Can Endometriotic Cystectomy reduce Ovarian Reserve? FSH value

Can Endometriotic Cystectomy Reduce Ovarian Reserve? FSH Value

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Summary

Controversial data are reported on the consequences of laparoscopic cystectomy on ovarian response during IVF/ICSI treatment. Cycle day 2 or 3 FSH, i.e. basal (b-) FSH, represents a simple parameter in the assessment of residual ovarian function after surgery.

Thirty-two women previous submitted to surgery for endometrioma were selected and compared with 59 patients who did not. B-FSH levels and pregnancies of these groups were compared.

b-FSH in the endometrioma group was significantly higher than in those patients who had no surgery for endometriotic cyst (8.5±4.7 *vs* 6.5±3 mIU/ml respectively) ($P<0.05$). Clinical pregnancy rates were similar (9.4% vs 11.9%), although the direction was toward improved pregnancy rates in the group of patients without history of ovarian surgery.

In our experience, although the history of endometriomas seems not to affect IVF/ICSI pregnancy rate results, excision of endometriomas is associated with a reduction in ovarian reserve. Couples should be informed that lower oocytes numbers would result in reduced, but still encouraging, pregnancy rates if the age is young.

Introduction

Laparoscopic surgery is the gold standard for the treatment of ovarian endometriomas. Controversial data are reported on the consequences of laparoscopic cystectomy on ovarian response during IVF/ICSI treatment.

In vitro fertilization has provided a powerful therapeutic tool for the treatment of infertility related endometriosis after failure of surgery *(Aboulghar MA et al., 2003).* The success of IVF is critically dependent on the appropri-

ate evaluation of ovarian function to optimize controlled ovarian stimulation (COS).

A variety of tests, such as the antral follicle count, the clomiphene challenge test and measurements of basal inhibin B, have been introduced as predictive of ovarian reserve; however, cycle day 2 or 3 FSH, i.e. basal (b-)FSH, is still the most widely used parameter in the assessment of ovarian function after surgery *(Weghofer A et al., 2005)*.

The aim of our study was to evaluate whether endometrioma surgery could reduce ovarian reserve and its effect on ART outcomes. We compared women submitted to endometrioma cystectomy *vs* women with stage I-II endometriosis or with tubal factor infertility, who had never undergone ovarian surgery, in terms of b-FSH levels and pregnancy rate.

Material and Methods

Data from infertile patients submitted to ART technique, referred to the Department of Gynaecology Perinatology and Human Reproduction of the University of Florence were reviewed. Inclusion criteria were: availability of a detailed description of the surgical intervention, diagnosis of endometrioma histologically confirmed, and post surgery b-FSH levels, for the study group; age ≤40 years and presence of both ovaries at the time of ovarian stimulation for both groups.

The study group consisted of 32 women who previously underwent laparoscopic cystectomy for an ovarian endometrioma. None of them had any other known factor of infertility factor besides endometriosis. The control group included 59 infertile women with stage I-II endometriosis or with tubal factor infertility who had never undergone ovarian surgery before ART treatment.

In patients who underwent conservative ovarian surgery for endometriosis, laparoscopic cystectomy was performed. Surgical treatment consisted of drainage of ovarian cyst, cystectomy and in case of bleeding coagulation.

b-FSH was measured on cycle days 2 or 3. The IVF-ET protocol used for ovarian stimulation was the long protocol with GnRH analogue plus gonadotropins. GnRHa (Decapeptyl® 0, 1 mg, IPSEN Italy) was injected subcutaneously starting on day 21 of the cycle. After down-regulation (adequate ovarian suppression at pelvic ultrasonography and circulating E_2 below 35 pg/ml), purified urinary FSH (Gonal -F®, 75 IU, sc Serono, Italy), 3 to 4 ampoules (225-300 IU), was administered. Human chorionic gonadotropins (hCG) 10.000 IU (Gonasi® 5000 IU, two ampules; AMSA, Italy) was injected when at least two or more follicles reached a diameter 17-18 mm at transvaginal ultrasound scans.

Women submitted to cystectomy and control group were compared in terms of b-FSH levels, parameters of stimulation (days, FSH IU of gonadotropins), and pregnancy rate.

Pregnancy was defined by a positive pregnancy test and confirmed by the presence of an intrauterine gestational sac with heart activity by ultrasonography.

All analyses were performed by using Statistical Package for the Social Science (SPSS for windows, Microsoft, version 13). Data are expressed in percentages or means ± SD, as required. Statistical analysis was performed with the *t* test for parametric data or χ^2 test for categorical data.

Statistical significance was set at $P<0.05$

Results

Patient clinical characteristics at the time of surgery are presented in Table 1.

