شبكة المعلومات الجامعية

بسم الله الرحمن الرحيم

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

شبكة المعلومات الجامعية

جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

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علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات

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شبكة المعلومات الجامعية

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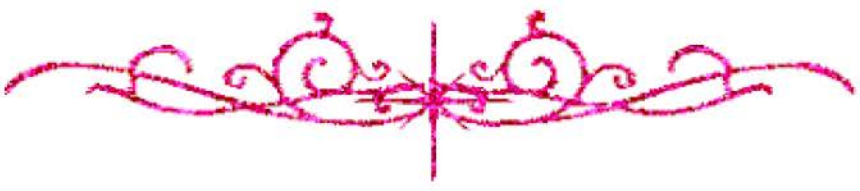

بالرسالة صفحات لم ترد بالأصل

Comparing parameters of ovarian reserve before & after laparoscopic ovarian drilling of polycystic ovaries

Thesis

Submitted for partial fulfillment of Doctoral in Obstetrics and Gynecology

By

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Introduction

The primary function of the female ovary is the production of a mature oocyte capable of fertilization and subsequent embryo development and implantation. At birth, the ovary contains a finite number of oocytes available for folliculogenesis. This finite number of available oocytes is termed “the ovarian reserve”. The determination of ovarian reserve is important in the assessment and treatment of infertility. As the ovary ages, the ovarian reserve will decline ***(Baird et al., 2005).***

Ovarian reserve (OR) refers to the number and quality of oocytes that, at any given age, are available to produce a dominant follicle late in the follicular phase of the menstrual cycle. By estimating the OR, a prediction of the remaining reproductive lifetime could be assessed as well as the likely success of assisted reproductive techniques (ART) such as *in vitro* fertilization (IVF) ***(Roudebush et al., 2008).***

Since the mid-twentieth century, when the progressive loss of follicular population between 30 and 40 years of age was estimated to be of approximately 75%, more attention has been devoted to the reproductive potential of women in the presence of ovarian aging. Considering modern trends of maternity postponement and the increasing demand for assisted reproduction techniques (ART), the evaluation of functional ovarian reserve has arisen in an attempt to better counsel interested couples and guide the elaboration of stimulation protocols, with a reduction of emotional and financial burdens of a hard and stressful process ***(De Carvalho et al., 2008).***

There are both indirect and direct measures of ovarian reserve. Indirect measures include day 3 follicular stimulating hormone (FSH), estradiol, and the FSH\LH ratios. These biomarkers are considered indirect measures, as they require stimulation from either a feedback inhibition or a stimulation loop. Essentially these biomarkers rely on the production of other hormones. Inhibin B and Anti-Müllerian hormone (AMH) are examples of direct measures of ovarian reserve as these hormones are produced during specific stages of follicular development, rather than by follicular stimulation ***(Roudebush et al., 2008).***

Biomarkers are desirable for assessing fertility because of the minimal invasiveness of blood collection in comparison to other procedures. The "magic bullet" biomarker for ovarian reserve has yet to be clearly defined, yet. However many biomarkers do provide significant insight as to ovarian reserve status. There are a few newly recognized biomarkers that look extremely promising, including AMH and inhibin-B ***(Roudebush et al., 2008).***

The inhibins are glycoprotein hormones of the superfamily of transforming growth factors β (TGF-β) secreted by granulosa and theca cells which are selectively responsible for pituitary inhibition of FSH secretion. Inhibin-B is particularly outstanding in the execution of this function and in its paracrine action on developing follicles, stimulated by the association of FSH itself with insulin-like growth factor I (IGF-I) ***(De Carvalho et al., 2008).***

In normal ovulatory cycles, the serum concentration of inhibin-B is inversely correlated with FSH concentration and

increases insidiously up to the mid-point of the follicular phase, when it reaches a maximum peak together with the mass of granulosa cells. A progressive decrease occurs thereafter to low concentrations that persist in the luteal phase, except for a brief new elevation after the LH surge .This behavior along the cycle permits us to assume that inhibin-B plays a role in follicular development, reflecting ovarian function and follicular reserve, thus acting as a marker of the functional reserve of the gonad. ***(De Carvalho et al., 2008).***

Seifer et al. demonstrated greater estrogen responses and number of oocytes obtained after stimulation among women with serum inhibin-B levels ≥45 pg/mL, whereas cancellations were three times more frequent among patients with lower levels ***(Seifer et al., 1997).***

Hofmann et al. comprised women with a supposedly adequate ovarian reserve based on the test of stimulation with clomiphene citrate and demonstrated that inhibin-B levels were more elevated among women with a normal response ***(Hoffman et al., 1998).***

Tinkanen et al. investigated infertile women aged 24 to 40 years and detected a significant negative correlation between serum inhibin-B levels and FSH, as well as a significant positive correlation between inhibin-B and initial antral follicles counted by ultrasound ***(Tinkanen et al., 2001).***

Anti-Müllerian hormone (AMH) is a glycoprotein hormone of the transforming growth factor-β (TGF-β) superfamily, known to be produced by testicular Sertoli cells and to be responsible for

the regression of the paramesonephric ducts during the sexual differentiation of male human embryos ***(Rajpert et al., 1999).***

