A Comparative Study between the Effect of Endometrial Injury at day 21 of previous Cycle and day 7 of the Same ICSI Cycle on Pregnancy Rate in Patients Undergoing ICSI

Thesis

Submitted for Partial Fulfillment of Master Degree in Obstetrics and Gynecology

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Introduction

In assisted reproductive technology, procedures for culturing and transferring embryos have been continually improved over the last two decades. Yet the clinical pregnancy rate has not substantially improved over the last ten years (currently only 32.4~33.0% per IVF transfer as reported by ESHRE in 2010) [(1)] and many patients have suffered repeated implantation failure even in the most successful Invitrofertilization (IVF) clinics. Although no practical solutions for repeated implantation failure have emerged, an improved ability to control the endometrial environment for implantation promises to have a significant, positive impact on IVF outcomes.

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. [(2)]

Management of repeated implantation failure despite transfer of good-quality embryos still remains a dilemma for ART specialists. Scrapping of endometrium in the nontransfer

cycle has been shown to improve the pregnancy rate in the subsequent IVF/ET cycle in recent studies.

It has been shown that endometrial receptivity could be modulated by a multitude of signaling molecules, including prostaglandins, [3] growth factors, cytokines, chemokines, integrins, leukemia inhibitory factor, [4,5] Wnt family ligands, [6] and E-cadherin. [7]

Whereas dysregulation of some of these factors could be associated with repeated implantation failure, key molecular mechanisms that underlie the regulation of endometrial receptivity remain to be elucidated. [8]

Interestingly, earlier studies have shown that prior incidences of hysteroscopic endometrium biopsy are associated with increased rates of implantation, clinical pregnancy, and live birth among women who experienced repeated implantation failure but without obvious endometrium defects, suggesting that a hysteroscopic procedure in the nonconceptual cycle itself could be beneficial for improving pregnancy in subsequent IVF cycles. [2] [9]

This hypothesis has been supported--directly or indirectly--in a number of clinical settings. [10]

Although earlier studies aiming to understand the effect of hysteroscopic endometrium biopsy on implantation have been methodologically diverse, studies showed that an endometrial biopsy induced injury leads to a successful implantation, [11] an endometrial biopsy-induced injury could produce just such a local inflammatory and angiogenic environment between the endometrium and the conceptus, which, in turn, facilitates embryo implantation and subsequent pregnancy in earlier studies. [12-14]

However, due to substantial variations in patient selection, timing, number and extent of endometrial injury applied, and techniques in earlier studies, [12] [9] [15] the merits of endometrial biopsy injury on clinical outcomes in IVF clinics remain controversial. [2]

Aim of The Work

The aim of this work is to compare the effect of endometrial injury on day 21 of preceding cycle to ICSI cycle and on day 7 of the same cycle of ICSI cycle on pregnancy rate in patients undergoing ICSI.

PROTOCOL OUTLINES:

Title:

The Effect of Endometrial Injury on Pregnancy in ICSI Cases.

Study Design:

Pilot Randomized control study.

Site of the study (Setting):

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

Study Duration:

Six Months may be extended to one year.

Recruitment and Randomization:

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

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.

Inclusion Criteria:

1- Age is between 25-35 years old.

1. BMI is between 20-30.
2. Cause of infertility:
    a. Tubal causes.
    b. Unexplained causes of infertility.
    c. Male factor.

Exclusion Criteria:

1. Age above 35 years old.
2. BMI > 30.
3. Endometriotic patients.
4. Poor responders.
5. Uterine cavity abnormalities.
6. Previous ICSI failure.
7. Hydrosalpinex and pyosalpinex.

Patients and Methods:

This Pilot randomized study consists of 60 patients are preparing to do ICSI and designed as the following 3 groups:

