A Comparative Study between Estradiol and Vaginal Progesterone with Induction of Ovulation in Unexplained Infertility

Thesis

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بسم الله الرحمن الرحيم

قالوا سبحانك لا علم لنا إلا مـا علمتنـا
إنـك انـت العليـم الـحكيـم

صدق اللـه العظيـم

البقرة آية ٣٢

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Ayman Hassan

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List of Abbreviations

ART : assisted reproductive technology
ASRM : American Society Of Reproductive Medicine
BBT : basal body temperature
BMI : body mass index
CC : clomiphene citrate
CCCT : clomiphene citrate challenge test
cGMP : cyclic guanosine monophosphate
CI : confidence interval
CL : corpus luteum
Cmax : maximum plasma concentration
CNS : central nervous system
COH : controlled ovarian hyperstimulation
CV : coefficient of variation
DIPI : direct intraperitoneal insemination
DNA : deoxy ribonucleic acid
E2 : estradiol
EE : ethinyl estradiol
eg. : example
ESHRE: European Society of Human Reproduction and Embryology
ET : embryo transfer
FDA : food and drug administration
FSH : follicle-stimulating hormone
FVW : flow velocity waveform
GIFT : gamete intra-fallopian transfer
GnRH : gonadotropin-releasing hormone
GnRHa: gonadotropin-releasing hormone agonist

GTN : glyceryl trinitrate

hCG : human chorionic gonadotropin

hMG : human menopausal gonadotropin

Ho : null hypothesis

HSG : hysterosalpingeography

HSSG : hysterosalpingosonography

ICD : international classification of diseases

ICSI : intracytoplasmic sperm injection

i.e. : that is to say (meaning)

IHD : ischemic heart disease

im : intramuscular

IU : international unit

IUI : intra-uterine insemination

IUGR : intra-uterine growth retardation

IVF : in-vitro fertilization

LH : luteinizing hormone

LUFS : luteinized unruptured follicle syndrome

mcg : microgram

mg : milligram

MHz : megahertz

Mm HG: millimeter mercury

MRI : magnetic resonance imaging

ng : nanogram

NHLBI : National Heart, Lung and Blood Institute

NO : nitrous oxide

OHSS : ovarian hyperstimulation syndrome

OI : ovulation induction

OPU : ovum pick-up

OR : odds ratio

P : Progesterone

PCOD : polycystic ovarian disease

PCT : post-coital test

PDE : phosphodiesterase

PEB : premenstrual endometrial biopsy

pg : pictogram

PI : pulsatility index

PRs : pregnancy rates

SA : Semen analysis

sc : subcutaneous

SE : standard error of mean

SEM : scanning electron microscope

SD : standard deviation

SGA : small for gestational age

SPSS : statistical package for social sciences

SRT : sperm recovery test

TI : timed intercourse

TIA : transient ischemic attack

Tmax : time to peak concentration

TVS : trans-vaginal sonography

UI : unexplained infertility

US : ultrasound

VOLss: volume of distribution

VTE : venous thromboembolism

WHO : world health organization

ZIFT : zygote intra-fallopian transfer

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Abstract

In the past few years, much interest has been focused on the possible effect of estradiol in reversing the antiestrogenic effect of CC on the endometrium, thus increasing the pregnancy rate. Another approach is the use of vaginal progesterone aiming as a luteal phase support.

Patients enrolled in this study were allocated to three groups; control group (*group I*) receiving CC induction alone, 2nd group (*group II*) receiving CC with ethinyl estradiol, 3rd group (*group III*) receiving CC with vaginal Progesterone, respectively.,

The use of ethinyl estradiol or vaginal Progesterone with ovulation induction by CC would improve the endometrial parameters which are believed to be one of the most important predictive factors of successful implantation and hence better pregnancy rates.

- ***Keywords:***

Unexplained Infertility – Clomiphene Citrate – Ethinyl Estradiol – Vaginal Progesterone.

Introduction

The assessment of the endometrium of infertile women undergoing induction of ovulation is one of the most controversial areas in the work of assisted reproduction. Adequate endometrial thickness and pattern at the time of ovulation assessed by ultrasonography and vascular impedance of the uterine artery using Doppler have been correlated with higher pregnancy rates in different studies (***Hock et al., 1997; Gerli et al., 2000; Tsai et al., 2000; Idriss et al., 2000; Sher and Fisch, 2000***).

Since the introduction of clomiphene citrate, a synthetic non steroidal estrogen agonist and antagonist, in reproductive medicine in **1961**, it has been widely used for induction of ovulation in anovulatory patients as well as super ovulation in patients with unexplained infertility. Although ovulation rate may reach up to 80%, pregnancy rate is much lower. This has been attributed to the adverse effects of CC on the endometrium leading to inadequate endometrial development that impairs implantation (***Phipps, 2001; Unfer et al., 2001; Elkind-Hirsch et al., 2002***).

The use of CC for induction of ovulation has long been described with high rates of ovulation but with discrepancy as regards pregnancy, partly attributed to the effect of Cc on the endometrium.

In the past few years, much interest has been focused on the possible effect of estradiol in reversing the antiestrogenic effect of CC on the endometrium, thus increasing the pregnancy rate (***Shimoya et al., 1999; Gerli et al., 2000; Unfer et al., 2001; Elkind-Hirsch et al., 2002***).

Another approach is the use of vaginal progesterone as luteal-phase support in ovulation induction. Although the benefit of P in the luteal phase has been well documented in IVF, there is little consensus among practitioners regarding the use of luteal-phase P supplementation in patients using oral medication ***(Montville et al. 2009).***

A study is needed to compare the effect of clomiphene citrate alone; as well as the effect of adding estradiol to compensate for the deleterious effects of CC on the endometrium or the use of Progesterone to attain the same beneficial effect on the endometrium thus helping in implantation.

Aim of Work

To compare the pregnancy rates in patients with unexplained infertility using clomiphene citrate, and the effect of adding oral ethinyl estradiol or vaginal progesterone on the endometrium in contrast to a control group.

Review of literature