Original Article

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A comparison of luteal phase support in graduated estradiol/progesterone replacement cycles using intramuscular progesterone alone versus combination with vaginal suppositories on outcome following frozen embryo transfer

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Summary

Purpose: To compare pregnancy outcome following frozen embryo transfer according to type of progesterone (P) support given in the luteal phase.

Methods: Retrospective cohort analysis of frozen embryo transfer (ET) cycles in which ovulation was suppressed by graduated estradiol in the follicular phase. Two P regimens in the luteal phase were compared: P vaginal suppositories and intramuscular P vs intramuscular alone.

Results: The clinical and viable pregnancy rates were significantly higher for the women receiving only intramuscular P (57.6% and 43.7%) vs those receiving combined therapy (45.9% and 35.6%, respectively). The implantation rates were not significantly different (22.6% vs 19.5%).

Conclusion: The increased pregnancy rates with intramuscular P may have been related to a higher number of embryos transferred (3.69 vs 3.26). Nevertheless, intramuscular P alone is at least as effective, if not more effective, than combined therapy for frozen embryo transfers.

Key words: Frozen embryo transfer; Luteal phase support; Vaginal progesterone; Intramuscular.

Introduction

One method to prepare the endometrium for frozen embryo transfer (ET) is to use a graduated estradiol regimen followed by luteal phase support with progesterone (P). Data suggest that using P vaginal suppositories in comparison to an intramuscular (IM) route, can produce a significantly higher P concentration in the endometrium (1). There have been studies comparing the use of the IM route vs P vaginal suppositories which have each reached different conclusions as to which is more efficacious; some have demonstrated the efficacy of the P vaginal suppositories [2, 3], while others advocate the usage of the IM P [4, 5], while still others demonstrate no difference [6, 7]. There have been few studies that have compared pregnancy outcomes with different routes of P administration in preparation for frozen ET in which there is no P contribution from the corpus luteum. The majority of our patients use both vaginal P and IM P during their frozen ET cycles but there is a subset that only receives IM P because of side-effects of the vaginal preparation. The study presented here compared pregnancy rates (PRs) between women receiving a combination of vaginal P and IM P vs those receiving IM P alone.

Materials and Methods

A retrospective review of the outcomes of first frozen ETs reported to the Society for Assisted Reproductive Technology (SART), for patients up to age 45 over a 5-year period was performed. Donor egg recipients were also included in the review. The age of the women used for the study was the age at the time of oocyte fertilization. The analysis included embryos fertilized by conventional insemination and intracytoplasmic sperm injection (ICSI).

Patients were placed in one of two groups depending on the type of luteal phase support they received in preparation for frozen ET. The first group included women who received both 200 mg vaginal P twice daily and 100 mg IM P, while the second group received the exact same dosage of only IM P. The cryopreservation technique used a simplified method in which a slow cooling program was begun at – 6°C in an alcohol bath freezer. The cryoprotectant used was 1,2 propanediol. A one-step fast thawing procedure at room temperature was used and the cryoprotectant was removed from the embryos in one-step [8]. All embryos studied were cryopreserved at the 2 pronuclear stage. The implantation, clinical pregnancy, and live delivery rates were all compared using chi-square analysis.

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Results

There was a significantly higher clinical and viable PR in the group receiving IM P (Table 1). Lower implantation rates were found with the combination group, though the differences were not significant (Table 1). The higher PR could be explained partially by the significantly larger number of embryos transferred in the IM P group (Table 2).

Table 1. — *Pregnancy outcome for frozen ET by type of luteal phase support.*

	P vaginal suppositories + IM	IM only
No. of transfers	713	111
Clinical pregnancies	312	64
% clinical/transfer (p = .006)	43.7%	57.6%
No. of live deliveries	254	51
% delivered/transfer (p = .036)	35.6%	45.9%
Total no. of embryos transferred	2322	410
Total no. of embryos implanted	453	93
Implantation rate (p = .138)	19.5%	22.6%

Table 2. — *Comparison of possible confounding variables.*

	P vaginal suppositories + IM	IM only
Age	34.8 ± 5.12	37.2 ± 6.3
No. of embryos transferred (p < .05)	3.26 ± 1.0	3.69 ± 1.1
Endometrial thickness immediately prior to starting P	10.4 ± 2.57	10.3 ± 2.9

Discussion

These data demonstrate that despite the absence of the corpora lutea, the use of higher dosages of P provided by the additional vaginal P therapy, does not improve outcome. Too much P may actually be detrimental because it may alter the time for window of implantation [9]. It has been suggested that premature trophoblast invasion into an endometrium that is not yet adequately prepared immunologically may lead to embryo rejection before the maternal immune system can be properly modulated [9]. Hopefully, this study will stimulate interest in performing a prospective comparison of both treatment regimens, or even better, to do a three way comparison of vaginal P only, IM P only, and combined therapy.

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