Routine Hysteroscopy before First Intra Cytoplasmic Sperm Injection Cycle: A Randomized Controlled Trial

Thesis

Submitted For Partial Fulfillment of Master Degree
In Obstetrics & Gynecology

Presented by:

Mohamed Hassan Ibrahim Marey
M.B.B.Ch. El Mansoura University (2009)
Resident of Obstetrics and Gynecology
Boulak El-DakrorGeneral Hospital

Supervised by

Prof. Dr. Amr Hassan El-Shalakany
Professor of Obstetrics & Gynecology
Faculty of Medicine – Ain ShamsUniversity

Dr. Ahmed Elsayed Hassan Elbohoty
Assistant professor of Obstetrics & Gynecology
Faculty of Medicine – Ain Shams University

Dr. Amr Helmy Yehia
Lecturer of Obstetrics & Gynecology
Faculty of Medicine – Ain Shams University

Ain Shams University
Faculty of Medicine
2015

Acknowledgment

Thanks Allah Almighty, the Gracious for blessing me with such a wonderful group of professors who instructed and guided me throughout my work.

I would like to express my sincere thanks to **Prof. Dr. Amr Hassan El-Shalakany**, *Professor of Obstetrics and Gynecology, Faculty of Medicine, Ain Sams University, for his supervision, guidance, valuable advice, helpful directions and continuous interest throughout the whole work.*

My thanks and gratefulness to **Dr. Ahmed Elsayed Hassan Elbohoty**, *Assistant professor of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University, for his keen interest, beneficial advice and constant support during the conduction of this work.*

I also wish to offer my warmest and deepest appreciation to **Dr. Amr Helmy Yehia**, *Lecturer of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University, for his unlimited, endless help and continuous encouragement.*

Table of Contents

List of Abbreviations

AMH	Anti-Müllerian hormone
ART	Asssisted Reproductive Techniques
BMI	Body Mass Index
CAM	Cellular Adhesion Molecules
cSET	Compulsory single embryo transfer
DET	Double embryo transfer
ET	Embryo transfer
eSBT	Elective single blastocyst transfer
eSET	Elective single top quality embryo transfer
FET	Frozen-thawed embryo transfer
FISH	Fluorescent in situ hybridisation
FSH	Follicle-stimulating hormone
GnRH	Gonadotropin Releasing Hormone
HCG	Human Chorionic Gonadotropin
HR	High ovarian response
HSG	Hysteroslapingiogram
ICSI	Intra cytoplasmic sperm injection
IGFBP-1	Insulin-like growth factor-binding protein-1
IR	Implantation rate
ICSI	In vitro fertilisation
IUA	Intrauterine Adhesions
LBR	Live birth rate
LR	Low response
LR→NR	Low response, followed by a normal Response in a consecutive cycle.
MBR	Multiple live birth rate
MR	Miscarriage rate

NR	Normal response
NR→LR	Normal response, followed by a low Response in a consecutive cycle.
nt-eSET	Elective single embryo transfer of Non-top quality embryo.
OD	Oocyte donatio
OH	Office Hysterosocopy
OHSS	OvarianHyperstimulation Syndrome
OPU	Ovum pick-up
PCOS	Polycystic Ovarian Syndrome
PCR	Polymerase chain reaction
PR	Pregnancy rate
ROS	Reactive oxygen species
SIS	Saline Infusion Sonography
TVS	Transvaginal sonography
TV/US	Transvaginal Ultrasound
tLBR	Term live birth rate
WHO	World Health Organisation

List of Tables

List of Figures

Introduction

Intra cytoplasmic sperm injection (ICSI) is an expensive treatment but results in a successful outcome in only a third of treatment cycles ***(Bouwmans et al., 2008).*** Assisted Reproductive Technology procedures for culturing and transferring embryos have been continually improved over the last two decades and the clinical pregnancy rate has not substantially improved over the last ten years ***(De Mouzon et al., 2010).*** Implantation failure could be due to a variety of reasons including embryo quality and uterine receptivity but remains unexplained in many cases ***(Margalioth et al., 2006).***

