Impact of Laparoscopic Ovarian Drilling on E_2 / FSH Ratio and Ovarian Stromal Blood Flow in Women with Polycystic Ovary Syndrome

Thesis

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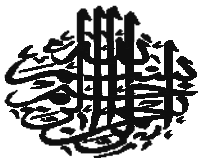

وأنـزل الله عليـك
الكتـاب والحكمة
وعَلَّمَكَ مَا لَمْ تَكُن
تَعْلَمُ وكَانَ فَضْلُ
اللَّهِ عَلَيْكَ عَظِيماً

صدق الله العظيم

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Aliaa Mohammad Ali Maaty

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List of Abbreviations

ADA	American diabetes association
ASRM	American Society for Reproductive Medicine
BMI	Body mass index
CC	Clomiphene citrate
DHEA	Dehydroepiandrosterone
E2	Estradiol
ESHRE	European Society of Human Reproduction and Embryology
FAI	Free androgen index
FI	Flow index
FSH	Follicle stimulating hormone
GnRH	Gonadotrophin releasing hormone
IGF	Insulin growth factor
IGFBP	Insulin-like growth factor-binding protein
IVF	In vitro fertilization
KTP laser	Potassium titanyl phosphate
LH	Luteinizing hormone
LOD	Laparoscopic ovarian drilling
MG	Mean grayness
mL	Milli liter
Nd YAG laser	Neodymium-doped yttrium aluminum garnet
Ng	Nanogram
NIH	National Institute of Health
OGTT	Oral glucose tolerance test

List of Abbreviations *(Cont...)*

PCOS	Polycystic ovary syndrome
Pg	Picogram
rFSH	Recombinant follicle stimulating hormone
SD	Standard deviation
SHBG	Sex hormone binding globulin
t_p	Paired t-test
U/S	Ultrasound
VFI	Vascularization flow index
VI	Vascularization index
VOCAL	Virtual organ computer aided analysis
W	Watt
WHO	World Health Organization
2D	Two dimensional
3D	Three dimensional

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Introduction

Polycystic ovary syndrome (PCOS) is one of the most common female endocrine disorders. PCOS is a complex, heterogeneous disorder of uncertain etiology, but there is strong evidence that it can to a large degree be classified as a genetic disease***(Legro and Strauss, 2002).***

The classic triad of the disorder includes hirsutism, menstrual dysfunction, and obesity. Some common symptoms of PCOS include: Menstrual disorders: PCOS mostly produces oligomenorrhea or amenorrhea, but other types of menstrual disorders may also occur.Infertility**:**this generally results directly from chronic anovulation. Hyperandrogenism: The most common signs are acne and hirsutism (male pattern of hair growth), but it may produce hypermenorrhea (very frequent menstrual periods) or other symptoms***(Teede et al., 2010).***

The exact pathophysiology of PCOS and itsinitiating event is still unproved. However, various biochemical abnormalities and hormonal changes have been described, and associations andlinkages of one to another have been established. Many of these abnormalities reinforce each other in vicious circles***(Melmed et al., 2011).***

In 2003, a workshop in Rotterdam indicated PCOS to be present if any 2 out of the following 3 criteria are met(***Rotterdam ESHRE/ASRM-sponsored PCOS consensus workshop group 2004), (Azziz 2006)*** *and* ***(Teede et al., 2010).***

1. Oligo ovulation and/or anovulation.

2. Excess androgen activity.

3. Polycystic ovaries (by gynecologic ultrasound). According to available literature, at least one of the following criteria should be present to establish polycystic ovaries: either 12 or more follicles measuring 2–9 mm in diameter, or increased ovarian volume (>10 cm3). Not all women with PCOS have polycystic ovaries, nor do all women with ovarian cysts have PCOS; although a pelvic ultrasound is a major diagnostic tool, it is not the only one***(Marrinan and Greg,2011).***

Three-dimensional (3D) ultrasound provides a new method for the objective quantitative assessment of follicle count, ovarian volume, stromal volume and blood flow within the ovary as a whole. The presence of PCOs on ultrasonography was not included in the definition despite this feature being mandatory in many centers***(Balen et al., 2003),*** and the associated clinical features such as menstrual disturbance, obesity and hyperandrogenism manifesting as hirsutism or acne vary considerably among women***(Polson et al., 1999),(Michelmore et al., 2002).***

Though surgery is not commonly performed, the polycystic ovaries can be treated with a laparoscopic procedure called "ovarian drilling" which often results in either resumption of spontaneous ovulations or ovulations after adjuvant treatment with clomiphene or FSH (Ovarian wedge resection is no longer used as much due to complications such as adhesions and the presence of frequently effective medications)***(Felemben et al., 2000).***

Laparoscopic ovarian drilling was first described in 1984 and involved the creation of 8 – 15 holes, each one 2 – 4mm deep on the surface and stroma of each ovary using a unipolar electrode at 300–400 W for 2–4 seconds. Several modifications of the technique have been reported including the use of laser (CO2, argon, KTP or Nd-YAG) with good results. However, the published results of laser surgery are inferior to those of electro cautery***(Ameret al., 2004).***

Aim of the Work

The aim of the current study is to study the impact of laparoscopic ovarian drilling on E2/FSH ratio and ovarian stromal blood flow in women with polycystic ovary syndrome.

