



Effect of Endometrial Injury before Frozen Embryo Transfer on Pregnancy Rate (Randomized Controlled Trial)

Thesis

*Submitted for Partial Fulfillment of Master Degree
in Obstetrics and Gynecology*

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List of Abbreviations

APC	: Antigen Presenting Cells
APOD	: Apolipoprotein D
ART	: Assisted reproductive technology
ART	: Assisted reproductive technology
B- hcg	: Beta Human chorionoc gonadotropin
BMI	: Body mass index
CI	: Confidence interval
CPA	: Cryoprotective additives
DSMO	: Dimethyl sulphoxide
EG	: Ethylene glycol
EI	: Endometrial injury
ET	: Embryo transfer
FET	: Frozen embryo transfer
FT	: Frozen thawed
GnRH	: Gonadotrophin-releasing hormone
Groa	: Growth related oncogene a
hCG	: Exogenous human chorionic gonadotrophin
ICM	: Inner cell mass
IL15	: Interleukin 15
ITGa6	: Integrin a 6
Iui	: Intra uterine insemination
LH	: Luteinizing hormone

LN	: Liquid nitrogen
MIP1B	: Macrophage inflammatory protein 1B
MUC1	: Mucin 1 transmembrane
OPN	: Osteopontin
PG	: Propylene glycol
PLA2	: Phospholipase A2
PN	: Pro nuclear
r-Hcg	: Recombinant Human chorionoc gonadotropin
TNFa	: Tumor necrosis factor a
UPIb	: Uroplakin Ib
USG	: Ultrasonography

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Protocol of Thesis

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Introduction

Frozen embryo transfer (FET) is assuming a greater role in the practice of infertility than it has in the past. In 2012, 28.4 % of cycles reported to the Society for Assisted Reproductive Technology and the Center for Disease Control and Prevention were frozen embryo transfers compared with 16.1 % in 2003. FET has been primarily utilized when more good quality embryos were produced than could safely be transferred, if there was concern regarding risk of ovarian hyperstimulation syndrome, or when endometrial development during the fresh IVF cycle was inadequate (*Lathi et al., 2015*).

The clinical value of embryo cryopreservation has steadily increased over the decades with significant technological advances made in our ability to freeze cleavage-stage and blastocyst stage embryos. The first live birth following the transfer of cryopreserved embryos was reported in 1984 and this strategy has been progressively used in assisted reproductive technology (ART) (*Zeilmaker et al., 1984*).

The number of cryotransfer cycles practiced has increased considerably in recent years for two main

reasons: first, the increased effectiveness (*Cobo et al., 2012*) and safety (*Liu et al., 2013*) of the process of embryo vitrification; second, the policy adopted of freezing all embryos in the stimulated cycle and transferring them in a natural or an artificial cycle, with the aim of reducing the risk of ovarian hyperstimulation (*Absalan et al., 2013*) and of ectopic pregnancy (*Decleer et al., 2014*).

Among the various potential causes of repeated implantation failure, uterine factors (e.g., thin endometrium, poor endometrial receptivity, and immunological incompatibility) have received the most attention in recent years and management of repeated implantation failure despite transfer of good-quality embryos still remains a dilemma for ART specialists (*Margalioth et al., 2006*).

Endometrial scratching which is intentional damage to the endometrium, such as biopsy or curettage, in women undergoing assisted reproduction technology (ART) associated with improvement in endometrial receptivity (*Nastri et al., 2012*).

The first non-randomized paper suggesting this association was published in 2003 reported that

endometrial sampling of IVF patients using a biopsy catheter substantially increases their chances to conceive at the following IVF-embryo transfer cycle. By transferring a similar number of embryos in the study and control groups, the authors achieved an implantation rate of 28 versus 14%, a clinical pregnancy rate of 67 versus 30% and a live birth rate per embryo transfer of 49 versus 23%. They concluded that local injury to the endometrium increased the incidence of implantation. This finding inspired us to perform the study on local injury to the endometrium (*Barash et al., 2003*).

Although in some previous studies concluded that local injury to endometrium in luteal phase prior to FET cycle had a negative impact on implantation and clinical pregnancy rates, currently there is lack of good evidence to support routine endometrial injury prior to FET treatment (*Aflatoonian et al., 2016*).

Aim of the Work

The aim of this work is to measure the efficacy of endometrial injury before frozen embryo transfer on pregnancy rate.

Research Question:

In women undergoing frozen embryo transfer, does routine endometrial injury before frozen embryo transfer increase clinical pregnancy rate?

Research Hypothesis:

(Null Hypothesis)

In women undergoing frozen embryo transfer Routine endometrial injury before frozen embryo transfer does not increase clinical pregnancy rate.

(Alternative Hypothesis)

In women undergoing frozen embryo transfer, endometrial injury before the transfer may increase pregnancy rate.

Protocol Outlines

Title:

The efficacy of endometrial injury before frozen embryo transfer on pregnancy rate in IVF and ICSI Cases.

Study Design:

Randomized control study.

Study Population:

Women planned to undergo frozen embryo transfer.

Site of the study (Setting):

ART unit at Faculty of Medicine - Ain -Shams University Hospital.

Study Duration:

Six Months may be extended to more than one year.

Outcome measures:

1. Primary outcome measure:

- Chemical pregnancy rate (serum B-hCG positive).

2. Secondary outcome measure:

- Clinical pregnancy (appearance of gestational sac on transvaginal ultrasound), Implantation rate, and multiple pregnancy rate.

Patients and Methods

During the pre-selection phase (after admission into the ART Unit at Ain Shams University hospital) inclusion and exclusion criteria will be applied.

Inclusion Criteria:

All infertile women have high quality frozen embryos.

Exclusion Criteria:

1. Age > 40
2. History of endocrine disease such as: diabetes;
Hyperthyroidism and Hyperprolactinemia
3. History of hysteroscopic surgery due to
intrauterine adhesions
4. History of cardiovascular, renal or liver disease
5. History of stroke or myocardial infarction
6. Poor quality embryos
7. Alcohol or Substance abuse

Suitable women will be invited to participate in the study then a signed and informed consent will be obtained from them. When the patient's consent is obtained, they are to be included into the study.