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Cetrorelix in ICSI Cycles of Women with one Ovary

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INTRODUCTION

A significant number of single ovary women participate in programs of assisted reproductive technologies (ART) and consequently a number of studies have tried to answer whether these women have the same capability for conception comparing with women having both ovaries (1-10). In all these studies, the stimulation protocols included either clomiphane citrate (CC) and human menopausal gonadotropins (hMG) or gonadotropin releasing hormone agonists (GnRHagonists) with hMG or recombinant follicular releasing hormone (rFSH). Recently, gonadotropin releasing hormone antagonists (GnRH-antagonists) have been introduced into the clinical practice, offering immediate suppression of serum luteinazing hormone (LH) and avoidance of the flare-up effect (11-16). So far, two GnRH-antagonists are available: cetrorelix and ganirelix. In the use of cetrorelix, two different stimulation protocols have been developed: the single dose protocol and the multiple dose one (11-16).

In the present study, the multiple protocol of cetrorelix was evaluated retrospectively in a group of women with one ovary.

MATERIALS AND METHODS

Seven women with one ovary underwent 12 treatment cycles (group A). The control group (group B) included 39 treatment cycles from 31 women of comparable age. Male factor was the cause of infertility in all cases. In both groups, the ovarian stimulation protocol included suppression with the GnRH-antagonist cetrorelix (Cetrotide ®, ASTA Medica AG, Frankfurt/Main, Germany and Serono International S.A., Geneva, Switzerland) in a multiple dose schedule (Lübeck protocol):

0.25mg per day from cycle day 6 onwards until ovulation induction. The stimulation was achieved with hMG (Menogon ®, Ferring Arzneimittel GmbH, Kiel, Germany) or rFSH (Gonal-F ®, Serono International S.A., Geneva, Switzerland). The administration of hMG/rFSH was individually adjusted according to serum estradiol levels and ovarian sonography. Ovulation was induced by injection of 10000 IU human chorionic gonadotropin (hCG) when the serum estradiol concentration increased to about 300-500 pg/ml per follicle >17mm. Oocyte retrieval was performed 36 hours following hCG injection.

Sperm preparation and Intracytoplasmic Sperm Injection (ICSI) were performed as previously described. (17,18). Embryo transfers were carried out 48 hours after oocyte retrieval. In each embryo transfer, according to the degree of embryos' fragmentation, the number of blastomeres and the regularity of blastomeres, the cumulative embryo score (CES) was calculated (19). Clinical pregnancies were defined by the presence of positive foetal heartbeats. In that case, progesterone was administrated up to 12th week of gestation.

RESULTS

There were no significant differences in any of the analysed parameters between the two groups. In group A, 2 pregnancies were achieved and 4 children were born. In group B, there were 10 pregnancies and 9 children were born.

CONCLUSIONS

Women with one ovary have the same response to multiple dose protocol of cetrore-lix/hMG/rFSH as women having both ovaries; al-

though they have a lower, but not statistical significant, pregnancy rate.

Table 1
Comparison of ovarian response and ICSI/ET outcome between women with one ovary and women with two ovaries

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	One ovary (group	two ovaries	р
	A)	(group B)	
No of cycles	12	39	
Age (years)	30.17±4.41	33.31±5.62	n.s.•
Cycles of poor response	3	9	n.s.#
Days of stimulation	11.22±1.48	11.25±2.78	n.s.*
No of gonadotropin ampoules	40.00±21.07	32.5±15.84	ก.ร.*
Peak estradiol	1836.33±1439.97	1534.42±979.4	n.s.*
(pg/ml)		1	,
No of follicles	8.78±2.49	9.56±3.95	n.s.∙
No of retrieved oocytes	6.58±4.1	6.54±3.32	n.s.•
No of 2PN occytes	4.08±3.37	3.95±2,21	n.s.*
Fertilisation rate (%)	62.03	60.39	n.s.#
No of transferred	2.17±1.19	2.41±0.68	n.s.*
embryos			
CES	17.25±13.92	23.51±11.59	n.s.∙
No of pregnancies	2	10	n.s.#
No of born children	4	9	n.s.#

All values are mean±SDdeviation. •: Student t-test was used. *: K-S and U-test were used. #: Chi-square and v-square were used.

