

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

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا سبحانك لا علم لنا إلا ما علمتنا
إنك انت العليم الحكيم

صدق الله

البقرة آية

العظيم

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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
GnRH_a	:	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