and signed a consent form for surgical manipulations and use of their data in medical research. Polycystic ovary syndrome was defined according to the Rotterdam consensus criteria and was diagnosed if at least 2 of the following 3 features were present: 1- oligo / amenorrhea, 2- clinical or biochemical signs of androgen excess, and 3- polycystic ovary in ultrasonographic findings (4, 12). In order to stimulate ovaries releasing ova, 150 units of Gonal-f (Sereno, Switzerland) were used daily. Trans-vaginal ultrasound guided oocyte collection was carried out when more than 80% of follicles were measured 9 to 14 mm in diameter. Products were aspirated at a pressure of 180 mmHg and follicular flushing was not performed. All of collected oocytes were filtered through a cell strainer with a 70-mm sized mesh. The Medicult medium (MediCult, IVM System, Denmark) was used for the oocyte culturing procedure by default. The cumulus oocyte complexes were cultured at 37°C in 6% CO_2 within a highly humid environment. After 24 hours, monitoring of the oocyte maturation was started under an inverted microscope and repeated every 6 to 8 hours within the next 48 hours. Only the oocytes with an extrusion of the first polar body were considered mature and then were separated of cumulus cells for preparation of intracytoplasmic sperm injection (ICSI). A single spermatozoon was injected in each metaphase II oocyte. After ICSI, each fertilized oocyte was transferred to its special cell cleavage medium. The fertilization process was assessed 16 to 18 hours after ICSI by the appearance of two distinct pro-nuclei and two polar bodies. Normal embryos were selected and subjected to laser-assisted hatching. These embryos were transferred to the uterine cavity on the second or third day after ICSI (4). To make endometrial preparation, rectal or vaginal progesterone suppositories (400 mg twice a day) were used accompanied with estradiol-valerate (6 mg/d), which was started after oocyte aspiration. Endometrium quality and thickness were recorded on day of embryo transfer (ET), utilizing the trans-vaginal ultrasound technique. Clinical pregnancy was defined as presence of a visible fetal sac in trans-vaginal ultrasonography at least 4 weeks after ET. Chemical pregnancy was also detected by positive serum level of β-hCG, at least two weeks after ET. All patients' records were reviewed and required data including demographics, total cost (including drug and laboratory procedures), outcome (chemical and clinical pregnancy), systemic complications (OHSS), anatomical view, and thickness of the endometrium at the time of ET and zygote division quality were obtained from the participants' medical file.

Statistical analysis was performed using the SPSS software, version 13 (IBM SPSS, Armonk, NY, USA). All quantitative data were expressed as mean $\pm$ standard deviation. Fisher exact test and Mann-Whitney U test were conducted to analyze respective and quantitative data. P values lower than 0.05 were considered statistically significant.

3. Results

The IVF and IVM groups included 22 and 20 patients, respectively. Mean age of the patients among the IVM and IVF group was respectively 29.35 $\pm$ 4.94 and 28.95 $\pm$ 3.84 years ($P > 0.05$); no case was above 39 years old. Mean number of used Gonal-f ampoules was 14.1 $\pm$ 4.2 and 25.3 $\pm$ 8.6 in IVM and IVF groups, respectively, with a statistically significant difference ($P < 0.001$). Total cost was significantly lower in IVM group than in IVF (201.63 $\pm$ 6011 USD versus 380.59 $\pm$ 143.89 USD, ($P < 0.001$). Positive outcomes were achieved significantly more frequently with the IVF method (1 chemical and no clinical pregnancy in IVM versus 7 and 6 in IVF group, respectively) ($P < 0.001$). Although the rate of OHSS was also higher in the IVF group compared to IVM, yet, it was not statistically significant ($P = 0.233$). Main outcome measurements are summarized in Table 1.