REFERENCES

- 1. Alper M.M., Seibel M.M., Oskowitz S.P., Smith B.D., Ransil B.J., Taymor M.L.: Comparison of follicular response in patients with one or two ovaries in a program of in vitro fertilization. *Fertil. Steril.* 44: 652-6555 (1985)
- Boutteville C., Muasher S.J., Acosta A.A., Jones H.W.Jr., Rosenwaks Z.: Results of in vitro fertilization attempts in patients with one or two ovaries. *Fertil. Steril.* 47: 821-827 (1987)
- 3. Diamond M.P., Colston Wentz A., Herbert C.M., Pittaway D.E., Maxson W.S., Daniell J.F.: One ovary or two: differences in ovulation induction, estradiol levels and follicular development in a program for in vitro fertilization. *Fertil. Steril.* 41: 524-529 (1984)
- 4. Dodds W.G., Chin N., Awadalla S.G., Miller F., Friedman C., Kim M.: In vitro fertilization and embryo transfer in patients with one ovary. *Fertil. Steril.* 48: 249-253 (1987)
- 5. Dodson M.G., Young R.L., Poindexter A.N., Gibbons W.E., Rossavik I.K., Findley W.E.: Comparison of in vitro fertilization results in women with one or two ovaries. *J. Reprod. Med. 32*: 359-362 (1987)
- 6. Khalifa E., Toner J.P., Muasher S.J., Acosta A.A.: Significance of basal follicle-stimulating hormone levels in women with one ovary in a program of in vitro fertilization. *Fertil. Steril.* 57: 835-839 (1992)
- Lass A., Paul M., Margara R., Winston R.M.L.: Women with one ovary have decreased response to GnRHa/HMG ovulation induction protocol in IVF but the same pregnancy rate as women with two ovaries. *Hum. Reprod.* 12: 298-300 (1997)

- 8. Levitas E., Furman B., Shoham-Vardi I., Lunenfeld E., Potashnik G.: Treatment outcome in women with a single ovary versus patients with two ovaries undergoing in vitro fertilisation and embryo transfer (IVF/ET). Eur. J. Obstet. Gyn. Reprod. Biol. 88: 197-200 (2000)
- 9. Nargund G., Bromhan D.: Comparison of endocrinological and clinical profiles and outcome of IVF cycles in patients with one ovary and two ovaries. *J. Assist. Reprod. Genet.* 12: 458-460 (1995)
- 10. Penzias A.S., Gutmann J.N., Shamma F.N., LaMorte A.I., DeCherney A.H.: Ovulation induction with GnRH agonist and human menopausal gonadotropins: response in patients with one versus two ovaries. *Int. J. Fertil. Menopausal. Stud. 38*: 270-273 (1993)
- 11. Albano C., Smitz J., Camus M., Riethmuller Winzen H., Van Steirteghem A., Devroey P.: Comparison of different doses of gonadotrophin-releasing hormone antagonist Cetrorelix during controlled ovarian hyperstimulation. Fertil. Steril. 67: 917-922 (1997)
- 12. Felberbaum R., Reissmann T., Küpker W., Al-Hasani S., Bauer O., Schill T., Zoll C., Diedrich C., Diedrich K.: Hormone profiles under ovarian stimulation with human menopausal gonadotropin (hMG) and concomitant administration of the gonadotropin releasing hormone (GnRH)-antagonist Cetrorelix at different dosages. *J. Assist. Reprod. Genet.* 13: 216-222 (1996)
- 13. Felberbaum R.E., Albano C., Ludwig M., Riethmüller-Winzen H., Grigat M., Devroey P., Diedrich K.: Controlled ovarian stimulation for assisted reproduction with hMG and concomitant midcycle administration of the LHRH-antagonist Cetrorelix (Cetrotide) according to the multiple dose protocol-results of a prospective non controlled phase III study. *Hum. Reprod.* 15: 1015-1020 (2000)
- 14. Ludwig M., Katalinic A., Diedrich K.: Use of GnRH antagonists in ovarian stimulation for assisted reproductive technologies compared to the long protocol. Meta-analysis. *Arch. Gynecol. Obstet. 265*: 175-182 (2001)
- 15. Nikolettos N., Al-Hasani S., Felberbaum R., Demirel L.C., Kupker W., Montzka P., Xia Y.X., Schopper B., Sturm R., Diedrich K.: Gonadotropin-releasing hormone antagonist protocol: a novel method of ovarian stimulation in poor responders. *Eur. J. Obstetr. Gynec. Repr. Biology 97*: 202-207 (2001)
- 16. Diedrich K., Felberbaum R.: New approaches to ovarian stimulation. *Hum. Reprod.* 13: 1s-13s (1998)
- 17. Al-Hasani S., Küpker W., Baschat A.A., Sturm R., Bauer O., Diedrich C., Diedrich K.: Mini-swim up: a new technique of sperm preparation for intra-cytoplasmic sperm injection. J. Assist. Reprod. Genet. 12: 428-433 (1995)
- 18. Al-Hasani S., Ludwig M., Karabulut O., Al-Dimassi F., Bauer O., Sturm R., Kahle D., Diedrich K.: Results of intracytoplasmic sperm injection (ICSI) using microprocessor controlled Transfer Man Eppendorf Manipulator system. *J. Middle East Fertil. Soc. 4*: 41-44 (1999)
- 19. Steer C.V., Mills C.L., Tan S.L., Campbell S., Edwards R.G.: The cumulative embryo score: a predictive embryo scoring technique to select the optimal number of embryos to transfer in an IVF-ET program. *Hum. Reprod. 7*: 117-119 (1992)