

Ovarian reserve in infertile women with chronic pelvic inflammatory disease

ABSTRACT

Yasser Abdel Daiem¹, Mohamed Nezar¹,
Raafat Abdel Fatah¹ and Ahmed Elawa²
Department of Obstetrics & Gynecology¹
Department of Clinical Pathology²
Faculty of Medicine, Mansoura University, Egypt

Objective: To assess ovarian reserve among infertile women with chronic pelvic inflammatory disease (PID).

Materials and Methods: A prospective study comprised of 35 women (study group A) with clinically and laparoscopically diagnosed PID and 15 cases as control. All cases were assayed for day 3 serum FSH, E2 and inhibin B.

Results: In group A, day 3 FSH & E2 were significantly higher than control (11.2 ± 6 mIU/ml and 68.5 ± 21 pg/ml versus 5.3 ± 3 mIU/ml and 41.2 ± 16 pg/ml, $P < 0.05$). While serum inhibin B was significantly reduced in group A (40 ± 19 pg/ml) compared to the control (60 ± 10 pg/ml). Serum inhibin B was negatively correlated with serum FSH in patients with PID.

Conclusion: Ovarian reserve appears to be relatively diminished in women with PID. This observation denotes progressive loss of ovarian reserve in cases of PID due to poor follicular development.

Key words: Ovarian reserve, Infertility, Chronic pelvic inflammatory disease .

INTRODUCTION

Ovarian reserve means the presence of sufficient number of follicles available for recruitment and development that will yield a cohort of eggs capable to lead successfully a conception cycle¹. Screening of ovarian reserve has been studied by many fertility centers to evaluate women reproductive potentials, both in the general fertility population², and for couples undergoing in vitro fertilization "IVF"³.

PID is a common benign gynaecological disease that affects about 30% of infertile women based on clinical and laparoscopic evaluation. The association between infertility and PID is well established⁴. The development of in vitro fertilization- embryo transfer (IVF-ET) has provided a new therapeutic approach for infertility. However, the results of IVF for patients with chronic PID are controversial. Several investigators had reported that the outcome of IVF was poorer for patients with PID if associated with poor ovarian reserve^{5, 6}.

Association between PID and poor follicular development has been proposed, resulting in abnormal steroid hormone production. So, ovarian reserve assessment is essential to identify the poor responder before initiation of controlled ovarian hyperstimulation or assisted reproductive programs, to lower the risk of cancellation and improve the pregnancy rates⁷. The aim of the present study was to determine ovarian reserve in infertile women with PID and compare that to normal fertile women as a control.

MATERIAL & METHODS

This study was carried out in Departments of Obstetrics & Gynecology and Clinical Pathology, Faculty of Medicine, Mansoura University from the period of May 2007 to October 2009. Thirty five 35 patients with clinically and laparoscopically diagnosed PID (pelvic adhesion, pre-tubal adhesion, hydrosalpinx and pyosalpinx, in cases of exacerbation, edema, hyperemia and dilated blood vessels of the pelvic structures)⁴ as study group. Fifteen women with normal reproductive outcome were as a control group, ultra-sonographic assessment was done to exclude any gross pelvic lesions. An informed consent was taken from all cases in the study.

At day 3 of menstruation, 3 blood samples were withdrawn from both patients and controls (2 ml) each at 10 minutes interval to avoid fluctuation into plain tubes. An equal volumes of the separated sera were pooled and kept frozen (-20°C) till analysis of serum FSH by chemiluminescence immunoassay using (immulite analyzer Dpc Los Angeles) according to Babson⁸, serum estradiol (E2) by electrochemiluminescence immunoassay using (Roche Elecsys 1010 immunoassay analyzer) according to method of Jonsen et al.⁹ and serum inhibin B was assayed by enzyme immunoassay Kit Biosource-Belgium) according to Groom et al.¹⁰.

Correspondence
Dr. Mohamed Nezar MD,
Professor of Obstetrics & Gynecology,
Faculty of Medicine, Mansoura University,
Egypt
Tel: 002 0101593863
E mail: Yasser_2002@hotmail.com

RESULTS

Table (I) show clinical data of study and control groups as regard age, BMI (body mass index) and cycle length. Table (II) show statistical data of hormonal assay comparison between study group A and control group. Table (III) for correlation coefficient between inhibin B and FSH & E2 in PID patients and control group confirmed the previous findings.