Research question:

Will bilateral ovarian drilling in patients with PCOS improve E2 / FSH ratio and ovarian stromal blood flow?

Research hypothesis:

Bilateral ovarian drilling in patients with PCOS improves E2 / FSH ratio and ovarian stromal blood flow.

Polycystic Ovary Syndrome

Polycystic ovary syndrome (PCOS) is one of the most common female endocrine disorders. PCOS is a complex, heterogeneous disorder of uncertain etiology, but there is strong evidence that it can to a large degree be classified as a genetic disease***(Legro and Strauss, 2002), (Fauser et al., 2011).***

The condition was first described in 1935 by American gynecologists Irving F. Stein and Michael L. Leventhal, from whom its original name of *Stein-Leventhal syndrome* is taken***(Marrinan and Greg, 2011),(Richard S., 2011).***

Other names for this syndrome include polycystic ovary disease, functional ovarian hyperandrogenism, ovarian hyper-thecosis, sclerocystic ovary syndrome, and Stein-Leventhal syndrome. The eponymous last option is the original name; it is now used, if at all, only for the subset of patients with all the symptoms of amenorrhea with infertility, hirsutism, and enlarged polycystic ovaries***(Marrinan and Greg, 2011).***

Symptoms of PCOS:

PCOS produces symptoms in approximately 5% to 10% of women of reproductive age (12–45 years old). It is thought to be one of the leading causes of female subfertility and the most frequent endocrine problem in women of reproductive age***(Azziz et al., 2004), (Boomsma et al., 2008), (Goldenberg and Glueck, 2008).***

The clinical severity of PCOS symptoms appears to be largely determined by factors such as obesity***(Kandarakis et al., 2006), (Teede et al., 2010).***

The principal features are anovulation, resulting in irregular menstruation, amenorrhea, ovulation-related infertility, and polycystic ovaries; excessive amounts or effects of androgenic hormones, resulting in acne and hirsutism; and insulin resistance, often associated with obesity, Type 2 diabetes, and high cholesterol levels.The symptoms and severity of the syndrome vary greatly among affected women***(Teede et al., 2010).***

The World Health Organization criteria for classification of anovulation include the determination of oligomenorrhea (menstrual cycle >35 days) or amenorrhea (menstrual cycle > 6 months) in combination with concentration of prolactin, follicle stimulating hormone (FSH) and estradiol. Almost 80% of anovulatory patients have normal serum FSH and estradiol levels and demonstrate very heterogeneous symptoms ranging from anovulation, obesity, biochemical or clinical hyperandrogenism and insulin resistance. PCOS is the most common cause of anovulation in women with normal serum FSH and estradiol levels***(Nadir and Kandarakis, 2009).***

Despite the heterogeneity in symptoms associated with PCOS, the essential feature is arrested follicular development at the stage when selection of the dominant follicle should normally occur***(Wafaa et al., 2012).***

PCOS includes a heterogeneous collection of signs and symptoms with varying degree of mildness and severity in affecting the reproductive, endocrine and metabolic functions***(Keith, 2011).*** The classic triad of the disorder includes hirsutism, menstrual dysfunction, and obesity. Some common symptoms of PCOS include:

- Menstrual disorders: PCOS mostly produces oligomenorrhea or amenorrhea, but other types of menstrual disorders may also occur***(Teede et al., 2010).***

- Infertility: This generally results directly from chronic anovulation (lack of ovulation)***(Teede et al., 2010).***

- Hyperandrogenism: The most common signs are acne and hirsutism (male pattern of hair growth), but it may produce hypermenorrhea (very frequent menstrual periods) or other symptoms***(Teede et al., 2010).***Approximately three-quarters of patients with PCOS (by the diagnostic criteria of NIH/NICHD 1990) have evidence of hyperandrogenemia***(Huang et al., 2010).***

- Metabolic syndrome: This appears as a tendency towards central obesity and other symptoms associated with insulin resistance***(Teede et al., 2010).*** Serum insulin, insulin resistance and homocysteine levels are higher in women with PCOS***(Nafiye et al., 2010).***