Group (A): consists of 20 patients as control group**.**

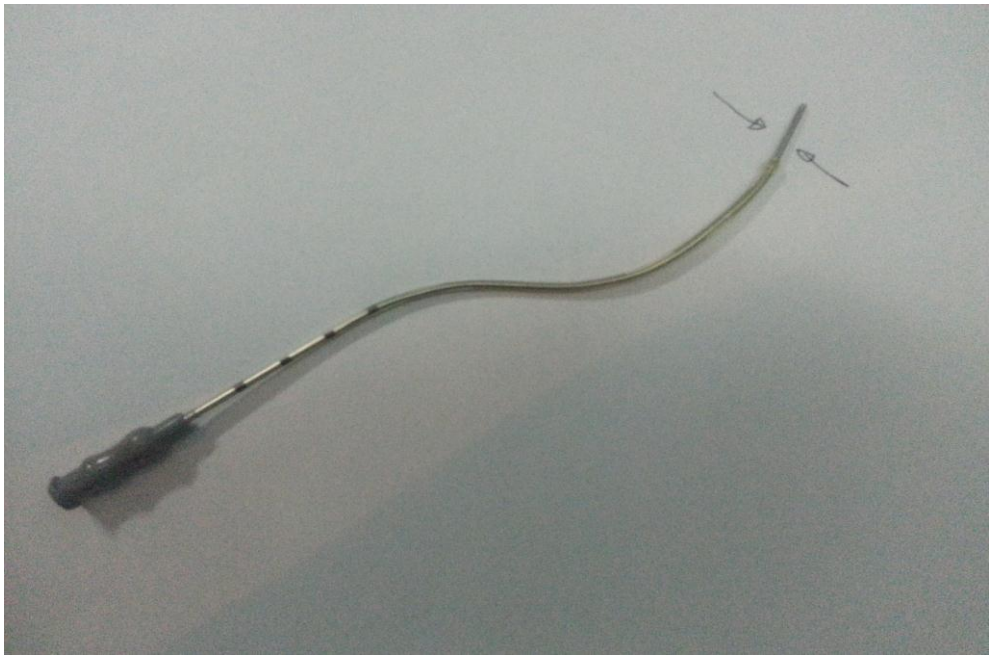
Group (B): consists of 20 patients will receive endometrial injury on day 21 in preceding cycle to ICSI cycle.

Group (C): consists of 20 patients will receive endometrial injury on day 7 of the ICSI cycle.

All patients will receive the long induction protocol as routine in IVF & ART Unit at Ain Shams University Hospital:

Depends on Age, BMI patients will receive C.O.C.P from day 2 or day 3 of previous cycle for 21 days then will receive Decapeptyle 0.1 mg. S.C daily dose from the last day of C.O.C.P till vaginal bleeding withdrawn as menstrual bleeding then HMG (FSH + LH) 2-6 ampoules daily from day 2 of menstrual bleeding, then folliclumetry will be done daily or every other day until Mature Graffian follicle reach 18-22 mm. then patient will receive HCG I/M and ovum pick up will be done after 36 hours.

A single induced injury will be done on the posterior endometrium by using modified Cook catheter as shown:



Data Collection:

Enrollment (recruitment) Data (Patient Characteristics) [Case Record Form (CRF)]:

During visit 1, all patients will undergo complete clinical examination and detailed medical history will be obtained. Each patient will have a Case Record Form (CRF) in which the following data will be recorded.

- Patient number (according to the randomization schedule).
- Age, BMI.
- Past medical and surgical history.

Ethical considerations:

Ethics: The study will get approval from Ethics & Research Committee (ERC), Ob/Gyn department, Faculty of Medicine, Ain Shams University. The clinical research study will be conducted in accordance with the current approved clinical protocol and relevant policies, requirements and regulations of the Ain shams University Maternity Hospital.

Consent procedure:

All patients will be given informed consent. The investigator will make an appropriate informed consent process

in place to insure that potential research objects or their authorized representatives are fully informed about the nature and objective of the clinical study, the potential risks and benefits of study participation, and their rights as research subject. The investigator will obtain the written signed informed consent of each subject, or the subjects authorized representative, prior to performing any study specific procedures on the subject. The investigator will retain the original signed informed consent form.

Subject confidentiality:

All evaluation forms, reports and other records will not include unique personal data to maintain subject confidentially.

Statistical analysis:

All analyses will be based on the intention-to-treat principle. Data will be collected, tabulated, coded using Excel 2007 (Microsoft, Redmond, WA, USA). Then, data will be analyzed by a computer software SPSS version 19.0.Numerical variables will be examined for normality then, will be expressed as mean (standard deviation) or median (AND inter quartile range) whenever appropriate. On the other hand, categorical variables will be presented as number of cases (percent). Between groups, comparison of continuous variables will be performed by Student's t test. Comparison of

categorical variables will be performed by Chi-Square or Fischer's test. Whitney U tests were used for variables that were not normally distributed. A 5% level of significance will be used throughout.

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