	Endometrioma previously removed	*Control group*
Patients (no.)	32	59
Mean age (yr±SD)	32.9±3.2	31.8±3.6
Duration of infertility (yr±SD)	3.9±2.5	3.5±2.7
Basal FSH (IU)	8.5±4.7*	6.5±3*
Days of stimulation	12.1±2	12.1±1.6
Total FSH(IU)	3827.4±1506*	3152.6±1366.5*
Peak E_2 levels (pg/ml)	1155.6±1040.1	1373.9±891.9
Pregnancies	3 (9.4%)	7 (11.9%)

Tab.1: *Patients characteristic. *P<0.05*

b-FSH in the endometrioma previously removed group was significantly higher than in those patients who had no surgery for endometriotic cyst (8.5±4.7 and 6.5±3 mIU/ml respectively) ($P<0.05$). Women were comparable in terms of age and duration of infertility. There were no significant differences in the length of stimulation phase. However, we noted a significant difference in the total doses of gonadotropins required in favour of patients who were never submitted to ovarian cystectomy. Clinical pregnancy rates were similar (9.4% vs 11.9%), although the tendency was toward improved pregnancy rates in the group of patients without history of ovarian surgery.

Conclusions

Several hypotheses have been proposed to clarify the association between endometriosis and infertility *(ASRM 2004)* but the precise mechanism remain unknown.

There is a controversy concerning the management of asymptomatic ovarian endometriomas in infertile women. It has been suggested that surgical

excision may increase the chance of spontaneous conception *(Adamson GD et al.,1994)*, it is unclear whether the benefits of cystectomy are produced by treatment of endometrioma or by adhesiolysis, ablation of peritoneal endometriosis, and chromoperturbation *(Garcia-Velasco JA et al., 2004)*.

Removal or ablation of endometrioma might injure normal ovarian tissue, as the lining of cyst is surrounded by follicles. It was reported that 54% of endometrioma cyst walls excised by stripping techniques also contained ovarian tissue *(Muzii L et al., 2002)*.

It seems that the damage to the ovarian tissue during surgery of endometriomas is strictly dependent on the expertise of the surgeon. Canis *et al.* suggested that in experienced hands laparoscopic ovarian cystectomy produces a reduced ovarian damage *(Canis M et al., 2001)*.

Another factor is the number of surgeries performed on the same patients before attempting IVF. Published data show that patients who had more than one attempt at surgical treatment for endometriosis has a significantly higher withdrawal rate because of poor response *(Aboulghar MA et al., 2003)*.

A recently published study shows that endometriomas do not seem to affect IVF outcomes adversely, though they come to different conclusions. Garcia-Velasco *et al.* propose that proceeding directly to COH in asymptomatic women with ovarian endometriomas might reduce the time to pregnancy, diminish patient costs and avoid potential complications of surgery *(Garcia-Velasco JA et al., 2004)*.

Still, no consistent guidelines emerge conclusively from the literature to date regarding the indication for the removal of endometriomas before performing IVF. However, laparoscopic ovarian cystectomy is recommended if an ovarian endometrioma ≥4 cm in diameter is present to confirm the diagnosis histologically; reduce the risk of infection; improve access to follicles and possibly improve ovarian response. The patients should be counseled regarding the risks of reduced ovarian surgery and the loss of the ovary *(ESHRE 2004)*.

A normal b-FSH level (≤10 mU/ml) and young chronological age (≤35 years) are generally acknowledged as the two most promising prognostic factors, reflecting ovarian function, in women initiating fertility treatment *(Weghofer A et al., 2005)*.

The data from our study showed that excision of endometriomas is associated with a reduction in ovarian reserve. Women who underwent ovarian cystectomy have b-FSH levels, as long as they are still <10.1 mU/ml, significantly higher than in those patients who had no surgery for endometriotic cyst (8.5±4.7 *vs* 6.5±3 mIU/ml respectively) ($P<0.05$), although the history of cystectomy for endometriomas does not appear to affect IVF/ICSI pregnancy-rates adversely.

B-FSH should be measured before surgery as an adjunct to antral follicle count. Couples should be informed that variations in b-FSH levels are also not predictive of clinical pregnancy rates. This finding should not be a surprise because, as long as patients are still capable of producing a minimal number of oocytes of acceptable quality, they will also produce adequate numbers of good quality embryos for a single embryo transfer.

Patients with diminished ovarian reserve could possibly benefit from treatment by flare up GnRHa protocol, large doses of gonadotropins, and reducing dose of GnRH agonist *(Aboulghar MA et al., 2003)*. Consequently, high b-FSH levels, especially in young patients, should be considered not as exclusion criteria from fertility treatment, but as guidance to individual patient counseling.

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