

THE USE OF GnRH AGONISTS IN THE TREATMENT OF ENDOMETRIOMAS WITH OR WITHOUT DRAINAGE

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SUMMARY

In order to assess the effectiveness of GnRH-agonist (GnRH-a) therapy in the treatment of endometriomas, with or without surgical intervention, 26 women with laparoscopically proven endometriomas, greater than 3 cm diameter were recruited to the study.

Fourteen women who had 19 endometriomas (5 of them were bilaterally), had drainage of endometrioma at the initial laparoscopy. After the procedure, they had ovarian suppression with GnRH-a therapy for 6 months.

The second group which consisted of 12 women, had 17 endometriomas. No surgical procedure was performed. They received only GnRH-A therapy for 6 months. At the second -look laparoscopy, the rates of decrease in ovarian AFS scores of endometriomas and complete resolution were found as 100% and 36.8% respectively. In the first group, in the second group the response was only 17.6% ($p < 0.0001$).

In this prospective study we found that drainage of the cyst (surgical therapy) combined with the postoperative GnRH-a suppression is a better treatment modality for endometriomas. Than the use of GnRH-a (medical therapy) alone.

Key Words: GnRH - agonist, endometriosis, endometrioma, laparoscopic surgery.

INTRODUCTION

After the report of Meldrum (1), the usage of GnRH - agonists (GnRH-a) has revealed a marked improvement in the medical treatment of endometriosis (1-7). Indeed GnRH-a therapy can reduce the size and score of endometriosis (1-7), but complete resolution of an endometrioma larger than 1 cm diameter is not expected (3,5-7). Previously, laparotomy was used for surgical approaches to endometriomas; now gynecologists have started using operative laparoscopy alone (8-11) or combined with medical ovarian suppression (3, 12).

In this study our aim was to compare the effectiveness of GnRH-a in the treatment of endometriomas, with or without surgical intervention.

MATERIALS AND METHODS

Twenty - six patients who were found to have ovarian endometrioma unilaterally or bilaterally more than 3 cm in diameter, were included in this study. Patients were randomly allocated into 2 groups. The first group, which consisted of 14 patients, had 19 endometriomas (5 patients had bilateral endometriomas). This group had a drainage of endometrioma plus adhesiolysis at the initial laparoscopy. They were opened with laparoscopic scissors at the most dependent part, to facilitate proper drainage. Immediate suction was routinely used to prevent spillage of the chocolate -like material outside the true pelvis. The cavities of endometriomas were irrigated with Ringer's lactate solution. All incisions were left open without suturing. At the completion of the procedure, 300 ml Ringer's lactate was left in the pelvic cavity to serve as hydroflotation medium (13). After the operative laparoscopy, they had ovarian suppression with GnRH-a for 6 months. At the end of this medical therapy, they underwent a second - look laparoscopy to assess the results. If needed, further surgery (elimination of inner lining) was performed.

The second group which consisted of 12 patients, had 17 endometriomas (5 patients had bilateral endometriomas). No surgical procedure was undertaken to endometriomas at the initial laparoscopy. This group received only GnRH-a therapy for 6 months after diagnostic laparoscopy, then a second - look laparoscopy was performed to assess the effectiveness of GnRH-a therapy. Drainage plus coagulation of the inner lining was performed during this procedure.

Both of the groups were treated with a delayed release formulation of D-Tryp 6-LHRH (Decapeptyl 3.75 mg Ferring - Switzerland). Injections were administered intramuscularly at four week intervals for a period of 6 months. The therapy was started on

the 21st day of the cycle. By the end of the first therapy serum estradiol fell significantly to the levels within the postmenopausal range and remained throughout the continued treatment.

At the laparoscopic view, the severity of disease was staged according to the revised AFS classification scheme (14). According to the diameter of endometrioma, the ovarian endometriosis scores were defined as 4, 16 or 20 points for each of the endometriomas. The response of the ovarian endometrioma to the treatment was assessed by using the changes in AFS ovarian (endometrioma) scores. The disappearance of endometrioma was accepted as complete cure and scored -0- points.

The mean age, stage, ovarian endometriosis score, AFS score, implant score and adhesion score of the two groups are shown in table I. There is no significant difference between two groups ($p>0.05$) except duration of infertility ($p<0.005$).

RESULTS

In the first group, which had drainage at the first laparoscopy and received the postoperative GnRH-a therapy, the scores of endometriomas were decreased in 12 endometriomas (63.15%). Complete resolution was found in 7 endometriomas (36.84%) (Table II). There was no increase in the scores of endometriomas. Therefore 12 endometriomas needed further surgical intervention at the second - look laparoscopy. As shown in table I, there was

statistically significant decrease in the mean values of rAFS, peritoneal implant, and adhesion scores.

