Int J Clin Exp Med 2015;8(11):21703-21706
www.ijcem.com /ISSN:1940-5901/IJCEM0014413

Original Article

Clinical analyses of endometriosis after conservative surgery

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Received August 10, 2015; Accepted November 7, 2015; Epub November 15, 2015; Published November 30, 2015

Abstract: Objective: To assess the remission rate and outcome of pregnancy of patients who had moderate and severe ovarian endometriosis after conservative surgery. We also wished to analyze the associated factors of recurrence. Methods: Weconducted retrospective analyses of 199 cases with stage II-IV ovarian endometriosis who had preserved fertility under laparoscopic surgical treatment. Postoperatively, the 199 patients were divided into three groups: 43 cases underwent surgical treatment alone (group A); 47 were given a gonadotropin-releasing hormone agonist (GnRH-α) (group B), and 109 were given mifepristone (group C). Ten cases in group A were infertile, 26 cases in group B, and 38 cases in group C. All patients were followed up for 3 years. This study was approved by the Ethics Committee of Yangpu District Central Hospital. Results: In groups A, B and C, the remission rate was 58.13%, 70.21% and 60.55% and the difference not significant (P=0.384); Recurrence rates were 27.90%, 12.76% and 24.77%, and the difference between them significant (P<0.05). The recurrence rate in group B was the lowest. The natural pregnancy rate after surgery in the three study groups (untreated, GnRH-α and mifepristone) was 30%, 34.61% and 28.94% but this difference was not significant. Conclusion: Surgery can improve the symptom remission rate and fertility of patients. Postoperative drug therapy does not improve the chance of pregnancy.

Keywords: Ovarian endometriosis, pregnancy, gonadotropin-releasing hormone agonist

Introduction

Endometriosis is a relatively common disease in women of reproductive age, and its incidence has been increasing in recent years. About 80% of patients with pelvic pain, and 30%-40% of patients with infertility. Medication and surgery have been used to treat endometriosis, but do not result in cure or eliminate symptoms for a long time. The prevalence of recurrence at 5 years is 36-57% [1]. About 50% of patients who undergo surgery to cure it fail to conceive. Most patients with ovarian endometriosis are young, so we often carry out conservative surgery to preserve fertility. Hence, conservative surgery has become the first-line treatment of endometriosis. Whether pharmacological treatment can improve the prevalence of remission after surgery, reduce the prevalence of recurrence, or increase the chance of conception is not known.

Methods and materials

Clinical data

Surgical exploration and postoperative pathological examination confirmed the diagnosis of ovarian endometriosis. Dysfunction of the liver and kidney, as well as hormone-associated disorders, was excluded. Exclude the factor of male infertility. Patients were aged 21-38 (mean, 31±5.76) years.

A total of 199 cases were divided into three groups according to postoperative adjuvant-drug treatment: 43 cases underwent surgical treatment alone (group A); 47 cases underwent treatment with a gonadotropin-releasing hormone agonist (GnRH-α) after surgery (group B); 109 cases underwent treatment with mifepristone after surgery (group C). Ten cases in group A were infertile, 26 cases in group B, and 38 cases in group C. All three groups were compa-

Table 1. Treatment of three patient groups (A, B and C)

	Drug treatment (%)			Chi square	*P* value
	A	B	C		
Remission	58.13% (25/43)	70.27% (26/47)	60.50% (72/109)	1.916	0.384
Recurrence	27.90% (18/28)	12.76% (6/47)	24.77% (27/109)	6.058	0.048

Group A: The cases underwent surgical treatment alone; Group B: The cases were given a gonadotropin-releasing hormone agonist (GnRH-α); Group C: The cases were given mifepristone.

Table 2. Pregnancy in untreated and treatment groups

Group	Total number of cases	Sterile	Pregnant at 3 years
Untreated	43	10	30% (3/10)
GnRH-α	47	26	34.61% (9/26)
Mifepristone	109	38	28.94% (11/38)

Table 3. Recurrence rate in different age groups

Group (years)	Total number of cases	Recurrence cases	Recurrence rate
<25	14	0	0%
25-29	21	4	19.04%
30-34	101	25	24.75%
34-38	63	16	25.39%

Table 4. Recurrence rate and relationship with clinical stage

Group	Total number of cases	Recurrence cases	Recurrence rate
II	71	8	11.26%
III	86	24	27.90%
IV	28	12	42.85%

II-IV: stage II-IV ovarian endometriosis.

rable with respect to age, serum level of cancer antigen CA125 and Retrospective American Fertility Society (rAFS) score. According to amendments made by the AFS in 1985, 78 cases were stage II, 93 cases were stage III, and 28 cases were stage IV.

Treatment methods

All 199 cases underwent routine laboratory tests and tests for biological markers (CA125, CA199, alpha-fetoprotein (AFP), carcinoembryonic antigen (CEA). Ultrasound and/or CT examination of the pelvis was also carried out. Liver function and kidney function were in the normal range. Conservative surgical treatment included: removal of ovarian endometrial cysts by laparoscopic means; adhesiolysis of pelvic adhesions; electric coagulation of ectopic lesions; and hydrotubation.

