The relationship of clinical response, oocyte number, and success in oocyte donor cycles¹

Gerard Letterie,^{2,3} Lorna Marshall,² and Marlane Angle²

Submitted July 12, 2004; accepted October 22, 2004

Purpose: The purpose of the study was to determine if there is a threshold of clinical response to ovarian stimulation below which pregnancy rates diminish in oocyte donation cycles.

Methods: Two hundred and seventy-six oocyte donor cycles were reviewed. Data were stratified by number of oocytes retrieved and divided into pregnant versus non-pregnant outcomes.

Results: There were no differences in fertilization rates or clinical pregnancy rates regardless of the number of oocytes retrieved ranging from 3 to >25. There was no difference in the mean age of the donors in pregnant versus non-pregnant cycles.

Conclusions: These data suggest that a lower threshold below which cycle cancellation should be considered donation cycles is different than standard IVF.

KEY WORDS: Clinical pregnancy rate; in vitro fertilization; oocyte donation.

INTRODUCTION

Oocyte donation is a treatment modality for a variety of complex reproductive problems. This procedure has made childbearing possible in women with age-related infertility and diminished ovarian reserve or lack of functional ovarian tissue (1). The process is unique in several clinical and ethical aspects (2–4). Management of ovarian stimulation in donors and embryo selection for recipients may require a paradigm distinct from that of standard in vitro fertilization cycles. Differences in cycle management for donors may include a broader interpretation of clinical response and indications for cycle cancellation different from commonly accepted criteria in non-donor cycles. A wider range of clinical responses may be acceptable in this group that result in high ongoing

clinical pregnancy rates. The purpose of this study was to determine if there is a threshold of clinical response to ovarian stimulation below which pregnancy rates diminish in oocyte donation cycles.

MATERIALS AND METHODS

A retrospective data analysis of oocyte donation cycles for 3 years at a tertiary care center was undertaken. Two hundred seventy-six oocyte donation cycles were reviewed. Data were stratified by the number of oocytes retrieved and divided into pregnant (group 1) versus non-pregnant (group 2) outcomes. Clinical pregnancy rates, peak serum estradiol concentrations, fertilization rates, and rates of embryo cryopreservation were calculated and compared for each group. Statistical analysis was made with Chi-square analysis and analysis of variance (ANOVA) using *InSTAT* software.

Stimulation Protocols

Donor Stimulation Donors were cycled with 21 days of combination oral contraceptives (ethinyl

¹ Presented at the 59th Annual Meeting of the American Society for Reproductive Medicine 2003, San Antonio, Texas.

² Center for Fertility and Reproductive Endocrinology, Virginia Mason Medical Center, Seattle, Washington.

³ To whom correspondence should be addressed at Northwest Center for Reproductive Sciences, 12040 NE 128th Street, Kirkland, Washington 98034-3098; e-mail: chowletterie@comcast.com.

estradiol/norethindrone). Pituitary suppression was initiated on day 14 of the oral contraceptive cycle with nafarelin or leuprolide acetate. The GnRH analog was continued through the stimulation protocol until the time of retrieval. Ovarian hyperstimulation was conducted using two to three ampules of recombinant follicle stimulating hormone, depending on body mass index (BMI) and one ampule of urinary gonadotropins regardless of BMI. Human chorionic gonadotropin (hCG) (10,000 IU intramuscularly) was administered when at least two follicles were 18 mm in diameter. Transvaginal oocyte retrieval was then performed 34 h after hCG under propofol intravenous sedation.

Recipient Stimulation Recipients were given 21 days of combination oral contraceptives (ethinyl estradiol/norethindrone). Pituitary suppression was accomplished using leuprolide acetate, beginning on day 14 of the oral contraceptive cycle. Leuprolide was continued through the start of endometrial stimulation with estradiol and discontinued on the day of hCG administration to the donor. Estradiol valerate 4 mg was administered intramuscularly. Serum estradiol concentrations were monitored throughout the cycle until 10 weeks gestation. Transvaginal ultrasound examination to assess endometrial thickness was performed beginning on day 8 of estradiol administration and continuing weekly, if necessary. All recipients had an endometrial thickness of at least 10 mm at the time of transfer.

RESULTS

Clinical outcomes for donors are summarized in Table I. Number of oocytes retrieved ranged from 4 to 42. There were no differences in the fertilization rates or clinical pregnancy rates regardless of

the number of oocytes retrieved. Significant differences, however, were noted in serum estradiol concentrations for donors having <10 oocytes and >25 oocytes retrieved ($p \leq 0.05$). The number of cycles that resulted in cryopreserved embryos was related to the number of oocytes retrieved. There was no difference in the mean age of the donors and the pregnant cycles versus non-pregnant cycles (26.1 vs. 25.2 years). No differences were noted in the serum estradiol concentrations in the recipients at the time of embryo transfer in pregnant versus non-pregnant cycles (981 ± 272 vs. 1011 ± 282 pg/mL) (mean $\pm$ standard deviation). All recipients had an endometrial thickness of 8–10 mm at the time of embryo transfer. There were no cycle cancellations.

