

Effectiveness of mind-body intervention on oocyte quality and serum cortisol level in sub-fertile women undergoing IVF treatment in Wardha region: A Study Protocol

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Abstract

In last 4 decades, the treatment of infertility has changed fundamentally and has been used increasingly in the whole world. Fresh embryo transfer and vitrified thawed embryo transfer are the two methods that are preferred. Nowadays, freeze all cycles are much more involved in the treatment of infertility. Maternal complications are found to be lesser in pregnancy arising from the cryopreserved thawed embryo transfers. Women undergoing frozen embryo transfer are found to have good ovarian reserve with a lower risk of preterm birth. But the occurrence of pregnancy-induced hypertension syndrome is found to be more in cryopreserved embryo transfer than in fresh embryo transfer. The ovarian hyperstimulation syndrome is found to be same in both types of embryo transfers. Objective of the study is to correlate the β -HCG outcome of fresh and frozen embryo shifting, to correlate pregnancy complications in patients with fresh and frozen embryo shifting, to identify various reasons for pregnancy complications and to establish criteria for selection of embryo transfer type (Fresh/Frozen). This invasive methodology includes a recording of the treatment history and the indications. Counseling of all the participants for research will be done. The further protocol includes evaluation of outcomes of both the techniques by comparing its complications in pregnancy.

Keywords: Fresh embryo transfer, frozen embryo transfer, blastocyst, day-03embryo, IVF, ICS.

INTRODUCTION

In this era of advancing medical science and technology, the field of artificial reproductive science has given opportunity to infertile couples to conceive baby as about 15% of population suffer infertility.(1) Intracytoplasmic sperm injection (ICSI) and in vitro fertilisation (IVF) has resulted in beyond 6 Million of births.(2) Artificial Reproductive Technology (ART) basically works on human oocyte and sperm and has represented one of the most successful intervention in field of medicine.

The embryo is formed by fusion of ovum and sperm outside the body (in vitro fertilisation) and is transferred to female body either freshly (Fresh Embryo Transfer) or by thawing the cryopreserved one (Frozen Embryo Transfer).(3)

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In 1984, the first baby by transfer of thawed cryopreserved embryo was conceived and by passing time this trend of transferring frozen embryo is increasing.(4)(5) Not just because of subtlety of the embryology laboratories, the procedure of FET (Frozen embryo transfer) is also preferred because of the protocols which are easier than that of the fresh embryo transfer. The main motive of frozen embryo transfer is to provide time for ovary to recover from controlled ovarian stimulation (COS) and to get suitable endometrium.(4)(6)

All the techniques of embryo transfer are successful but are still under controversial findings and comparative studies. As the altercations prevail regarding the complications in pregnancy, Maheshwari et al. manifested that pregnancies arising from FET have lower risks of maternal complications like it is associated with lesser risk of placental abruption (disassociation of placenta from innermost wall of womb before the parturition)(7), postpartum haemorrhage(heavy blood loss during parturition), ectopic pregnancy (site of pregnancy other than uterus) (8) and preterm delivery than fresh embryo transfer. Chances of lesser birth weight newborns and pre-eclampsia(onset of high blood pressure after 20 weeks of pregnancy)(9) has also reduced by cryopreserved embryo transfer.(10)(5) It is said that women undergoing cryopreserved embryo transfer have good ovarian reserve and better prognosis.(1) According to Yezhou Su et al. the occurrence of placental accreta(abnormal implantation of chorionic villi on myometrium)(11) and pregnancy- induced hypertension syndrome is more in frozen embryo transfer.

Whereas, opposite conclusion was given by Shavit et al. that pre-eclampsia and gestational diabetes mellitus (GDM) is seen more in FET than fresh embryo transfer.(10)

The possibility of ovarian hyperstimulation syndrome was found to be almost similar in both types of transfers i.e. fresh embryo transfer and cryopreserved thawed embryo transfer. (10)(12)

One reason for preferring frozen embryo transfer can be that we can alter the conditions of endometrium. Endometrial scratching one of the major technique ,that can be performed antecedent to the embryo transfer, which helps in increasing the receptivity of endometrium and in response implantation rates are increased. (13) Treatment with platelet rich plasma also improves the health of endometrium thus improving the rates of conception.(14)

So here I compare the complications in pregnancy following the fresh embryo transfer and vitrified embryo transfer in my study. This will be a cohort study.

