THE EFFECT OF LAPAROSCOPIC OVARIAN DRILLING ON SERUM PROLACTIN LEVEL IN PATIENTS WITH POLYCYSTIC OVARIAN SYNDROME

Submitted for the Partial Fulfillment of Master Degree (MSc) in Obstetrics and Gynecology

Presented by

Mohammed Samaan Khattab
(M. B. B. Ch.)

Supervised by

Prof. Dr. Ismael Ibrahem Abo El-Foutouh
Professor of Obstetrics and Gynecology
Faculty of Medicine, Cairo University

Prof. Dr. Ahmed Nehad Askalany
Assistant Professor of Obstetrics and Gynecology
Faculty of Medicine, Cairo University

Prof. Dr. Dina Sabry Abd-El-Fatah
Prof. of Biochemistry
Faculty of Medicine, Cairo University

Faculty of Medicine
Cairo University
2013

بسم الله الرحمن الرحيم

قَالُوا سُبْحَانَكَ لاَ عِلْمَ لَنَا
إِلاَّ مَا عَلَّمْتَنَا إِنَّكَ أَنتَ الْعَلِيمُ
الْحَكِيمُ

صدق الله العظيم
سورة البقرة الآية (32)

Acknowledgment

First and above all thanks to ***ALLAH,*** *the most beneficial and merciful for helping me to bring this work to light.*

I am greatly honored to express my deepest thanks, gratitude and respect to ***Prof. Dr. Ismael Ibrahem Abo El-Foutouh*** *Professor of Obstertrics and Gynecology, Faculty of Medicine, Cairo University, for his kind guidance, supervision, advice and continuous encouragement.*

My deepest thanks and appreciation go to ***Prof. Dr. Ahmed Nehad Askalany,*** *Assistant Professor of Obstertrics and Gynecology, Faculty of Medicine, Cairo University, for his unlimited help, keen supervision, valuable advice, and extreme patience to complete this work.*

I am also expressing my sincere appreciation and deepest gratitude to ***Prof. Dr. Dina Sabry Abd-El-Fatah,*** *Professor of Biochemistry, Faculty of Medicine, Cairo University, for her continuous supervision and excellent guidance.*

Finally, I would like to express my deepest gratitude and thanks to all my family especially my wife for her for her help and effort to finish this work.

Abstract

Background:

The effect of ovarian drilling on the serum levels of proloctin and gonadotropins hormones have been studied previously.

The aim of this study is to evaluate the effect of ovarian drilling on the serum proloctin levels and its relation to ovulation in women with polycystic ovarian syndrome.

Methods:

This is a prospective study, fifty women with PCOS underwent laparoscopic ovarian drilling in Ashmoun and other private hospitals. Hormonal assessment for prolactin, FSH and LH were done before LOD, and 3 months after LOD for prolactin hormone, folliculometry was also performed for detecting the ovulation.

Results:

3 months after drilling the mean serum prolactin levels was increased in all patients from(257.2±230mIU/ml)(range 42.7-2471) to (426±360mIU/ml)(range 53-3162).

Approximately the non ovulation rate was 34%, hyperprolactineamia was detected in 29.4% 3 months after drilling.

Conclusion:

Hyperprolactinemia after LOD may be considered as a possible cause of anovulation in women with PCOS. The cause of hyperprolactineamia is unknown .Hormonal assay particulary PRL in anovulatory patients after LOD in recommended .

Key words:

Laparoscopic – Ovarian – Drilling – Hyperprolactinemia-Anovulation

List Of Contents

List of Abbreviations

ACTH	Adrenocorticotrophic hormone
ASRM	American Society for Reproductive Medicine
ART	Assisted reproductive technology
BMI	Body mass index
CC	Clomiphene citrate
Cm3	Centemeter
CT	Computed Tomography
DHEAS	Dehydroepiandrosterone sulphate
DA	Dopamine agonist
DXA	Dual-energy X-ray absorptiometry
et al.	et alii (and others)
FSH	Follicle stimulating hormone
GH	Growth hormone
GNRH	Gonadotropin releasing hormone
Hb A1C	Glycosylated haemoglobin
HCG	Human chorionic gonadotropin
HDL-C	High-density lipoprotein cholesterol
HIV	Human immunodeficiency virus
HMG	Human menopausal gonadotropin
HPG	Human pituitary gonadotropin
HRP	Horse radish peroxidase
HPO	Hypothalamic- Pitutary- Ovarian axis
IGF-1	Insulin like growth factor-1
IgG	Immunoglobulin G
IVF	In vitro fertilization
IU	International unit
kg/m2	kilogram/m2
LH	Luteinizing hormone
LOD	Laparoscopic ovarian drilling
mg/ dl	miligram/ deciliter
ng/dl	nanogram/ deciliter
NICHD	National Institute of Child Health and Human Disease
NIH	National Institutes of Health
PAI-1	Plasminogen activator inhibitor-1
PCOS	Polycystic ovary syndrome
SHBG	Sex hormone binding globulin
TRH	Thyrotropin releasing hormon
TSH	Thyroid stimulating hormone
VEGF	Vascular endothelial growth factor