4. Discussion

Our findings showed superiority of execution of IVF approach compared with the IVM method in infertile females with PCOS, who planned to have a child. However, the IVM approach is cheaper than IVF and is also associated with lower risk of OHSS. Although IVM can help females with reproductive disorders such as PCOS to achieve pregnancy, yet, the rate of pregnancy using IVM/IVF approaches is still low in PCOS, which may be due to poor maturation of oocytes and lack of synchronization with implantation window (13). Using the IVM method seems to be more economical, simple, and less stressful for females with shorter treatment cycles, and there is also no request for administration of ova stimulatory drugs and no risk of OHSS. The puncture procedure is simple and safe and it can improve the disrupted endocrine environment and induce a spontaneous recovery of ovulation and pregnancy in females with PCOS, who have no other combined infertility problem (4). Several studies have suggested that immature oocyte retrieval followed by IVM is a successful treatment

Table 1. Comparison of Clinical and Outcome Variables Between the Study Groups

Variables	IVM	IVF	P Value
Chemical pregnancy, n (%)	1 (5%)	7 (31.8%)	0.027[a]
Clinical pregnancy, n(%)	0	6 (27.3%)	0.012[a]
Number of follicle > 9 mm	5.4 ± 3.56	11.68 ± 8.35	0.003[d]
Conception rate	2.19 ± 1.27	6.95 ± 4.86	< 0.001[d]
Quality of embryo A to B	7 (43.8%)	21 (95.5%)	< 0.001[a]
On the day of transfer C to D	4 (25%)	7 (31.8%)	0.642[b]
Endometrial thickness, mm	7.75 ± 0.9	10.32 ± 1.9	< 0.001[d]
Three layers endometrium	15 (75%)	90.9%	0.167[b]
At the time of embryo transfer OHSS[c], n (%)	0	3 (13.6%)	0.233[b]

[a] Difference was significant between the 2 groups.
[b] Difference was not significant between the 2 groups.
[c] Ovarian Hyper stimulation syndrome.
[d] Difference was highly significant between the 2 groups.

for infertile females with PCOS (4,14,15). In the study conducted by Lin et al. (14), pregnancy was achieved in 33.8% of the females with PCOS using the mentioned method. In another study by Child et al. (15), implantation, pregnancy, and live birth rates per transfer were respectively 9.6%, 29.9%, and 14.9% for females with PCOS that had undergone IVM. In the present study, we failed to achieve clinical pregnancy in females with PCOS using IVM and only one chemical pregnancy occurred in this group. Our findings showed that results of IVM in PCOS were not appropriate and pregnancy rates using IVF were significantly higher. In a similar study by Child et al. (11), the success rates of IVM and IVF were compared. In this case-control study, 107 IVM and 107 IVF cycles were evaluated. The number of mature oocytes and obtained embryos were significantly lower in the IVM group compared to IVF. The IVM and live birth rates per retrieval were 26.2% and 15.9% compared with 38.3% and 26.2% for IVF ($P < 0.05$). Also, a significantly higher rate of implantation was seen in IVF derived embryos ($P < 0.05$). The rate of pregnancy in both IVF and IVM techniques was lower in our study. In brief, it seems that IVM is less effective than conventional IVF (8). In IVF, up to 59% of delivery rates have been achieved after fresh and subsequent frozen embryo transfers (16), whereas in IVM, delivery rates of 13% to 15% have been achieved (17, 18). In some studies, the lower rates of pregnancy were attributed to lower quality of endometrium for implantation (19), which may be critical in assisted reproductive technology results (20). In the study by Child et al. (11), 12 cases (11.2%) of moderate or severe OHSS were observed in IVF patients while the syndrome did not occur in the IVM group, which was statistically significant. In our study, although we found a lower rate of OHSS in the IVM group, yet, it was not statistically significant. Further studies with larger sample sizes are needed to determine the exact effects of IVM on the rate of OHSS. The effects of follicular stimulating hormone (FSH) priming on human IVM are controversial (21), although some researchers have shown beneficial effects (22). In the present study, we also did not find any beneficial effect with the use of FSH priming. Our findings showed that the total cost in IVM cycles was significantly lower than IVF. As no expensive hormones are required for IVM, the total cost of an IVM cycle is significantly lower than that of an IVF cycle (8). The present study was limited by small sample size due to obtaining data from past registered patients' medical files. In conclusion, our findings failed to show superiority of IVM compared to IVF in infertile females with PCOS regarding pregnancy rate. The results of our study revealed that IVM is cheaper than IVF and may be associated with lower OHSS compared to IVF. However, we suggest this technique as an alternative technique for IVF in infertile females with PCOS. Conducting further studies to compare outcome of IVM and IVF in infertile females with PCOS, particularly randomized controlled trials, is recommended.

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Footnote

Conflict of interests: All authors have confirmed that they had no conflict of interest in this project.

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