

Comparison of *In Vitro* Fertilization Cycle Outcome between Patients with Polycystic Ovary Syndrome and Tubal Factor

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Abstract

Background: Infertility with an incidence of about 15% has been considered one of the major burdens on the community and has even been a threat to the continuity of the family life. One of the most prevalent causes of women infertility is ovarian causes particularly PCOS. The objective of this study was to determine the outcome of IVF & ET in women with PCOS in comparison with tubal factor.

Material and Methods: This historical cohort study was performed from 2000 to 2002, in Royan Institute. Our cases consisted of 33 patients with PCOS (without any other causes of infertility) who failed standard ovulation induction treatment with clomiphene citrate (≥ 6 cycles) and had undergone 33 cycles of IVF & ET. Control group consisted of 76 patients with only tubal factor infertility. Our study was performed during the first cycle of IVF in two groups, using long protocol with Buserelin (GnRH α and HMG). IVF and ET cycle characteristics were compared using student's t-test, χ^2 and Fisher's exact test.

Results: The results of this research showed that a statistically significant difference existed in mean age and incidence of OHSS between the two groups. But there were no statistically significant differences in duration of follicular phase, the duration of GnRH α use up to onset of HMG, cyst number after using GnRH α , the percentage of cyst aspiration, HMG ampule consumption, retrieved oocyte, number of embryo per patient, embryo transfer per patient, cycle cancellation and pregnancy rate per embryo transfer in two groups.

Conclusion: The result of this study showed that IVF/ET can be a successful treatment in PCOS patients resistant to other usual treatments and that hormonal disturbance of PCOs patients had no significant effect on IVF/ET outcome in comparison to patients with tubal factor.

Keywords: Polycystic Ovarian Syndrome, Tubal Factor, IVF & ET Outcome

Introduction

Infertility is a serious problem affecting familial life. About 30-40% of the causes are due to failure in ovarian function, with Polycystic Ovarian Syndrome (PCOS) being the most prevalent (1). PCOS, with a prevalence of 5%, is one of the causes of anovulation among women during reproductive age. The diagnosis of PCOS requires the presence of hyperandrogenism and chronic anovulation (2). The best treatment for ovulation stimulation in PCOS patients is using clomiphene which often ends up in high incidence of ovulation and pregnancy. In vitro fertilization and embryo transfer (IVF-ET) is an accepted form of treatment for 10-20% of PCOS refractory to

standard methods of ovulation induction.

Patients with different etiologies for infertility like endometriosis, male factor, tubal factor and PCOS have undergone IVF and intracytoplasmic sperm injection (ICSI). Many researches about the effect of infertility cause on the outcome of pregnancy have been done and had different results. The issue of endocrinological disturbances in patients with PCOS and its effect on the outcome of IVF-ET is important and it seems that the raised concentration of luteinizing hormone (LH), as well as premature LH surge have adverse effect on follicle and oocyte development, and are believed to be responsible for the relatively

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low pregnancy rate in this group of patients (2-6).

Therefore, in this study pregnancy rate was compared between two groups of PCOS and tubal factor (T.F) patients who underwent IVF cycles.

Material and Methods

In this historical cohort study, the outcome of IVF-ET was compared between 33 patients with PCOS and 76 women with TF. This study was approved by ethics committee of Royan Institute.

Spermaograms were normal in both groups. The diagnosis of PCOS was established by the presence of hyperandrogenism and anovulation while tubal factor, was diagnosed by hysterosalpingography (HSG) and laparoscopy. In all patients hormonal evaluation (FSH, LH, Estradiol, Prolactin and DHEA in third day of menstruation cycle) and sonography (third day of menstruation) were performed. Thereafter, they underwent long GnRH agonist protocol (Superfact, Hoechst, Germany). GnRHa (500 μ g) was injected subcutaneously from day 21 of the previous cycle for two weeks. After ovarian suppression, Buserelin was reduced to 200 μ g and HMG, two ampoules daily, (Pregonal, Serono, Italy or Humegoen, Organon) was started. The dose of HMG was adjusted using daily ultrasound (Aloka -600, Japan) monitoring. Human Chorionic Gonadotropin (Pregnyl, Organon, Holland) was administered intramuscularly as a single dose of 10,000U when at least three follicles, 18-20mm in diameter, were detected. Oocyte retrieval was performed after 48 hours and In vitro fertilization and embryo transfer were performed, 48-72 hours after fertilization.

Intramuscular progesterone (100mg/day) was administered for luteal phase support. Pregnancy was confirmed by measurement of β HCG on day 9 and day 12 after embryo transfer and detecting gestational sac by sonography. If more than 15 follicles were detected in each ovary or $E_2 > 3000$ pg/ml, the patient was considered as prone to ovarian hyperstimulation syndrome (OHSS). Among PCOS patients who were at risk of developing OHSS, gonadotropin was discontinued for 3-5 days (coasting). If Estradiol reduction was achieved, HCG was injected and the cycle continued otherwise, the cycle was cancelled.