List of Tables

List of figures

INTRODUCTION

The major features of polycystic ovarian syndrome (PCOS) include menstrual dysfunction, anovulation, and signs of hyperandrogenism ***(Azziz et al., 2009)***.

Although the exact etiopathophysiology of this condition is unclear, PCOS can result from abnormal function of the hypothalamic-pituitary-ovarian (HPO) axis.A key characteristic of PCOS is inappropriate gonadotropin secretion, which is more likely a result of, rather than a cause of, ovarian dysfunction. In addition, one of the most consistent biochemical features of PCOS is a raised plasma testosterone level ***(Barber et al., 2010)***.

Polycystic ovary syndrome (PCOS) is one of the most common causes of anovulatory infertility and affects 5 - 10% of women of reproductive age. Women with this syndrome of chronic anovulation and hyperandrogenism are at increased risk of obesity, diabetes, infertility, and miscarriage ***(Neveu et al., 2007)***.

Clomiphene citrate (CC) has been the standard treatment for ovulation induction in these patients for many years. Ovulation rates of 60 - 85 % and pregnancy rates of 30 - 40 % have been reported with this medication ***(Zawadzki and Dunaif, 1992)***. However, clomiphene citrate has been shown to be associated with cervical mucus abnormalities, luteal phase defects, ovarian cysts, and multiple gestations. Moreover, hot flushes and visual symptoms are

other side effects of this medication ***(Palomba et al., 2006)***.

In 75% of patients with PCOS, ovulation induction occurs with clomiphene citrate treatment; however 25% of patients are clomiphene citrate resistant and require alternative treatment ***(Palomba et al., 2006)***.

For many years ago, the second line treatment in CC resistant PCOS women consisted of laparoscopic ovarian drilling or gonadotrophin use. The two approaches are similar in terms of ovulation and pregnancy rates. Furthermore, during gonadotrophin administration, a particular experience of the doctor is needed as well as careful sonographic and biochemical monitoring to avoid or to reduce the risk of ovarian hyperstimulation and multiple pregnancies. In addition, the treatment with gonadotrophins requires a relevant investment of time and money ***(Gleicher, 2000)***. On the contrary, with the advent of laparoscopic techniques and with their wide use, LOD has been proposed as a once-only procedure to induce ovulation in CC-resistant PCOS women ***(Felemban et al., 2000)***.

Laparoscopic ovarian drilling is a day-surgery procedure characterized not only by effectiveness in ovulation induction comparable to gonadotrophin use but also by few side effects and no need for ongoing monitoring ***(Farquhar et al., 2000)***. In addition, LOD has beneficial effects at the metabolic level but effectiveness does not seem to be maintained after a long term follow up ***(Saleh et al., 2001)***.

The proportion of ovulation after LOD is about 77% but the chance of conception at 12 months after LOD was 54% only ***(Mustafa and Tulay, 2005)***. This can be attributed to post-operative adhesion formation.

Although there was marked improvement of hormonal profile in most patients after LOD ***(Godinjak et al., 2007)*** (LH and testosterone levels decreased in 75% and 70% of PCO patients respectively), the reported ovulation rate after LOD remain around 52.8 % only ***(Parsanezhad et al., 2005)***. Many studies concerning the endocrine effects of LOD have been performed ***(Vicino et al., 2000 and Alborzi et al., 2001)***, but few have emphasized on the cause of disparity between hormonal changes and ovulation rate. There is controversy whether the cause of this disparity is due to post-LOD hyperprolactinemia or not ***(Parsanezhad et al., 2005)***.

Aim of the Work

The aim of the study is to detect the changes in serum prolactin level in relation to ovulation rate after laparoscopic ovarian drilling in patients with polycystic ovary syndrome. This will be done in order to determine whether or not hyperprolactinemia is a cause of persistent anovulation after LOD.