Absent during female differentiation, AMH is expressed in granulosa cells as soon as the first primordial follicles are recruited, at about the 36th week of intrauterine life, and at higher concentrations at puberty ***(Visser et al., 2005).***

After activation of the hypothalamus–pituitary–ovarian axis, its expression is maintained until the follicles reach about 6 mm in diameter, when the differentiation into antral follicles itself is enough for dominance and follicular growth follows controlled by FSH action ***(Weenen et al., 2004).***

AMH will in all probability become the hormone of choice for assessing OR. It has been suggested that AMH is the single best predictor of poor response for ART ***(Muttukrishna et al., 2005).***

The fact that AMH is secreted without dependence on other hormones, particularly the gonadotropins, and that AMH is expressed at a constant level, independent of cycle day make AMH very attractive as a direct measurement of OR. ***(La Marca et al., 2006& La Marca et al., 2007).***

The freedom that AMH testing offers both clinicians and patients by allowing collections to be performed on any day during the menstrual cycle is a vast logistical advantage over other biomarkers ***(Feyereisen et al., 2006& Hehenkamp et al., 2006).***

A study demonstrated not only a strong relationship between AMH and AFC (antral follicular count) and this

relationship was stronger than the other typical biomarkers relationships with AFC ***(Feyereisen et al. 2006).***

In addition to being a good biomarker for the quantity of follicles, another study illustrated that AMH is also suggestive of the quality of the remaining oocytes ***(Ebner et al., 2006).***

Women with normal reproductive performance were examined twice within an average of four years and assessed the AFC and various endocrine markers. It was demonstrated that serum AMH, followed by the AFC showed the most consistent correlation to the age-related decline of reproductive capacity ***(Van Rooij et al., 2005).***

Anti-Müllerian hormone (AMH) is involved in the regulation of follicular growth and development. Serum and follicular fluid AMH concentration is increased in women with polycystic ovary syndrome (PCOS), which correlates with the extent of ovarian dysfunction and clinical manifestation of the syndrome. It is unclear whether the higher AMH levels in PCOS are due to the higher number of preantral follicles or result from a specific disorder in the synthesis of AMH causing follicular arrest in PCOS ***(Pehlivanov & Orbetzova .,2011).***

AMH determination has high specificity and sensitivity as a diagnostic marker for PCOS. The AMH level can also be used to predict the effect of treatment in PCOS women, the higher values implying more difficulties in the therapeutic management of the disease ***(Pehlivanov & Orbetzova., 2011).***

The interest of serum AMH assay is also clinically important because AMH level is more sensitive, more specific and reproducible from one center to another as the follicle count. Rates above 5ng/ml or 35pmol/l may be considered as a diagnostic criterion for PCOS ***(Catteau&, Dewailly., 2011).***

AMH appears to correspond well with antral follicle counts (AFCs) and ovarian response to hyperstimulation in IVF **(*Gnoth et al., 2008 & Visser et al., 2006).***

Follicular fluid anti mullerian hormone (FF AMH) levels are greater in women with PCOS compared to normo-ovulatory women, which may suggest increased per follicle AMH secretion in PCOS ***(Fanchin et al., 2005).***

A lot of studies have confirmed the utility of early follicular phase serum AMH concentration as a predictor of the number of retrieved oocytes, which could support the concept of a direct relation between serum AMH levels and AFCs in an IVF cycle . However, data on serum or FF AMH levels in relation to oocyte quality are still contradictory ***(Arabzadeh et al., 2010, Nelson., 2009, La Marca et al.,2007,Pigny et al., 2006, Eldar-Geva et al.,2005,Fanchin et al., 2005,Peñarrubia et al.,2005 , Fanchin .,2003&Seifer et al.,2002).***

Serum basal AMH levels could be a good marker for oocyte number in both PCOS and infertile normo-ovulatory women **(*Arabzadeh et al., 2010).***

It is suggested that serum AMH level may be a predictive marker of oocyte maturation and implantation rate in normal women ***(Arabzadeh et al., 2010)***

The lack of consistency between AMH levels and qualitative IVF outcomes in PCOS patients may be influenced by the presence of differing PCOS phenotypes, with either primary ovarian dysfunction or insulin and obesity being the major contributor to reproductive dysfunction ***(Arabzadeh et al., 2010).***

Problems in inducing ovulation in women with polycystic ovary syndrome (PCOS) are well recognized. Surgical ovarian wedge resection was the first established treatment for anovulatory PCOS patients but was largely abandoned because of the risk of post-surgical adhesion formation. It was replaced by medical ovulation induction with clomiphene and gonadotrophins. However patients with PCOS treated with gonadotrophins often have a polyfollicular response and are exposed to the risks of ovarian hyperstimulation syndrome (OHSS) and multiple pregnancies. Although effective, it is an expensive, stressful and time consuming form of treatment requiring intensive monitoring ***(Berek et al., 2012).***

Treating women with clomiphene-resistant polycystic ovarian syndrome with laparoscopic ovarian diathermy results in reduced direct and indirect costs. The reduction in multiple pregnancies makes the alternative of surgery particularly attractive ***(Farquhar, 2005).***

Laparoscopic ovarian electrocautery is used as an alternative to wedge resection in patients with severe PCOS whose condition is resistant to clomiphene citrate ***(Berek et al., 2012).***

There were statistically significant differences between Day 3 FSH, inhibin B levels, ovarian volume and antral follicle count