Effect of Follicular Flushing During Oocyte Retrieval on Clinical Outcome of Assisted Reproductive Technology

Thesis

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Mohamed Mahmoud Ahmed Salman

Contents

List of Abbreviations

ABPs	:	Androgen-binding proteins
AFC	:	Antral Follicle Count
AI	:	Artificial insemination
AMH	:	Anti-Müllerian Hormone
ART	:	Assisted reproductive techniques
AZH	:	Assisted zona hatching
BMI	:	Body Mass Index
CDC	:	Centers for Disease Control and Prevention
CG	:	Chorionic gonadotropin
CGH	:	Comparative Genomic Hybridization
DES	:	Diethylstilbestrol
DLN	:	Double-lumen needle
DNA	:	Deoxyribonucleic acid
EMT	:	Endometrial thickness
FDA	:	Food and Drug Administration
FISH	:	Fluorescent In Situ Hybridization
FSH	:	Follicle-Stimulating Hormone
GIFT	:	Gamete Intrafallopian Transfer
GnRH	:	Gonadotrophin-releasing hormone
GnRHa	:	Administration of a gonadotropin releasing hormone agonist
hCG	:	Human Chorionic Gonadotropin
HFEA	:	Human Fertilisation and Embryology Authority
HIV	:	Human immune deficiency virus
HMG	:	Human menopausal gonadotropin
HPGA	:	Hypothalamic-Pituitary-Gonadal Axis
ICSH	:	Interstitial cell-stimulating hormone
ICSI	:	Intracytoplasmic sperm injection
Ig	:	Immunoglobulin
IM	:	Injected intra-muscularily

List of Abbreviations (Cont.)

IU	:	International Units
IUI	:	Intrauterine insemination
IV	:	Intravenous
IVF	:	In vitro fertilization
LH	:	Luteinizing hormone
LHRH	:	Luteinizing-hormone-releasing hormone
MIP	:	Maximal implantation potential
NICE	:	National Institute for health and care excellence
OCR	:	Transvaginal ovum retrieval
OHSS	:	Ovarian Hyperstimulation Syndrome
ORU	:	Oocyte recovery unit
PGD	:	Preimplantation genetic diagnosis
PGS	:	Preimplantation genetic screening
PZD	:	Partial zona dissection
r-hCG	:	recombinant human Chorionic Gonadotropin
rLH	:	recombinant luteinizing hormone
SART	:	Society for Assisted Reproductive Technology
SC	:	Sub-cutaneously
SERM	:	Selective Estrogen Receptor Modulator
SLN	:	Single-lumen needle
SSR	:	Surgical Sperm Retrieval
SUZI	:	Sub zonal insemination
TV	:	Transvaginal
US	:	Ultrasound
VOC	:	Volatile organic compounds
ZIFT	:	Zygote Intrafallopian Transfer

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Introduction

The union of male and female gametes during the process of fertilization makes the creation of new individual, a unique event that insures genetic immortality by transferring information from one generation to the next. It also creates variation, which introduces the effect of evolutionary forces. During the first half of nineteenth century, fertilization and the creation of early embryos was studied in a variety of marine, amphibians and mammalians species, and by the early 1960s had been successfully achieved in rabbits ***(Chang, 1959)***,The golden hamster ***(Yanagimachi and chang, 1964)*** and mice ***(Whittingham,1968).***

Following the decade of extensive researches in mouse, rat and rabbit reproductive biology and genetics, Robert Edwards began to study in vitro maturation of human oocyte in the early 1960s ***(Edwards,1965).*** On February 15, 1969, the journal Nature published a paper published by R. G. Edwards, B. D.Bavister and P. C. Stepoe: (early stages of fertilization in vitro of human oocytes matured in vitro, Edwards et al., 1969).