Table I : Clinical data of study group (35 cases) and control group (15 cases)

Parameter	Group		FSH	E2
Inhibin B	Control Group	r	-0.1	0.09
		p	> 0.05	> 0.05
Inhibin B	Study Group	r	-0.3 *	0.1
		p	< 0.05	> 0.05

95% CI= Confidence interval. P value: Not significant

Table II : Comparison of hormonal assay between study group and control group

Parameter	Study group (No= 35) M±SD	Control group (No=15) M±SD	95% CI	P value
Age (y)	30 ± 2.6	31 ± 3.2	27.6 - 31.8	0.12
Body mass index BMI (Kg/m2)	21.9 ± 3.1	20.12 ± 4.2	18.3 - 22.6	0.09
Cycle length (d)	29±4	28 ± 5	25.2 - 30.1	0.13

Table III : Correlation coefficient between inhibin B and FSH & E2 in PID patients and control group

Parameter	Study group (No= 35) M±SD	Control group (No=15) M±SD	P value
Day 3 FSH (mIU/ml)	11.2 ± 6	5.3 ± 3	0.05
Day 3 E2 (pg/ml)	68.5 ± 21	41.2 ± 16	0.05
Day 3 Inhibin B (pg/ml)	40 ± 18	60 ± 10	0.05

* Inhibin B is negatively correlated with FSH level in study group

DISCUSSION

Test for ovarian reserve is an important first step for many patients who are seeking for infertility treatment. Identification of patient with diminished ovarian reserve may identify the couple with decreased chance for getting pregnancy 11. To our knowledge and computer search, no information had been reported about assessment of ovarian reserve in patients with chronic PID.

In our work, study and control groups have the same mean age and body mass index. Age has been found to be a risk factor for low ovarian response due to aging ovary progressively loses its follicular pool and pituitary reacts by increasing F.S.H. secretion which in turn leads to an increase in basal E2 resulting in diminished ovarian reserve 12, also, BMI (25-28 Kg/m2) had significant higher rate of anovulation than women with normal BMI 17. So no effect for either age or BMI on the fertility in the present study (Table 1).

Also, in the present study relatively diminished ovarian reserve was observed in PID patients (F.S.H. 11.2±6 mIU/ml, E2 68.5±21 pg/ml) as compared to control group (F.S.H. 5.3±3 mIU/ml, E2 41.2±16 pg/ml). Serum FSH is an indirect indicator of ovarian reserve and its elevation reflects a decrease in the negative feedback

of the ovary on the pituitary gonadotropin secretion 13. Basal serum FSH had been reported to be the best marker for assessing ovarian reserve and predicting the response to superovulation with a good correlation to pregnancy rate 14. Measurement of basal E2 in addition to FSH might improve the ability to predict fertility potential. Buyalos et al. reported that day 3 E2 level less than 80pg/m1 with normal FSH level in women of 38-42 years gives a good prognosis of successful treatment 15.

Inhibin B is one of the ovarian peptide (a heterodimeric glycoprotein) released by granulosa cells of the follicle early in the menstrual cycle having an inhibitory effect on the pituitary FSH release 8. So, it is considered as a direct marker of ovarian function. Low inhibin level was associated with poor response to superovulation (16) Measurement of basal inhibin B level serves as an attractive indicator of ovarian function as it probably precedes the increase in FSH precipitating its release 8.

Serum inhibin B was significantly reduced in group B PID (40 ± 18 pg/ml) compared to control (60 ± 10 pg/ml) but did not differ in group A compared to control. Inhibin B was negatively correlated with FSH level in patient with advanced PID in group B (Table 3). Defective follicular growth in PID results in reduction of inhibin B and defective steroidogenic activity. As the natural cycles in women with PID have been shown to have longer follicular phase 8. Diminished ovarian reserve in PID may appear quite logic. This may be attributed to the local destructive process that may be associated with chronic PID and/or fibrosis associated with inactive old lesions. Added to this explanation PID associated with chemical and cellular local ovarian and pelvic milieu related to increased number of prostaglandins, activated macrophages and oxygen free radicals resulting in decreased inhibin B levels leading to increasing FSH which in turn increasing basal E2 17,18,19.