In the second group, which received GnRH-a therapy alone, we found 14 unchanged endometriomas (82%). In 3 endometriomas the ovarian AFS scores were decreased (17.64%) (Table II). The mean AFS scores of endometriomas were not changed significantly ($p>0.05$) (Table I). The reason for this may be our wrong time for the second look laparoscopy. Which was performed after the first menstruation following the end of GnRH-a treatment. Therefore we possibly have allowed the haemorrhage into the cavity of endometrioma. This could have increased AFS ovarian scores again. In another view of this study, as a proof of the effectiveness of GnRH-a therapy, we found a decrease in the scores of peritoneal implants reflecting the ovarian suppression ($p<0.001$). Conflicting with the classical information, we found a decrease in adhesion score ($p<0.02$) (Table I). This may be due to intra and inter observer error or due to decrease in pelvic vascularity after GnRH agonist treatment.

Seven patients in the first group who were cured completely were followed for 12 months and 3 pregnancies occurred in this group (1 spontaneous, 2 with clomiphene). of the remaining 4 patients 3 developed recurrence of the disease with endometrioma formation. Patients other than these 7 patients who were cured completely were not included in the results of this study because they received additional surgical intervention for their endometriomas at the second - look laparoscopy.

Table I: Changes in endometriosis parameters

	Group I		Group II	
	first look	second look	first look	second look
Age	27.92 ± 4.66		31.33 ± 6.09	
Duration of infertility	4.83 ± 2.65		8.36 ± 3.13	
Stage	3.64 ± 0.49	2.71 ± 0.82	3.50 ± 0.52	3.41 ± 0.51
Scores				
Endometrioma	19.57 ± 1.26 *	7.78 ± 7.36	18.58 ± 1.97 **	17.88 ± 2.05
Implant	3.00 ± 1.70 ***	1.14 ± 3.2	4.33 ± 1.66 ***	1.14 ± 1.58
Adhesion	14.42 ± 12.35 *	10.30 ± 8.97	13.16 ± 12.60 ****	12.33 ± 12.35
Total	44.28 ± 19.73 ***	18.85 ± 13.55	43.83 ± 18.24 *	38.83 ± 17.42

Values are means ± SD of scores according to rAFS classification

Group I drainage and GnRH-a, Group II GnRH-a only

(* $p<0.01$), (** $p>0.05$), (***) $p<0.001$), (**** $p<0.02$)

Table II: Comparison of the results of treatment in two groups.

	group I (drainage first)	group II (analog first)
unchanged	0	14 (82.3%)
decreased	12 (63.2%)	3(17.6%)
complete resolution	7 (36.8%)	0
total	19	17
chi-square: 26.3704, p<0.0001 (1.878 E-06)		

DISCUSSION

In this prospective study we found that drainage of the cyst (surgical therapy) combined with the postoperative GnRH - suppression is a better treatment modality for endometriomas (medical therapy) alone. Results of the second group which received GnRH-a therapy alone, showed that only 3 of the 17 endometriomas (17.64%) decreased in their ovarian AFS scores by shrinkage. These results are worse than the ones in the literature. According to the literature GnRH-a therapy cannot cure an endometrioma greater than 1 cm, completely (3,5 - 7). Donnez found that the size of ovarian endometriosis was decreased (more than >25%) in 73% of cases after buserelin therapy (3). Buserelin was unable to completely suppress endometriotic cells, because the ectopic foci are not governed by the normal control mechanisms that govern the uterine endometrial glands and stroma (15). Therefore all authors suggested the necessity of surgical approach to endometriomas (7, 11, 14 - 17).

In the other study group, we used drainage in addition to GnRH-a therapy. However, most recent reports about the laparoscopic management of endometriomas have describe the laparoscopic stripping of ovarian endometrioma (16, 17). Other methods, such as drainage, drainage plus vaporization of lining an drainage plus coagulation of lining, have been used for a long time. We chose the drainage method since of excision of endometriomas brings an additional risk of postoperative adhesions. Fayez (18) compared different laparoscopic methods for the treatment of endometriomas, and did not suggest excision of endometriomas because the least adhesions were found in the drainage group with or without elimination of the inner lining. In addition to this we did not want any other factor affecting the endometriotic cells of the inner lining of endometrioma.

By using drainage plus postoperative GnRH-a therapy in spite of decrease in ovarian AFS scores (100%) for all endometriomas (Table II) we found 12 of, 19 endometriomas had persistence (63.15%). Wood found that endometriomas persisted or recurred in 13.4% of cases in his study group which were treated either by surgical excision at

laparotomy, or drainage by laparoscopy plus removal through laparoscope or electrocautery, or CO2 laser without any medical therapy (19).

Fayez found persisted endometriomas in 21% of the drainage plus postoperative danazol therapy group (18). The reason for our high persistence rate, might be due to the possibility of re-closing of drainage incision and the possibility of hemorrhage into the cavity due to the menstruation that could be allowed by the first GnRH-a injection.

In another study of Donnez, it was shown that drainage alone is ineffective since the ovarian cyst after drainage shows quick recurrence. Drainage followed by GnRH-a was effective in the reduction of cyst size (20).

As a conclusion, this paper reports a comparison of the effect of GnRH agonist alone vs. surgical drainage plus GnRH agonist in the treatment of endometriomas. It was shown that the drainage of endometriomas led to a better suppression in the endometrioma size and resolution compared with the agonist alone. Moreover, drainage is an easier procedure which does not require additional surgical experience and can be applied to all of the cases.

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