DISCUSSION

Oocyte donation has emerged as a widely used technique in reproductive medicine. In the United States, 5,162 oocyte donation cycles were performed in 1996 and 6,643 in 1997 (5). The protocol for ovarian stimulation in donors and endometrial stimulation in recipients is well understood and precisely described in multiple studies (6,7,8). Clinical decisions regarding cycle cancellation may, however, differ from non-donor cycles and require a management paradigm different than that in non-donor cycles. Data from shared oocyte donation cycles provide some insight regarding a lower limit. A response of 8–10 oocytes resulted in no change in pregnancy rates. In this study, there were no differences in pregnancy rates when at least 8 oocytes were retrieved and divided, 4 to each recipient versus at least 12 oocytes retrieved and divided 6 to each recipient. The reduction in the lower limit of oocytes eligible for retrieval did, however, result in a lower

Table I. Clinical Outcomes by Oocyte Number

	Oocytes retrieved					
	0–5	6–10	11–15	16–20	21–25	>25
Pregnant cycles						
Serum $E_s^{\dagger,*}$	1351 $\pm$ 814	2179 $\pm$ 1469	2556 $\pm$ 1686	3091 $\pm$ 1421	2910 $\pm$ 1112	5112 $\pm$ 1710
Fertilization rate (%)	74	80	67	69	74	65
Clinical PR (%)	67	50	44	56	49	61
Cryopreservation	0	51	55	50	42	60
Non-pregnant cycles						
Serum $E_2^{\dagger,*}$	1402 $\pm$ 941	2312 $\pm$ 1014	3286 $\pm$ 1221	2472 $\pm$ 910	2491 $\pm$ 1004	5317 $\pm$ 1716
Fertilization rate (%)	50	61	76	75	71	69
Cryopreservation (% cycles)	0	0	15	52	50	61

*Mean $\pm$ Standard deviation.

† pg/ml.

cycle cancellation rate from 30% when at least 12 oocytes were anticipated versus 10% when 8 or more oocytes were anticipated.

In the present study, the lower limit for the number of oocytes retrieved was defined. In this setting, a diminishing number of oocytes did not impact overall pregnancy rates. It did, however, result in fewer embryos available for cryopreservation when five or fewer oocytes were available. Clinical outcome based on predicted number of oocytes retrieved was not a reliable indicator of pregnancy rate. These data suggest a lower threshold below which cycle cancellation should be considered may not be the same for oocyte donation cycles versus non-donor cycles. By reducing the absolute number of oocytes required for retrieval in donor cycles, a reduction in overall cycle cancellation rates may be appreciated. This paradigm differs from that of standard in vitro fertilization (IVF) cycles.

In summary, no differences in pregnancy rates were noted when total number of oocytes retrieved was compared ranging from a minimum of 4 to >25. These findings suggest a potential role for minimal stimulation of donors to avoid hyperstimulation syndrome in a non-shared donor programs. Significant differences, however, were noted in the percent of cycles that resulted in cryopreserved embryos, depending on the number of oocytes retrieved. The

enhanced cryopreservation with increasing oocyte number may improve efficiency of the donor cycle.

REFERENCES

1. Pados G, Camus M, Van Steirteghem A, Bonduelle M, Devroey P: The evolution and outcome of pregnancies from oocyte donation. *Hum Reprod* 1994;9:538–542
2. Ahuja KK, Simons EG, Edwards RG: Money, morals and medical risks: Conflicting notions underlying the recruitment of egg donors. *Hum Reprod* 1999;14:279–284
3. Ahuja KK, Simons EG, Fiamanya W, Dalton M, Armar NA, Kirkpatrick P, Sharp S, Arian-Schad M, Seaton A, Watters WJ: Egg-sharing in assisted conception: Ethical and practical considerations. *Hum Reprod* 1996;11:1126–1131
4. Faber BM, Mercan B, Hamacher P, Muasher SJ, Toner JP: The impact of an egg donor's age and her prior fertility on recipient pregnancy outcome. *Fertil Steril* 1997;68:370–372.
5. Toner JP, Grainger DA, Frazier LM: Clinical outcomes among recipients of donated eggs: An analysis of the U.S. national experience, 1996–1998. *Fertil Steril* 2002;78:1038–1045
6. Marina S, Exposito R, Marina E, Nadal J, Masramon M, Verges A: Oocyte donor selection for 554 candidates. *Hum Reprod* 1999;14:2770–2776
7. Abdalla HI, Billett A, Kan AK, Baig S, Wren M, Korea L, Studd JW: Obstetric outcome in 232 ovum donation pregnancies. *Br J Obstet Gynaecol* 1998;105:332–337
8. Kolibianakis EM, Tournaye H, Osmanagaoglu K, Camus M, Van Waesberghe L, Van Steirteghem A, Devroey P: Outcome for donors and recipients in two egg-sharing policies. *Fertil Steril* 2003;79:69–73