OVARAIN RESERVE AFTER SURGICAL MANAGMENT OF INFERTILE WOMEN WITH OVARIAN ENDOMETRIOSIS

Thesis

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بسم الله الرحمن الرحيم

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

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LIST OF ABBREVIATIONS

(AFC)	**:**	Antral follicle count
(AFS)	**:**	American Fertility Society
(AMH)	**:**	Anti-Mullerian Hormone.
(ART)	**:**	Assisted reproductive techniques
(ASRM)	**:**	American society of reproduction and menopause
(BOV)	**:**	Basal ovarian volume
(CA-125)	**:**	Cancer antigen -125
(CCCT)	**:**	Clomiphene citrate challenge test
(COH)	**:**	Controlled ovarian hyperstimulation
(d(V))	**:**	Volume-based diameter
(DSL)	**:**	Diagnostic Systems Laboratories
(E2)	**:**	Estradiol
(ECLIA)	**:**	Electrochemiluminescence
(EFORT)	**:**	The exogenous FSH ovarian reserve test
(ESHRE)	**:**	European society of human reproduction and embryology
(FSH)	**:**	Follicular stimulating hormone
(GALT)	**:**	Galactose phosphate uridyltransferase
(GAST)	**:**	Gonadotropin releasing hormone analogue stimulation test
(GSTMI)	**:**	Glutathione-s-transferase Pi-1
(GnRH)	**:**	Gonadotropin releasing hormone
(IgG)	**:**	Immunoglobulin G
(IgM)	**:**	Immunoglobulin M
(IL-1)	**:**	Interleukin-1
(IL-6)	**:**	Interleukin-6
(IL-8)	**:**	Interleukin-8
(IUI)	**:**	Intrauterine insimination
(IVF)	**:**	In vitro fertilization
(LH)	**:**	Luteinizing hormone

LIST OF ABBREVIATIONS (Cont.)

(LUF)	**:**	Luteinized unruptured follicle
(MCL)	**:**	Menstrual cycle length
(MFD)	**:**	Mean follicle diameter
(MRI)	**:**	Magenetic resonance imaging
(NAT2)	**:**	Anylamine-n-acetyltransferase natarylamine acetylase
(OBF)	**:**	Ovarian blood flow
(OV)	**:**	Ovarian volume
(PI)	**:**	Pulsatility index
(PID)	**:**	Pelvic inflammatory disease
(PROGINS)	**:**	Gene coding for progesterone receptor
(PSV)	**:**	Peak systolic velocity
(rFSH)	**:**	Recombinant FSH
(SonoAVC)	**:**	Sonography-based Automated Volume Calculation
(TGF-β)	**:**	Transforming growth factors β
(TNF-α)	**:**	Tumour necroting factor-α
(TVS)	**:**	Transvaginal sonography
(U/S)	**:**	Ultrasonography
(2D)	**:**	Two-dimensional
(2D-RTE)	**:**	Two-dimensional real-time equivalent
(3D)	**:**	Three –dimensional
(VEGF)	**:**	Vascular endothelial growth factor

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Abstract

Objective: To investigate the effect of two different laparoscopic methods on ovarian reserve in patients with ovarian endometriomas.

Design: Prospective, randomized clinical trial.

Setting: Endoscopy unit of Al Husein Hospital.

Patients:104 infertile women aged (18-35 years) with laparoscopically diagnosed ovarian endometriosis.

Methods: Patients were randomly selected to undergo either laparoscopic cystectomy for endometrioma (group 1) or laparoscopic coagulation of endometrioma for(group 2). Before and 6 months after laparoscopy all patients were evaluated. .

Main Outcomes: The primary end point was ovarian reserve damage based on the alterations of anti-Müllerian hormone (AMH). Secondary end points were the changes of antral follicle count and serum concentration of FSH, LH, E(2), and inhibin B..

Results: Mean serum AMH was reduced significantly from 3.9-2.9 ng/mL in group 1 compared with the reduction from 4.5-3.99 ng/mL in group 2.

Conclusions: Ovarian reserve determined by AMH is less diminished after the coagulation procedure compared with cystectomy of endometriomas.

Keywords: Endometriosis, Infertility, Classification of endometriosis, Laparoscopy,Ovarian reserve, AMH,FSH,E2,Inhibin B .

