

UTERINE PREPARATION PRIOR TO FROZEN EMBRYO TRANSFER USING LETROZOLE: A CASE SERIES

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Background:

Many clinics in the United States use a “programmed” regimen of oral estradiol and vaginal or intramuscular progesterone to prepare the uterine lining prior to a frozen embryo transfer (FET). However, artificial cycles can be complicated by risk of cycle cancellation due to inadequate lining, and require increased ultrasound monitoring and medication needs. For these reasons, patients and clinics continue to investigate the utility of natural cycles for uterine lining preparation. Several studies suggest no difference in clinical outcomes after FET using a natural cycle versus one with exogenous estrogen and progesterone administration.^{1,2} However, purely natural cycles can be quite variable and may result in missing the optimal window for embryo transfer. A pilot study³ in anovulatory women suggested that letrozole can be used successfully to prepare the uterine lining and result in successful FET cycles. A large meta-analysis comparing FET cycle preparation methods suggested evidence in favor of mild ovarian stimulation.⁴

Objective:

The purpose of our study was to evaluate pregnancy rates for FET cycles at our center, in which uterine lining was prepared using letrozole for ovarian stimulation, followed by embryo transfer and low-dose luteal support. These results were compared to our pregnancy rates for FET cycles using traditional estradiol/progesterone preparation protocols.

Materials and Methods:

For women undergoing this protocol, letrozole 5 mg was administered daily for 5 days starting on cycle day 3. Transvaginal ultrasound was performed on cycle day 12 (1-2 days earlier for patients with menstrual cycles <27 days in length). A dominant follicle ≥ 17 mm was triggered using Ovidrel 250ug, once the endometrial lining was ≥ 7 mm and serum progesterone was confirmed to be ≤ 1.0 ng/mL. Embryo transfer was performed 7 days after trigger, with luteal support (progesterone vaginal suppositories 200mg, Crinone 0.8% gel, or progesterone-in-oil 50mg) administered every evening starting 4 days after trigger. Oral estradiol (2mg) was added daily starting two days after the embryo transfer. The clinical pregnancy rate (CPR) was defined as the proportion of transfers with an intrauterine gestational sac at first ultrasound. Differences in groups were analyzed using Chi-square, with Fisher’s exact test where appropriate.

Results:

Fifty-three women between ages 28-43 underwent 55 embryo transfers using the letrozole protocol. The CPR for letrozole cycles was 63.6%, as compared to 57.1% for transfers using our center’s traditional oral estradiol protocol ($p = 0.347$). Among FET cycles using the letrozole

protocol, there were no differences in CPR between cycles using vaginal progesterone (62.5%) and progesterone-in-oil (71.4%) for luteal support ($p = 0.994$). The letrozole protocol required fewer days of administration of medication in the preparation phase and required fewer days of luteal support.

Conclusions:

Frozen embryo transfer cycles using letrozole for preparation are associated with a clinical pregnancy rate comparable to that of traditional exogenous estrogen and progesterone preparation. This protocol may simplify and shorten the endometrial preparation process for both the patient and the clinic. Further investigation with a randomized trial could elucidate whether there is clinical advantage to this regimen in our center or others.

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References:

- ¹ Lathi RB, Chi YY, Liu J, et al. Frozen blastocyst embryo transfer using a supplemented natural cycle protocol has a similar live birth rate compared to a programmed cycle protocol. *J Assist Reprod Genet.* 2015(32):1057-62.
- ² Groenewould ER, Cohlen BJ, Al-Oraiby A, et al. A randomized controlled, non-inferiority trial of modified natural versus artificial cycle for cryo-thawed embryo transfer." *Hum Reprod.* 2016(31):1483-92.
- ³ Hu YJ, Chen YZ, Zhu YM, et al. Letrozole stimulation in endometrial preparation for cryopreserved–thawed embryo transfer in women with polycystic ovarian syndrome: A pilot study. *Clin Endo.* 2014(80):283-9.
- ⁴ Yarali H, Polat M, Mumusoglu S, et al. Preparation of endometrium for frozen embryo replacement cycles: a systematic review and meta-analysis. *J Assist Reprod Genet.* 2016(33):1287-1304.