Rationale:

A study by YEZHOU SU et al. published on September 30, 2018 compares the pregnancy complications after fresh and vitrified embryo transfer. According to the study they state that cryopreserved embryo transfer had lower risks placental abruptions(disassociation of placenta from inmost wall of

uterus before the parturition) (7), ectopic pregnancy(site of pregnancy occurring other than uterus)(8)(OR=0.42;95% CI=0.37-0.49), still births(OR=0.83;95% CI=0.73-0.75) , lesser birth weight(OR=0.76;95% CI=0.71-0.81).Higher risks of placenta accreta and pregnancy-induced hypertension syndrome are seen in frozen embryo transfer. Occurrence of miscarriage (OR=1.10; 95% CI=1.58-3.25) is found to be almost same in both types of pregnancy. According to this study, vitrified thawed embryo transfer is a superior alternative than fresh embryo transfer for Asian population.(4)

MEILING YANG et al. conducted a study that compares the fresh and cryopreserved embryo transfer and also which one is better for mother and babies. According to the study, lesser implantation rate, pregnancy rate, clinical gestation and ongoing pregnancy outcome is seen more in case of fresh embryo transfer. Report of 6 random controlled trials have been considered in this study which states that rate of implantation is lower in fresh embryo transfer. Frozen embryo transfer is considered to have lesser risk of placental abruption, placental previa and preterm delivery of the baby. Gestational diabetes mellitus occurrence is almost same in both types of embryo transfer. In this study there is contradiction in ideas of Maheshwari et al. and Shavit et al. If we see the neonatal outcomes, low birth weight babies are seen in fresh embryo transfer. Also, some say that the newborns after frozen thawed embryo transfer have much more threat of congenital impairments and organ system abnormalities but according to this study no such cases are seen after both types of embryo transfer. The past meta-analysis conclusions are considered still to be controversial because of limited sample size.(10)

There is another study in July 2014 by MARYAM E FTEKHAR et al. Yazd, Iran. In this study data of 372 women was reviewed who underwent the cryopreserved thawed embryo transfer. Some of the clinical parameters like primary IVF protocol, IVF procedure, endometrial thickness, treatment duration to fetal transfer found to be unrelated to cryopreserved thawed embryo transfer outcomes .The end result was given that the age of female and basal FSH (follicle stimulating hormone) levels are the utmost crucial elements determining the clinical gestation rates following the cryopreserved thawed embryo shifting.(15-21)

A retrospective clinical study from 1st January 2014 to 30th September 2015 was conducted. They studied a total of 516(fresh=286 and frozen=230) embryo shifting cycles, in which Intracytoplasmic sperm injection (ICSI) was carried out initially due to male barrenness. The females in the study were seen to have disorders of fallopian tube and most of them were normal. The clinical facts with its gestation outcomes of two types of study groups, i.e. the fresh embryo transfer group and the frozen-thawed embryo transfer (FET) group were compared. The rate of failure of gestation in the frozen embryo transfer group was found to be lesser than that of fresh embryo transfer group. The frozen embryo transfer had greater nascency rates than the fresh embryo transfer

(56.10% vs. 47.21%). No differences were noted in the embedding rate, clinical gestation rate, biochemical gestation outcomes, multiple pregnancy rates, and premature parturition rate between these two types of embryo transfers. The gestational age, single neonatal weight, or congenital anomalies between these two transfer groups had no difference and were found to be of same rates. (22-28)

There is one study in November 2016 in Cochrane Gynecology and Fertility Group. They reviewed four studies comparing the cryopreserve all strategies in cumulative 1890 women comparing the vitrifying all the embryos (cryopreserve-all) policy with a traditional IVF/ICSI strategy. The prevalence of OHSS (ovarian hyperstimulation syndrome) was found to be lesser after the cryopreserved-all plan in comparison to the strategy of standard IVF/ICSI. After study and obtaining report of 1633 women it is suggested that if the rate of ovarian hyperstimulation syndrome is higher in cryopreserved-all strategy than basic IVF/ICSI techniques. The vitrified-all strategy is said to be associated with fewer miscarriages as studied in 1892 women comparatively excess incidence of gestation complication was recorded. It was suggested by study of 1630 women that the multiple gestation rate was found to be same. (28)

Aim:

To study the pregnancy complications in fresh and frozen embryo transfer.