The presence of uterine pathology may negatively affect the chance of implantation ***(Cenksoy et al., 2013).*** The prevalence of unsuspected uterine pathology in asymptomatic women with implantation failure has been reported to be as high as 50% ***(Chen et al., 2012).*** Hysteroscopy doesn't only provide accurate visual assessment of the uterine cavity, but also gives a chance to treat any pathology detected during the examination and availability of hysteroscopy with smaller diameter has made the use of office hysteroscopy feasible as a routine examination ***(De Placido et al., 2007).***

Infertility related to uterine cavity abnormalities has been estimated to be the causal factor in as many as 10% to 15% of

couples seeking treatment. Moreover, abnormal uterine findings have been found in 34% to 62% of infertile women ***(Brown et al., 2000).*** Hysteroscopy is considered the gold standard for evaluating the uterine cavity, and due to improved endoscopic developments, can be performed reliably and safely as an office procedure ***(Gordts et al., 2002).***

Direct view of the uterine cavity offers a significant advantage over other blind or indirect diagnostic methods, although hysterosalpingography (HSG) is to be as accurate as hysteroscopy in the diagnosis of normal and abnormal cavities, the nature of the intrauterine filling defects is more accurately revealed by hysteroscopy ***(Prevedourakis et al., 1994).*** The correlation is only 65% between findings diagnosed with HSG compared with those diagnosed with hysteroscopy**.** Role of hysteroscopy in infertility investigation is to detect possible intrauterine changes that could interfere with implantation or growth, or both, of the conceptus, and to evaluate the benefit of different treatment modalities in restoring a normal endometrial environment ***(Campo et al., 2009).***

It is clear why many authors believe that uterine and endometrial integrity should be evaluated primarily by hysteroscopy in the infertile and ICSI treated population ***(Oliveira et al., 2003).*** It is generally performed as a definitive diagnostic tool to evaluate abnormal findings on hysterosalpingogram or salinehysterosonography performed

during the course of investigation of subfertile women ***(Roma et al., 2004).*** Still, Many consider hysteroscopy as only a complementary procedure in case of abnormal findings detected by other methods (primarily hysterosalpingography and ultrasound) ***(Fabre et al., 1998).***

Lastly, there is evidence that performing hysteroscopy before starting ICSI treatment could increase the chance of pregnancy in the subsequent ICSI cycle in women who had one or more failed ICSI cycles ***(Bosteels et al., 2010).*** However, recommendations regarding the efficacy of routine use of hysteroscopy prior to starting the first ICSI treatment cycle are lacking.

Aim of the Work

The aim of this work is to assess the role of routine hysteroscopy prior to the first ICSI cycle and whether it increases chemical and clinical pregnancy rate or not.

Chapter (1)
Assisted Reproductive Technologies

Infertility is a reproductive disorder defined clinically as the failure to achieve a clinical pregnancy following at least 12 months of unprotected sexual intercourse ***(Gurunath et al., 2011)***. It can be related to female factors (35% to 40% of couples), male factors (20× to 40% of couples), both (20% to 30% of couples), or remain unexplained ***(Jose-Miller et al., 2007)***. Infertility is commonly caused by ovulatory dysfunction, tubal obstructions, and/or endometriosis. In recent years, efforts to optimize maternal and infant outcomes have focused on ICSI/ICSI and specific procedure related factors, such as the number of embryos transferred and whether sperm, eggs or embryos used should be fresh or frozen ***(Homan et al., 2007)***.

