



## COMPARISON BETWEEN TWO FET CYCLE METHODS WITH AND WITHOUT URINARY LH SURGE MEASUREMENT WITH URINARY LH KIT

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### ABSTRACT

The objective of this study is to assess the effectiveness of adding urinary LH surge kit to hormonal prepared frozen embryo transfer (FET) cycles. In this prospective clinical trial, 48 patients enrolled in two groups. Endometrial hormone priming in both groups was similar; but in group A, from day 10 of cycle, urinary LH surge detection was started embryo transfer (ET) scheduled after first positive test. In group B, ET was done after reaching endometrium thickness to at least 7 mm. The duration of cycle, the frequency of ultrasound monitoring, the total dosage of estrogen consumption and the result of cycle were measured. The duration of cycle before ET in group A was shorter ( $8.79 \pm 1.14$  VS  $11 \pm 1.47$  days, P Value: 0.0005), the number of ultrasound repetition also was lesser ( $2.42 \pm 0.58$  VS  $3.67 \pm 0.86$ , P Value: 0.001). Respectively, in group A the total dosage estrogen consumption was less than group B ( $35.58 \pm 5.2$  VS  $46.83 \pm 5.27$  mg, P value: 0.0005). The pregnancy rate in group A was more than group B, although it was not significantly different ( $37.5\%$  VS  $25\%$ , P value: 0.52). It seems except endometrial characters, assurance about the best time for embryo implantation prevent wasting valuable frozen embryo by incorrect timing of thawing and transfer.

**Keywords:** FET, LH kit, ICSI.

### INTRODUCTION

Embryo cryopreservation is an important progress in recent decades adjust to *in vitro* fertilization (IVF) or intra cytoplasmic sperm injection (ICSI) cycles, which means freezing the embryos at a temperature which all of the metabolic cell function have been arrested.<sup>1</sup> Embryo cryopreservation has several advantages at first, during fresh embryo transfer cycle, excess embryos with acceptable quality didn't throw away and could be used in future, in frozen embryo transfer (FET) cycle which is so cheaper than fresh cycle and increase the cumulative chance of pregnancy from one ovarian stimulation cycle for the same patient or other by donation. Secondary, in cases with ovarian hyper stimulation syndrome (OHSS), embryo cryopreservation could be a life saving attempt without elimination the chance of pregnancy or cycle cancelation. Also, in cases with unpredicted difficult embryo transfer or unfavorable endometrium it could be a wisely step<sup>2</sup>. There are some hormonal protocols for endometrium preparation in FET cycle, which in menstrual cycle endometrial growth monitor by intermittent ultrasound and when the endometrium reaches to the specific thickness (with or without improvement of ovulation by LH surge measurement<sup>3</sup>) thawed embryos have been transferred.<sup>4</sup> For endometrium priming usually two hormones are utilized: estrogens and progesterone. When menstruation started, estrogens (pills, patches, injection or vaginal form) are administrated for maturation and thicken the uterine inner layer. When the endometrium thickness reach to 7-8 mm<sup>5</sup>, progesterone started, mostly, 3 days before transfer of thawed embryos.<sup>6</sup> in order to optimized the chance of pregnancy rate during FET cycle, there are several new published study, like using prostaglandins<sup>7</sup>, sildenafil citrate<sup>8</sup> or prevent the spontaneous ovulation by gonadotropin-releasing hormone (GnRH) agonist injection.<sup>9</sup> Another way,

is monitoring for LH surge during follicular phase, via blood or urine. The usage of home LH surge kit is easier, noninvasive and more cost benefit. 12-36 hours after plasma LH surge, urinary LH surge kit will be positive<sup>10</sup>. LH surge occur in three manner: spike, plateau and biphasic<sup>11</sup>, despite variation in LH surge, most of the time ovulation occurs up to 48 hours after detection<sup>12</sup> and as we know implantation window is around 6 days after the peak of LH<sup>13</sup>, therefore we decided to transfer thawed embryo three days after first positive result in urinary LH kit which is approximately during uterine implantation window. By this intervention in comparison with traditional monitoring the endometrial appearance and thickness by serial ultrasound, we suggested this way is more convenient for patients and medical staff and may be more physiological and increase the chance of pregnancy.

### MATERIAL AND METHODS

In this prospective randomized clinical trial, 48 patients have enrolled in two groups based on close envelope randomization method. The study was conducted at the infertility department of the teaching hospital (Imam Khomeini hospital affiliated with Ahvaz Jundishapur University of medical science "AJUMS"), Ahvaz, Iran from January to October 2013. The university medical ethics review committee approved this study and registered in Iranian clinical trials system (www.IRCT.ir, IRCT 201310091496 N1). Written informed consent was obtained from participants. All of patients had at least two frozen embryos from their previous ICSI cycle and had normal level of prolactin and thyroid stimulating hormone (TSH) according to the recent check up. The patients were candidate for embryo donation were excluded from the study. In all of patients, transvaginal ultrasound (TVS) was performed on the