Hypothesis:

We hypothesized that cryopreserved thawed embryo transfer may provide lesser complications in pregnancy and better rate of implantation in IVF in relation to fresh embryo transfer.

Null Hypothesis:

Vitrified embryo transfer doesn't bring any alteration in increasing the rate of implantation.

Methods:

Study design: Observational Study (Cohort study)

Methodology:

As we have to compare the pregnancy complications of the patients who suffer from infertility enrolling into "Wardha Test Tube Baby Center, AVBRH". The very first option for the patient is to undergo intrauterine insemination (IUI) in which the prepared semen sample with good quality of sperm is directly injected into the uterine cavity of women. The outcome of IUI can be either conception or failure. If the procedure is failed, ovarian stimulation is done on the 2nd day of menstruation with either long agonist or short antagonist protocols. On 10th or 12th day of menstruation ovum aspiration is performed. Good grade ova are selected from the follicular fluid. After the selection, either in vitro

fertilisation (IVF) or Intracytoplasmic sperm injection (ICSI) is conducted. After the fusion of sperm and ovum by artificial technology, the embryo is formed. The embryo formed is either transferred freshly to women's uterine cavity (fresh embryo transfer) or are cryopreserved then thawed and transferred (frozen embryo transfer). Outcome of pregnancy for both types of transfer is checked by seeing the levels of β -HCG. If the outcome is positive i.e. the women has conceived, the clinical complications are seen for both the types of embryo transfer. The complications in pregnancy for both the types of embryo transfer are then compared and the various reasons for complications in pregnancy are studied.

Setting:

Location: Wardha Test Tube Baby Centre, Sawangi (Meghe), Wardha

Participants: Infertile couple visiting WARDHA TEST TUBE BABY CENTRE, , Sawangi (Meghe), Wardha

Inclusion Criteria:

- Couples enrolled for fresh embryo transfer.
- Patients giving consent for cryopreservation of embryos.
- Patients with regular follow up.

Exclusion Criteria:

- Patients not giving consent for IVF.
- Patients having uterus agenesis.
- Patients having infections like HIV, HbsAg.
- Patients with complicated systemic diseases.
- Patients having advanced and irreversible pathology.

Sample size: 50 infertile couple

$$N = \frac{\chi^2 * N * p(1-p)}{C^2(N-1) + \chi^2 p(1-p)}$$

Total population = N=120 during 36 months

χ^2 = The value Chi-square for 1 degree at some desired probability level. This is 3.84 at 5% level of significance

P = 50% proportion Q = 100 - p

= 50

C = Confidence interval of the one choice (95% CI)

= 0.05

N = 3.84 * 120 * 0.5 * 0.5

(0.05)² * 24 + 3.84 * (0.5 * 0.5)

= 50

Expected Outcomes:

50 women will be included. Transfer of embryo in 25 women will be the via fresh embryo transfer and in 25 women, we will conduct frozen embryo transfer procedure. Further β -hcg will be tested on 14th day of transfer to get the confirmation of pregnancy and the track of ongoing pregnancy is kept to

check for the complications. Thus, by performing frozen embryo transfer, better implantation rates are seen and complications in pregnancy are also lesser.

Discussion:

The principal objective of this study is to compare the complication of clinical gestation in both types of embryos transfer i.e. fresh and frozen and to decide which technique is better than another and helps to increase the implantation rates. The frozen embryo transfer is preferred as in this transfer the endometrial receptivity can be increased by means of endometrial scratching, providing platelet rich plasma to endometrium and thus better conceiving rates are seen with fewer complications in pregnancy.

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