Information about age, duration of infertility, cause of infertility, duration of using GnRHa up to onset of HMG, number of cyst after starting Buserelin, duration of follicular phase from onset of HMG up to HCG, number of retrieved oocytes, number of transferred embryos and pregnancy were obtained from patient's file and were compared between the two groups.

Pregnancy was diagnosed by measuring β HCG concentration 9 and 12 days after embryo transfer and presence of intrauterine gestational sac detected by transvaginal ultrasound.

For data entry SPSS version 11 was used. Student's t-test, χ^2 and Fisher exact test were used for statistical analysis. P-value less than 0.05 was considered as statistically significant.

Results

In this study, 33 PCOS patients and 76 T.F patients were evaluated. Mean duration of infertility was 9 ± 3.7 years in PCOS women and 9.1 ± 5.2 years in T.F group with no statistically significant difference ($P=0.46$). Primary infertility was 85.3% in PCOS and 73.3% in TF patients, again with no statistically significant difference ($P=0.16$).

Mean age in PCOS and T.F patients was 28.5 ± 4.2 and 32 ± 5.3 years, respectively with statistically significant difference ($P=0.00007$). There was no statistically significant difference between the two groups considering duration of follicular phase stimulation from onset of HMG till initiation of HCG, number of retrieved oocytes, duration of GnRH agonist administration up to starting HMG, number of HMG ampoules used, number of embryos per patient and number of transferred embryos per patient (Table 1), percentage of cyst development after Buserlin administration, cyst aspiration, conception per embryo transfer and cancelled cycles.

There was significant difference between the two groups with respect to OHSS development (Table 2). In this study, cycle was considered cancelled if patients didn't refer, were poor responders to gonadotropins, estradiol was less than 300pg/ml or more than 3000pg/ml.

Table 1: Characteristics of women with PCOS and T.F

Characteristics	PCOS (n=33)	T.F (n=76)	P-Value	Power
Duration of GnRH α upto starting HMG (Day)	13.3 \pm 3.5	12.6 \pm 2.5	0.4	18%
Duration of follicular phase induction from starting HMG up to HCG (Day)	12.3 \pm 2.83	10.9 \pm 3.2	0.23	62%
Number of HMG ampoules administered	31.8 \pm 10.8	29.1 \pm 11.05	0.16	22%
Number of retrieved oocytes	7.7 \pm 5.7	6.7 \pm 65.7	0.41	13%
Number of embryos	5.1 \pm 4.5	4.6 \pm 3.6	0.96	9%
Number of transferred embryos	2.7 \pm 1.4	3.6 \pm 1.3	0.17	24%

No significant difference in any result

Table 2: Comparison of results between the two groups (PCOs and T.F)

Characteristics	PCOS (n=33)	T.F (n=76)	P-Value	Power
The percentage of cyst formation after Buserelin	12.1%	23%	29%	16%
The percentage of cyst aspiration	3.03%	10.5%	0.44	10%
The percentage of OHSS	17.6%	2.7%	0.004*	62%
Pregnancy per embryo transfer	20%	18%	0.73	3%
Cancelled cycles	0%	5.9%	1	5%

*Significant difference between the two groups

Discussion

The objective of this study was to evaluate and compare the fertility rate in PCOS patients and those with tubal factor and normal ovarian function. We used the long GnRH agonist protocol which is confirmed by most researchers (1, 7-9). The results of this study showed that pregnancy rate per embryo transfer (ET) was 20% and 18% in PCOS and TF groups, respectively, with no statistically significant difference and similar to findings by Homburg et al., Mac Dougal et al., Dor et al and Grochowski et al (8, 10-12).

Mean ages in PCOS and T.F groups were statistically different but as there is no difference in fertility rate between the ages 28 and 32 years (13, 14), it seems that this difference has no adverse effect on pregnancy outcome. Although, it is better to adjust different groups by age in future studies.

Results of this study showed no statistically significant difference between the two groups considering the duration of follicle stimulating (from starting HMG till initiation of HCG) which is similar to findings of Engmann et al (15).

Also there was no significant difference in number of retrieved oocytes between the two groups while previous studies have shown that more oocytes were retrieved in PCOS group (Homburg et al, Mac Dougal et al., Salat et al.) (10, 11, 16).

This difference can be due to: 1) using coasting protocol in patients at risk of OHSS which may cause less number and less quality of oocytes, 2) low power of this study 3) Partial Empty Follicle Syndrome secondary to severe ovarian responses and follicle development in PCOS group in comparison to TF group.