days 3 of menstruation cycle and in woman with normal TVS, estradiolvalerate (Estrofem, tablet 2 mg, Novonordisk Ltd. Turkey) twice a day were administrated, seven days after drug consumption new TVS was done. In both groups, according to the endometrial thickness the dosage of drug was adjusted. In group A, from this day, patients started checking the urine sample two times in a day (8-10 AM and 4-6 PM), by urinary LH kit (Medi smart, lobeck medical Ltd, 5070Frick/Switzerland) with sensitivity threshold 20 ml/m IU. Twice daily testing decreased the chance of false-negative results in urinary LH kit<sup>14</sup>. When the urinary LH kit gets positive result, vaginal Cyclogest (400 mg suppository Actavis, Barnastaple Ltd.uk) twice a day was started, then 72 hours later embryo transfer (ET) was done. The duration of cycle until reaching the positive in urinary LH kit, the thickness and appearance (triplet layer or echogenic) of endometrium and total dosage of estradiol valerate until this day were recorded. In group B, when the endometrial thickness reach to at least 7 mm, vaginal Cyclogest twice a day was administrated and again 72 hours later ET was done. The mention data, in addition to frequency of repeated TVS in both groups, were recorded. Two weeks after ET,

pregnancy status was measured by serum beta human chorionic gonadotropin (BhCG) checking; in patients with positive results, all of drugs were continue until 7 weeks of gestational age and then the first pregnancy ultrasound was done. Ongoing pregnancy was defined as alive fetus until 13-14 weeks of gestational age. In both groups the rate of abortion and ectopic pregnancy were reported. Because there was not any published study for comparison of LH urinary kit usage -and without it, in hormone prepared cycle for frozen embryo transfer, the sample size of study was chosen on arbitrary bases with 90 % power of study p-value < 0.05 was consider as significant. Statistical analysis was performed using SPSS19.0 for windows. Student's t-tests for unpaired data and Chi-square and Fisher's tests were used to assess frequency distribution and clinical outcome. Regression and Anova tests were used for comparison between the groups.

**RESULTS**

Ultimately, 10 patients (6 patients in group A and 4 patients in group B) replaced by new patients due to no embryo for transfer after thawing frozen. Embryo of 48 patients in both groups had not any demographic differences (Table 1).

**Table 1: Demographic data in study population (the superior data are mean ± SD)**

	Group A	Group B	P-V
Age (year)	28.5 ± 5.99	28.5 ± 5.60	0.23
BMI (kg/m <sup>2</sup> )	22.32 ± 1.79	22.44 ± 1.70	0.48
Infertility duration (year)	6.4 ± 4.07	6.2 ± 4.25	0.70
Type of infertility	primary	14 (58.3 %)	0.35
	secondary	10 (41.7 %)	

In two groups the day of progesterone administration was final day for comparison; there was not any significant difference between the appearance of endometrium triplet layer and echogen or endometrial thickness between two groups; but the duration of cycle in group A was significantly

shorter than group B, also the total dosage of estrogen and the frequency of ultrasound repeat were lesser (Table 2). Of course the pregnancy rate between two groups did not reach to significantly different level, but in group A was more than in group B.

**Table 2: Clinical result in study population (the superior data are mean ± SD)\* p-value significant: < 0.05**

	Group A	Group B	P-value
Pregnancy test	negative	62.5 (15 person)	0.52
	positive	37.5 (9 person)	
Endometrial view	Triple	79.2 (19)	1.000
	Echogen	20.8 (5)	
Endometrial thickness (mm)	7.70 ± 1.65	8.08 ± 1.47	0.54
The duration of cycle (day)	8.79 ± 1.14	11.00 ± 1.47	0.0005*
Number of ultrasound in cycle	2.42 ± 0.584	3.67 ± 0.868	0.001*
Estrogen dose (mg)	35.58 ± 5.20	46.83 ± 5.27	0.0005*

**DISCUSSION**

Through recent years which freezing the excess embryos with acceptable quality during fresh IVF or ICSI cycle being a complementary step; synchronously, different protocols for preparing the endometrium before ET and maximize the FET success were challenging subject. According to Cochrane data base system review there is not sufficient evidence to recommend any specific method for endometrial priming before FET<sup>9</sup>; despite increasing tendency toward natural cycle<sup>15</sup>, still exogenous hormonal administration before FET is the most utilized method<sup>16</sup>. LH surges are the primary events for reaching to endometrial implantation window and detection of those surges could lead to more correct timing for embryo thawing transfer. Of course, in natural cycle no

adverse influence of spontaneous LH surge before ET has been reported<sup>17</sup>, but there was not any report about its effect in hormonal preparative cycles. To the best of our knowledge, our work is the first published study about using urinary LH surge kit before FET in exogenous hormonal preparative cycle. With urinary LH surge kit usage which is very easy, the duration of cycle before embryo transfer was lesser and the frequency of ultrasound monitoring also was lesser which not only is more cost benefit, but also is more convinced for patients and medical staffs. Total dosage of administrated estrogen was decreased significantly, but may be due to small sample size of our study the between two groups in pregnancy rate was not significantly different, although it was more in group A. We suggested that

prediction of LH surge and determination of ovulation time. Neither in natural cycle but in hormonal primed FET cycle could lead to better result due to most accurate time for transfer. We think if repeat the study in larger population of patients the positive result of cycle would be increased; in addition, it's obvious except endometrial characters, assurance about the best time for implantation will be more important and applicative and prevent wasting valuable frozen embryo by incorrect timing of thawing and transfer. Acknowledge: this study did with a grant from fertility infertility and perinatology research center, Ahvaz Jundishapur University of medical sciences, Ahvaz, Iran

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