POLYCYSTIC OVARIAN SYNDROME

Background

The major features of polycystic ovarian syndrome (PCOS) include menstrual dysfunction, anovulation, and signs of hyperandrogenism ***(Azziz et al., 2009).***

Although the exact etiopathophysiology of this condition is unclear, PCOS can result from abnormal function of the hypothalamic-pituitary-ovarian (HPO) axis. A key characteristic of PCOS is inappropriate gonadotropin secretion, which is more likely a result of, rather than a cause of, ovarian dysfunction. In addition, one of the most consistent biochemical features of PCOS is a raised plasma testosterone level ***(Barber et al.,2010)***.

Stein and Leventhal were the first to recognize an association between the presence of polycystic ovaries and signs of hirsutism and amenorrhea (eg, oligomenorrhea, obesity) ***(Stein et al.,1935).*** After women diagnosed with Stein-Leventhal syndrome underwent successful wedge resection of the ovaries, their menstrual cycles became regular, and they were able to conceive ***(Stien,1964).***

As a consequence, a primary ovarian defect was thought to be the main culprit, and the disorder came to be known as polycystic ovarian disease. Further biochemical, clinical, and endocrinologic studies revealed an array of underlying abnormalities. As a result, the condition is now referred to as PCOS, although it may occur in

women without ovarian cysts and although ovarian morphology is no longer an essential requirement for diagnosis. A woman is diagnosed with polycystic ovaries (as opposed to PCOS) if she has 12 or more follicles in at least 1 ovary—measuring 2-9mm in diameter—or a total ovarian volume greater than 10 cm^3

Diagnostic criteria

A 1990 expert conference sponsored by the National Institute of Child Health and Human Disease (NICHD) of the United States National Institutes of Health (NIH) proposed the following criteria for the diagnosis of PCOS:

- Oligo-ovulation or anovulation manifested by oligomenorrhea or amenorrhea
- Hyperandrogenism (clinical evidence of androgen excess) or hyperandrogenemia (biochemical evidence of androgen excess)
- Exclusion of other disorders that can result in menstrual irregularity and hyperandrogenism

In 2003, the European Society for Human Reproduction and Embryology (ESHRE) and the American Society for Reproductive Medicine (ASRM) recommended that at least 2 of the following 3 features are required for PCOS to be diagnosed ***(ESHRE/ASRM, 2004)*** .

- Oligo-ovulation or anovulation manifested as oligomenorrhea or amenorrhea
- Hyperandrogenism (clinical evidence of androgen excess) or hyperandrogenemia (biochemical evidence of androgen excess)
- Polycystic ovaries (as defined on ultrasonography)

The Androgen Excess and PCOS Society (AE-PCOS) published a position statement in 2006***(Azziz et al., 2006)*** and its criteria in 2009 ***(Azziz et al., 2009)*** emphasizing that, in the society's opinion, PCOS should be considered a disorder of androgen excess, as defined by the following:

- Clinical/biochemical evidence of hyperandrogenism
- Evidence of ovarian dysfunction (oligo-ovulation and/or polycystic ovaries)
- Exclusion of related disorders

The Society of Obstetricians and Gynaecologists of Canada (SOGC) indicated that a diagnosis of polycystic ovarian syndrome (PCOS) is made in the presence of at least 2 of the following 3 criteria, when congenital adrenal hyperplasia, androgen-secreting tumors, or Cushing syndrome have been excluded ***(Vause et al., 2010):***

- Oligo-ovulation or anovulation
- Clinical/biochemical evidence of hyperandrogenism

- Polycystic ovaries on ultrasonograms (>12 small antral follicles in an ovary)

Etiology

Women with polycystic ovarian syndrome (PCOS) have abnormalities in the metabolism of androgens and estrogen and in the control of androgen production. High serum concentrations of androgenic hormones, such as testosterone, androstenedione, and dehydroepiandrosterone sulfate (DHEA-S), may be encountered in these patients. However, individual variation is considerable, and a particular patient might have normal androgen levels. PCOS is also associated with peripheral insulin resistance and hyperinsulinemia, and obesity amplifies the degree of both abnormalities. Insulin resistance in PCOS can be secondary to a postbinding defect in insulin receptor signaling pathways, and elevated insulin levels may have gonadotropin-augmenting effects on ovarian function. Hyperinsulinemia may also result in suppression of hepatic generation of sex hormone–binding globulin (SHBG), which in turn may increase androgenicity ***(Barber et al., 2006).***

In addition, insulin resistance in PCOS has been associated with adiponectin, a hormone secreted by adipocytes that regulates lipid metabolism and glucose levels. Lean and obese women with PCOS have lower adiponectin levels than do women without PCOS ***(Toulis et al., 2009).***

A proposed mechanism for anovulation and elevated androgen levels suggests that, under the increased stimulatory effect