In conclusion, women with chronic PID have relatively diminished ovarian reserve. So, evaluation of patients with PID for ovarian reserve via serum inhibin B, FSH and E2 is essential before initiation of infertility treatment.

REFERENCES

- Hofmann GE, Sosnowski JA, Scott RT and Thie J 1996 Efficacy of screening criteria for ovarian reserve in a tertiary infertility center population. *Fertil Steril.* 66: 49-53.
- Toner JP, Philput CB, Jones GS and Muasher SJ. 1999 Basal follicle stimulating hormone level is a better predictor of in vitro fertilization performance than age. *Fertil. Steril.* 55: 784-91.
- Ebrahim A, Rienhardt G, Morris S, Krug TF and Lombard CJ 1993 Follicle stimulating hormone levels on day 3 predict stimulation response. *J Assist Reprod* 10: 130-6.
- Ryan KJ, Berkowitz RS, Barbieri RL and Dunaif A: *Kistner's Gynaecology*. 7th ed. Mosby St. Louis 1999, 492-518.
- Ross DC. 2005 Is *Mycoplasma genitalium* a cause of pelvic inflammatory "disease"? *Infect Dis Clin N Ant* 19:407-13.
- Fenkci V, Yilmazer M. Aktepe OC. 2002 Have *Ureaplasma urealyticum* and *Mycoplasma hominis* infections any significant effect on women fertility? *Infect Med* 10:220-3.
- Barri PN, Martinez F and Coroleu 1998 Managing non-responders. *Fertility and reproductive medicine., proceeding of the 16th World Congress on Fertil Steril.* San Francisco, 13: 127-37.
- Babson AI 1991 The immulite immunoassay system. *J Clin Immunoassay* 14: 83-88.
- Johnson MR, Corter G, Grint C and Lightman SL 1993 Relationship between ovarian steroid gonadotropin and relating during the menstrual cycle. *Acta endocrinol* 12912: 121-125.
- Groome NP Ittingworth PG and O'Brien M: Measurement of dimeric inhibin B through the human menstrual cycle. *J Clin Endocrinol Metab* 1996; 81: 1401-5.
- Hansen LM, Batzer and Gutmana JN 1996 Evaluating ovarian reserve: FSH and E2 variability during day 3. *Hum. Reprod* 11(3): 486-89.
- Alrayves S, Fakh H and Khan I 1997 Effect of age and cycle responsive

ness in patients undergoing ICSI. *Fertil Steril* 68: 123-27.

13. Danforth DR, Arbogast LK, Jamil Mrouch, Kim, MK Kennard EA, Seifer DB and Frideman CI 1998 Dimeric inhibin B: A direct marker of ovarian ageing. *Fertil, Steril* 70(1): 119-123.
14. Scott RT and Hofmann GE 1995 Prognostic assessment of ovarian reserve. *Fertil Steril* 63: 1-11.
15. Buyalos RP, Daneshmand and Brzechffa PR 1997 Basal estradiol and follicle stimulating hormone predict fecundity in women of advanced reproductive age undergoing ovulation induction therapy. *Fertil. Steril* 68: 272-7.

16. Hemmings R, Falcone T, Billiar R and Tulandi T 1992 Peritoneal fluid inhibin B during the menstrual cycle. *Obstet Gynecol* 80(1): 27-9.
17. Maisey K, Nardocci G, Immarai M. 2003 Expression of pro-inflammatory, cytokines and receptors by human Fallopian tubes in organ culture following challenge with *Neisseria gonorrhoea*. *Infect Immun* 71:527-32.
18. Equils O, Lti D, Ganef M. 2006 Chlamydia heat shock protein 60 induces trophoblast apoptosis through TLR4. *J Immunol* 2006; 177: 1257-03.
19. Donatella P, Ioannis M, Giulio B and Cristina F 2006 Genital tract and infection. 2008 *European J of Obstet & Gyn Rep Biol* (140) 3-11