INTRODUCTION

Endometriosis is characterised by the presence, outside the endometrial cavity, of tissue that is morphologically and biologically similar to normal endometrium. This ectopic endometrial tissue responds to ovarian hormones undergoing cyclical changes similar to those seen in eutopic endometrium. The cyclical bleeding from endometriotic deposits appears to contribute to the induction of an inflammatory reaction and fibrous adhesion formation, and in the case of deep ovarian implants, leads to the formation of endometriomas or chocolate cysts ***(Caroline et al., 2007).*** The current prevalence of endometriosis is estimated to be up to 10% ***(Vigano et al., 2004).*** The incidence has not increased in the last 30 years and remains at 2.37-2.49 per 1000 women per year, equating to an approximate prevalence of 6-8% ***(Hummelshoj et al., 2006).***

The main clinical symptoms of endometriosis are infertility, dysmenorrhoea, dyspareunia, dyschezia and chronic pelvic pain (defined as pain of greater than 6- month duration and not cyclical in nature) ***(Treloar et al., 2005).*** The gold standard for diagnosing endometriosis in the abdomen and pelvis is the visual identification of characteristic lesions at laparoscopy. In one study, this means of diagnosis was shown to be 97% sensitive and 77% specific ***(Buchweitz et al., 2003).***

Although many hypotheses exist to explain the condition between endometriosis and infertility, the precise mechanisms by which endometriosis leads to infertility remain unclear. While more extensive endometriosis may simply impair fertility by mechanical means, hypotheses concerning subtler forms of endometriosis have suggested that infertility is impaired due to disruption of ovum transport, interference with hormone support, ovulation

dysfunction, detrimental effects on gametes and/or reduced granulosa cell steroidogenesis ***(Toya et al., 2000).***

Reduced granulosa cell steroidogenesis has also been noted with diminished ovarian reserve ***(Toya et al., 2000).*** To evaluate the ovarian follicular status, classically, early follicular phase serum FSH, inhibin B, and E2 levels have been measured. However, the usefulness of those measurements and its clinical utility is limited ***(Broekmans et al., 2006).*** In addition, the assessment of the number of antral follicles by ultrasonography may predict the number of retrieved oocytes after controlled ovarian hyperstimulation (COM) ***(Hendriks et al., 2005).***

Anti-Mullerian hormone (AMH) is produced by small, early antral follicles and was strongly connected to the number of small antral follicles than FSH, E2, and even inhibin B levels ***(Fanchin et al., 2003).*** In vivo and in vitro studies showed that AMH has an inhibitory effect on primordial follicle recruitment and it decreases the sensitivity of follicles for the FSH-dependent selection for dominance. Besides its functional role in the ovary, serum AMH level serves as an excellent candidate marker of ovarian reserve ***(Visser et al., 2006).*** In addition, AMH is a marker for ovarian reserve and, as previously demonstrated, a better predictor of the number of early antral follicles as FSH, inhibin B, E2, and LH ***(Eldar-Geva et al., 2005).***

The laparoscopic excision of ovarian endometriotic cysts is associated with a statistically significant reduction in ovarian reserve, which is partly a consequence of the damage to the ovarian vascular system ***(Li et al., 2008).***

AIM OF THE WORK

To evaluate the effect of surgical managment, either using laparoscopic ovarian cystectomy or using fenestration aspiration and endocoagulation on ovarian reserve in infertile women with ovarian endometriosis.

Review of Literature

Ovarian endometriomas usually present as a pelvic mass arising from growth of ectopic endometrial tissue within the ovary. They typically contain thick brown tar-like fluid (hence the name "chocolate cyst") and are often densely adherent to surrounding structures, such as the peritoneum, fallopian tubes, and bowel. An endometrioma may be associated with symptoms of endometriosis (eg, pelvic pain, dysmenorrhea, and dyspareunia) or identified at the time of evaluation for a pelvic mass or infertility (***Giudice and Kao, 2004)***.

The pathogenesis of endometriomas is not clear. One hypothesis is that retrograde passage of menstrual blood or shedding from endometriosis implants deposit on the ovary of an endometrioma, which is actually a pseudocyst. The cyst contents of endometriomas contain high concentrations of iron, presumably from chronic bleeding into the cyst, possibly at the time of menses (***Giudice and Kao, 2004).***

Histopathology is required to make a definitive diagnosis of endometrioma. However, a clinical diagnosis can often be made with a high degree of certainty in a woman with histologically confirmed endometriosis and an adnexal mass, since 50 percent of women with endometriosis develop endometriomas, which are often bilateral (***Busacca et al., 2006).***

Ultrasound findings suggestive of an endometrioma include homogeneous low to medium level echoes in a thick walled, cystic mass (unilocular or multilocular) (Figure 1). There may be varying degrees of echogenicity in the different locules and fluid levels may be present. A ground glass appearance is typical (***Ghezzi et al., 2005)***.