This study showed no significant difference between the two groups considering number of embryos which is similar to the results of Salat (16), Dor (12) and Urman et al (6).

In this study 17.6% of cycles in PCOS group resulted in moderate OHSS which was significantly higher than TF group (2.7%). This finding was similar to Dougal et al., Dale et al., Urman et al and Wada et al studies (6, 11, 17, 18).

Conclusion

This study suggests that IVF-ET is an acceptable form of treatment for PCOS patients who did not respond to standard methods of ovulation induction, although, these patients have a tendency toward progressing OHSS because of hormonal disturbances. Therefore, they should be followed by sonographic monitoring and Estradiol measurement to prevent OHSS. In summary, IVF-ET in patients with PCOS

result in pregnancy rates comparable with those of women with pure tubal factor infertility and it could be the same or even higher than other groups.

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References

1. Speroff L, Glass RH, Kase NG. Clinical gynecologic endocrinology and infertility. 6th Edition, Baltimore, Lippincott Williams & Wilkins. 1999; 1097-1133
2. Ryan KJ, Berkowitz RS, Barbieri RL, Dunaif A. Kistner's Gynecology & women's 7th Edition, Mosby, ST. Louis Baltimore, Boston Philadelphia 1999
3. Keye WR, Chang RJ, Reber RW, Soules MR. Infertility Evaluation and Treatment. W. B. Saunders Company, 1995
4. Csemiczky G, Landgren BM, Fried G, Wramsby H. High tubal damage grade is associated with low pregnancy rate in women undergoing in-vitro fertilization treatment. Hum Reprod. 1996; 11(11): 2438-2440
5. Oehninger S, Scatt R, Muasher SJ. Effect of the severity of tubo-ovarian disease and previous tubal surgery on the results of IVF and ET. Fertil Steril. 1989; 51: 126-130
6. Urman B, Fluker MR, Yuen BH, Fleige-Zahradka BG, Zouves CG, Moon YS. The outcome of in vitro fertilization and embryo transfer in women with polycystic ovary syndrome failing to conceive after ovulation induction with exogenous gonadotropins. Fertil Steril. 1992;57(6):1269-1273
7. Hughes E, Collins J, Vandekerckhove P. Gonadotrophin-releasing hormone analogue as an adjunct to gonadotropin therapy for clomiphene-

resistant polycystic ovarian syndrome. Cochrane Database Syst Rev. 2000;(2):CD000097. Review

8. Grochowski D, Kulikowski M, Wolczynski S. The outcome of IVF program in women with PCOS. Gynecol Endocrinol. 1997; 11: 259-262
9. Turhan NO, Artini PG, D'Ambrogio G, Droghini F, Battaglia C, Genazzani AD, Volpe A, Genazzani AR. A comparative study of three ovulation induction protocols in polycystic ovarian disease patients in an in vitro fertilization/embryo transfer program. J Assist Reprod Genet. 1993 Jan; 10(1): 15-20
10. Homburg R, Berkowitz D, Levey T, Feldberg D, Ashkenazi J, Ber-Rafael Z. IVF and ET for treatment of infertility associated with PCOS. Fertil Steril. 1993; 60: 858-863
11. Mac Dougall MJ, Tan SL, Balen A, Jacobs HS. A controlled study comparing patients with and without PCO undergoing IVF. Hum Reprod. 1993; 8: 233-270
12. Dor J, Shulman A, Levran D, Ben-Rafael Z. The treatment of patients with PCOS by IVF and ET: a comparison of results with those of patients with tubal infertility. Hum Reprod. 1990; 5: 816-818
13. Osmanagaoglu K, Tournaye H, Kolibianakis E, Camus M, Van Steirteghem A, Devroey P. Cumulative delivery rates after ICSI in women aged >37 years. Hum Reprod. 2002; 17(4): 940-944
14. Auyeung A, Klein ME, Ratts VS, Odem RR, Williams DB. Fertility treatment in the forty and older woman. J Assist Reprod Genet. 2001; 18(12): 638-643
15. Engmann L, Maconochie N, Sladkkevicius P. The outcome of IVF treatment in women with sonographic evidence of PCO morphology. Hum Reprod 1999; 14: 167-171
16. Salat-Baroox J, Alvarez S, Antonie JM, Cornet D, Tibi C, Plachot M. Result of IVF in the treatment of PCOD. Hum Reprod. 1988; 3: 331-333
17. Dale PO, Tanbo T, Abyholm T. In-vitro fertilization in infertile women with the polycystic ovarian syndrome. Hum Reprod. 1991; 6(2): 238-241
18. Wada I, Matson PL, Troup SA. Assisted conception using buserelin and HMG in women with PCOS. Br J Obstet Gynecol. 1993; 100: 365-369
