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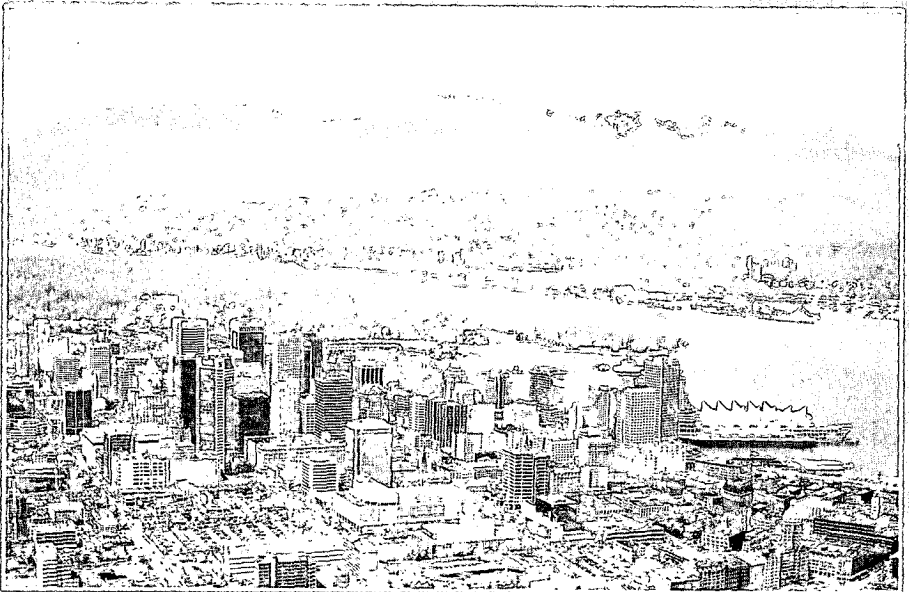
IN VITRO FERTILIZATION AND ASSISTED REPRODUCTION

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A comparison of pregnancy rates (PRs) following frozen embryo transfer (ET) in women receiving estrogen in gradually rising doses by use of down regulation of gonadotropin with leuprolide acetate (LA) in the luteal phase

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SUMMARY

The pregnancy outcome following frozen embryo transfer (ET) in 35 hormone replacement (HRT) cycles was compared to that of 71 HRT cycles with down regulation with gonadotropin releasing hormone agonist (GnRHa) in women with normal menstrual and ovulatory function. The number of embryos transferred was the same in both groups. The clinical pregnancy rates (PRs) were 31.4% (11/35) in the HRT group and 28.2% (20/71) in the down regulated/HRT group ($p=NS$). The implantation rates were 13.9% and 10.7%, respectively ($p=NS$). These data demonstrated no beneficial or detrimental effects of down regulation on pregnancy or implantation rates following frozen ET.

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INTRODUCTION

With the increased use of cryopreservation of human embryos, the need to properly prepare the patient undergoing frozen ET to assure that the thawed embryos are placed into the best uterine environment is crucial. Research on preparation of ovum recipients for ET, has shown that for recipients who still have menstrual function, hormone replacement cycles are superior to natural cycles in producing an adequate endometrium (Check et al, 1991). Edwards et al, (1991) have shown that oocyte recipients who have amenorrhea have higher success rates than their menstruating counterparts. They suggested that the elevation of luteinizing hormone (LH) and other changes associated with ovulation may have an adverse effect on implantation.

The objective of this study was to investigate the possible benefits of down regulation with GnRHa in women with normal ovulatory and menstrual function in improving the success rates following frozen ET.

MATERIALS AND METHODS

A retrospective clinical study was conducted comparing the outcome of frozen ETs for 35 women using the HRT stimulation protocol and 71 women using the HRT protocol in conjunction with down regulation. All the women were at most 38 years old and demonstrated normal menstrual and ovarian function. They were undergoing in vitro fertilization (IVF) therapy for either tubal factor, endometriosis, male factor or unexplained infertility. Patients with severe male factor, who used intracytoplasmic sperm injection were excluded. The first frozen ET for each woman was used in the study.

In the HRT protocol, patients were given Estrace (2mg) on days 1-5 of the cycle, 4mg on days 6-9 and 6mg on days 10-14. Progesterone (P) supplementation began on day 15 with an initial daily dose of 25mg IM and continued from day 16 on at a daily dose of 50mg IM. Protocol were adjusted based on serum hormone levels and sonographic monitoring as needed. In down regulation/HRT cycles, leuprolide acetate (LA) 1mg SC was administered for 10 days beginning in the luteal phase (day 21 of cycle before transfer). HRT began on day 11 of LA at which time the LA dosage was decreased to .5mg daily. LA was then administered for 5 additional days.

Embryos were cryopreserved and thawed using a one-step addition and dilution of cryoprotectant. The cryopreservation method involved a slow cooling program starting at the seeding temperature of -6.0°C in an alcohol bath controlled freezer. 1.5 M 1,2 propanediol was added to pronuclear stage embryos before cooling. A fast thawing technique at room temperature was used and the cryoprotectant was removed from the embryos in one step with a 1.08 M sucrose solution (Baker et al, 1997).

The main outcome measures were clinical PRs (evidence of gestational sac in the uterus) and implantation rates (number of sacs/embryos transferred). Chi-square analysis was used to compare the PR and implantation rates by stimulation protocol used. A p value of .05 was used.

RESULTS AND CONCLUSIONS

The 35 women using the HRT protocol ranged in age from 25 to 38 years with a mean \pm SD of 31.8 ± 3.8 years. The 71 women using the HRT

protocol with down regulation ranged in age from 28 to 38 with a mean \pm SD of 33.7 ± 3.0 .

The groups were similar in terms of the average number of embryos thawed per cycle and the average number of embryos transferred. In the HRT group, an average of $3.9 \pm .7$ embryos were thawed per cycle and $3.7 \pm .7$ were transferred; in the down regulated/HRT group, an average of $3.8 \pm .8$ embryos were thawed and $3.5 \pm .7$ were transferred.

The clinical PRs were 31.4% (11/35) in the HRT group and 28.2% (20/71) in the down regulated/HRT group ($p = \text{NS}$, chi-square). The corresponding implantation rates were 13.9% (18/29) and 10.7% (27/252), respectively ($p = \text{NS}$, chi-square).

Despite reports that down regulation with GnRHa may have some beneficial impact on implantation, eugonadotropic women with normal menstrual and ovulatory function did not demonstrate increased PRs with the use of down regulation with GnRHa following frozen ET. The use of graduated doses of estrogen in ovulating women from the early follicular phase appears to suppress premature luteinization as well as down regulation with LA starting in the luteal phase for at least 10 days prior to starting estrogen treatment in preparation for frozen ET.

The data presented herein showed that the use of estrogen replacement alone is a very effective, inexpensive method of preparing the uterus for frozen ET. Thus, as a first line of treatment, it would seem to make sense to not include GnRHa down regulation in order to reduce costs and avoid the discomfort to the patients of LA injections.

REFERENCES

1. Baker AF, Check JH, Hourani C. Survival and pregnancy rates of pronuclear stage human embryos cryopreserved and thawed using a single step addition and removal of cryoprotectant, Hum Reprod Update in press;1997.
2. Check JH, Nowroozi K, Choe J, Dietterich C. Influence of endometrial thickness and echo patterns on pregnancy rates during in vitro fertilization. Fertil Steril 56:1173-1175;1991.
3. Edwards RG, Morcos S, Macnamee M, Balmaceda JP, Walters DE, Asch R. High fecundity of amenorrhoeic women in embryo transfer programmes. Lancet 338:292-294;1991.

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