Assisted Reproductive Technology ART procedures for culturing and transferring embryos have been continually improved over the last two decades ***(De Mouzon et al., 2010).*** The efficacy of assisted reproductive technologies (ART) has improved significantly since the first reports of successful pregnancies and live births after in vitro fertilization (ICSI) ***(Edwards et al., 1978).***

In the USA, the live birth rate has increased from 38% to 48% among women under the age of 35 years treated with ART over the past decade ***(Centers for disease control and prevention. 2008).***

The European ICSI-monitoring consortium and the International Committee for Monitoring Assisted Reproductive Technology also observed similar trends in ART success ***(De Mouzon et al., 2006)***. The most common ART procedure is ICSI, which involves controlled ovarian hyperstimulation (COH) with gonadotropin administration to stimulate ovarian follicle development, followed by transvaginal oocyte retrieval, fertilization of the oocytes with sperm in vitro, culture of the resultant embryos, and transfer of the embryo(s) to the recipient ***(Palermo et al., 1992).*** ICSI is an expensive treatment but results in a successful outcome in only a third of treatment cycles ***(Bouwmans et al., 2008).*** Implantation failure could be due to a variety of reasons including embryo quality and uterine receptivity but remains unexplained in many cases ***(Margalioth et al., 2006).***

ICSI is a micromanipulation technique that involves injection of a sperm in to the center of mature oocyte under a microscope.ICSI has been primarily developed for treatment of male infertility with abnormal sperm parameters, which are generally not effectively treated by other methods of ICSI. However, its use has now been extended to treat other factors of infertility, tubal factor where sperms cannot reach

the mature ovum and unexplained infertility ***(Khalaf et al., 2010).*** Fertilization rate after ICSI is at about 70 to 80% in all ages combined ***(Palermo et al., 2009).***

Indications for Intra cytoplasmic sperm injection:-

ICSI was first reported as a treatment option for women with severe tubal disease ***(Steptoe et al., 1978).*** With improved efficacy after the introduction of gonadotropin stimulation and ICSI, the indications for ICSI have expanded to include infertility caused by severe male factor, diminished ovarian reserve, ovulatory dysfunction, severe endometriosis, and infertility of unexplained cause. In fact, ICSI is the most effective treatment option for couples with multi-factorial infertility problems.

- **Tubal factor:-**

Tubal-factor infertility accounts for 30% of cases of female infertility ***(Centers for disease control and prevention. 2008).*** ICSI is the treatment of choice for women over the age of 35 years with significant tubal disease and those with other co-existing infertility problems ***(Benadiva et al., 1995).***

- **Male factor:-**

Abnormal semen parameters may be a contributing factor in up to 40% of infertile couples ***(Thonneau et al., 1991).*** In cases of severe oligospermia (fewer than 5 million motile sperm/ml), severe asthenospermia (less than 5%

progressive motility), and severe teratospermia (less than 4% normal morphology based on strict Kruger criteria), these semen parameters are associated with poor success with artificial insemination ***(Voorhis et al., 2001).*** For men with obstructive or non-obstructive azoospermia, ICSI is indicated to achieve fertilization using surgically retrieved spermatozoa from either microsurgical epididymal sperm aspiration or testicular sperm extraction ***(Schlegel et al., 1997).***

Table (1): WHO 2010 Seminal Fluid Analysis Reference Values

Cut-off reference values for semen characteristics as published in consecutive WHO manuals

Semen characteristics	WHO 1980	WHO 1987	WHO 1992	WHO 1999	WHO 2010
Volume (mL)	ND	≥ 2	≥ 2	≥ 2	≥ 1.5
Sperm count (10^6/mL)	20-200	≥ 20	≥ 20	≥ 20	≥ 15
Total sperm count (10^6)	ND	≥ 40	≥ 40	≥ 40	≥ 39
Total motility (%)	≥ 60	≥ 50	≥ 50	≥ 50	≥ 40
Progressive motility	≥ 2	≥ 25%	≥ 25% (a)	≥ 25% (a)	≥ 32% (a+b)
Vitality (%)	ND	≥ 50	≥ 75	≥ 75	≥ 58
Morphology (%)	80.5	≥ 50	≥ 30	(14)*	≥ 4*
Leukocyte count (10^6/mL)	< 4.7	< 1.0	< 1.0	< 1.0	< 1.0