Assisted reproductive techniques are an accepted form of treatment for infertility and the procedures used are generally assumed to be relatively constant in the way they are performed between centers. Transvaginal ultrasound guided oocyte collection is now almost universal ***(Scott et al., 2001).***

In early stages of assisted reproductive technologies (ART), oocyte retrieval was performed via laparoscopy, a cumbersome and expensive process requiring general anesthesia ***(Lenz et al., 2001)***. Today, transvaginal oocyte retrieval for ART is a routine procedure performed under ultrasound guidance. Double lumen retrieval needles, which are capable of flushing ovarian follicles, were developed to overcome the possibility of oocyte retention within the ovarian follicles and retrieval collection system ***(Knight et al., 2001).***

The overall aim of ART is to increase the chances of conception, with the desired outcome a live baby, while not placing the woman at undue risk. Variations in accepted methodology are often attempted in order to improve the desired outcome. It is important to evaluate whether these variations do improve outcome. ultrasound guided transvaginal needle collection of oocytes has become the preferred method of oocyte retrieval for ART and has improved the collection rate per follicle from 19.8% and 46% when laparoscopic methods were used to between 52% and 64% and more recently 82.% ***(Baber et al., 2001).***

The aspiration of follicular fluid alone, or aspiration and flushing, both continue in different clinics suggests neither technique has overriding advantages or disadvantages when compared with the other. This may reflect historical methodology, inertia or the preference of the surgeons involved ***(Hill MJ et al., 2010).***

Follicular flushing at oocyte retrieval is based on the premise that more oocyte would be collected than by aspiration of follicular fluid alone, and the subsequent inference that this will increase pregnancy rates. Waterstone and Parsons found that 14% of total numbers of oocytes were collected in first three flushes and a further 3% in the next three when flushing was performed continuously after aspiration ***(Waterstone and Parsons, 2010).***

Studies that performed routine flushing after aspiration of the follicle reported that additional oocytes could always be obtained. For example, Bagtharia 2005 found 40% of the oocyte in the primary aspiration without flushing of the follicle, while up to 82% of oocyte were retrieved with two flushes and 97% retrieved in up to four flushes. Mendez Lozano 2008 observed 46.8% oocyte recovery rate with aspiration only, compared with 84.6% with additional follicular flushing in 165 infertile women with low ovarian

reserve, undergoing 271 consecutive minimal stimulation IVF cycles.

If no advantage in overall outcome is seen with aspiration and flushing, what impetus is there for abandonment or continuation of flushing? Techniques that do not include flushing have a number of theoretical advantages. Although sterile culture media is used for flushing, with antibiotic usually added, the potential exists for risk of pelvic infection. While of the same overall gauge the double lumen needle used for flushing presents a smaller diameter than the single lumen needle, theoretically increasing the risk of oocyte damage ad patient tissue damage at collection ***(Dahl 2009).***

First principle of surgery advocate the shortest possible operating time, the simplest procedure and minimum amount of tissue handling as maxims for reducing complications. Thus, since a decrease in operating time and amount of analgesia or anesthetic agent required when aspiration alone is used has been reported ***(Scott et al., 1989)*** and economic issues are becoming increasingly important in the provision of health care, flushing will generally increasing costs. Risk reduction is also obtained by minimizing procedures to which the patient is exposed. There are few published reports assessing complications associated with surgical retrieval of oocyte which suggests that it is a relatively safe procedure ***(Curtis et al.,1991).***

Aim of the Work

The aim of this study is to determine whether follicular aspiration and flushing increase the number of oocytes yield and pregnancy outcome over aspiration alone in women undergoing ICSI.

In vitro Fertilization

Introduction

Assisted reproductive technology (ART) is methods used to achieve pregnancy by artificial or partially artificial means. It is reproductive technology used primarily for infertility treatments, and is also known as fertility treatment. Some forms of ART are also used with regard to fertile couples for genetic reasons (preimplantation genetic diagnosis). ART is also used for couples who are discordant for certain communicable diseases; for example, AIDS to reduce the risk of infection when a pregnancy is desired. Examples of ART include in vitro fertilization, intracytoplasmic sperm injection (ICSI), cryopreservation and intrauterine insemination (IUI). There is yet no strict definition of the term *ART*; its usage mainly belongs to the field of reproductive endocrinology and infertility ***(Illmensee K et al., 2009).***

Definitions

While there is no consensus on the definition, generally the process of sexual intercourse is bypassed either by artificial Insemination or fertilization of the oocytes in the laboratory environment (i.e., in vitro fertilization). The Centers for Disease Control and Prevention (CDC) which is required as a result of the 1992 Fertility Clinic Success Rate and Certification Act to publish the annual ART success rates at U.S. fertility clinics-defines ART to include "all fertility treatments in which both eggs and sperm are handled. In general, ART procedures involve surgically removing eggs from a woman's ovaries, combining them with sperm in the laboratory, and returning them to the woman's body or donating them to another woman." According to CDC, "they do not include treatments in which only sperm are handled