Evaluation of infertility

We measured the levels of the sex hormones. B-ultrasound monitoring of ovulation was carried out. Upon confirmation of pelvic disease antibiotics were given for 3 days after surgery. Group-B patients on postoperative day (POD)7 were administered a GnRH-α (LeiDeZhen, 3.6 mg, i.m.) once per 28 days.Group-C patients were given mifepristone (12.5 mg, p.o.) on POD7 once-daily for 3-6 months.

Follow-up

All patients were followed up 1 month after surgery, then at 3 months, and then at 1 year. Follow-up comprised: pelvic examination, postoperative medication, pregnancy/birth outcomes (Refers to Natural pregnancy), B-ultrasound of the pelvis, and measurement of serum levels of CA125. The final follow-up was 3 years after surgery.

Criteria for evaluation of the prognosis

We used a three-point scale for the evaluation: 1. Remission (no symptoms, no positive signs, and auxiliary examination does not show abnormalities). 2. Improvement (symptoms remain, no positive signs, and auxiliary examination does not show abnormalities). 3. Recurrence. The recurrence diagnostic criteria for: (1) Was symptom relapse or exacerbation after remission for 3 months. (2) Positive signs appeared again in the pelvis. (3) B-type ultrasound shows new lesions.

Statistical analyses

SPSS v12.0 (SPSS, Chicago, IL, USA) was used for all analyses. Numerical data were evaluated

Table 5. Recurrence rate and the relationship between postoperative adjuvants

Postoperative Medication	Total number of cases	Recurrence cases	Recurrence rate	Time interval of recurrence
Untreated	43	12	27.90%	7±3
GnRH	47	6	12.76%	14±3
Mifepristone	109	27	24.77%	13±4

using the chi-square test. The Student's *t*-test was used to compare measurement data.

Results

The three groups of patients had a total remission rate of 61.81%. The difference in the remission rate was not significant. The three groups of patients had a total recurrence rate of 25.63%, and the difference was significant (χ^2=6.058. P=0.048) (**Table 1**).

Some patients are fertile but at follow-up are unmarried with no children. We analyzed women who became pregnant but who had been diagnosed preoperatively as being infertile. In untreated, GnRH-α and mifepristone groups, the proportion of patients that were pregnant at 3 years after surgery was 30% (3/10), 35% (9/26) and 29% (11/38) and the difference between groups was not significant, or between the untreated group and the combined treatment group (**Table 2**).

Age was no associated with the recurrence rate (P=0.188), but only in those aged <25 years (P=000); no significant differences between the other three age groups were observed (**Table 3**).

We found that the recurrence rate increased with clinical stage, χ^2=12.478, P=0.000 (**Table 4**).

The recurrence rate in the untreated, GnRH-α group, and mifepristone was 27.90% (12/43), 12.76% (6/47), and 24.77% (27/109). With mifepristone and GnRH-α, the recurrence intervals were (13±4) months and (14±3) months. The interval of recurrence in the untreated group was (7±3) months, and the difference between three groups was significant, variance analysis F=32.57, P=0.000 (**Table 5**).

Discussion

Endometriosis is an estrogen-dependent disease. Laparoscopy has become first-line treatment of endometriosis [2]. Laparoscopic procedures can remove small lesions and separate pelvic adhesions to restore the normal anatomy of the pelvic cavity [3]. The overall recurrence rate in the present study of 199 cases with ovarian endometriosis was 25.63%, and was consistent with the literature [4].

The present study showed that the recurrence rate of ovarian endometriosis increased with increasing rAFS score. The recurrence rate could have been high because deep lesions and atypical lesions were not removed by surgery. This research shows that: the more r-AFS stage, the more endometriosis recurrence rate.

The primary treatment of ovarian endometriosis is surgery. However, radical surgery should not be undertaken in women of reproductive age. We can preserve ovarian tissue by surgical removal of cells. Ectopic lesions can be identified and removed, though this can be difficult in the retroperitoneum. Unfortunately, the remnants of ectopic lesions can survive and be maintained by hormones.

Auxiliary therapy after surgery to eliminate or suppress residual lesions, prevent iatrogenic transmission, and prevent recurrence is very important. The recurrence rate in the treatment group was lower than that in the untreated group, and the time interval longer. Murphy [5] and others authors showed no direct inhibitory influence on the growth of human endometrial tissue through mifepristone. Han [6] believes that taking mifepristone suppresses concentrations of sex hormones, prompting residual small focal atrophy that is undetectable by the naked eye. The effects of different types of GnRH-α are the same as GnRH in the body. The mechanism of action of GnRH-α is mainly through inhibition of synthetic estrogen. That is, to cut-off stimulation of the hypothalamus-pituitary-ovarian axis and bleeding cycle of ectopic endometrial tissue [7, 8]. Yuka [9] analyzed randomized controlled trials of postoperative drug treatment. They found that postoperative recurrence time could be delayed by using GnRH, with the mean time of postoperative recurrence in the GnRH group being longer by 12 months. Hence, patients with ovarian endometriosis underwent conservative surgery combined with GnRH treatment.

Improving the fertility of patients with ovarian endometriosis is difficult. It has been reported that GnRH-α can reduce the extent of endometriosis of infertile patients due to increased expression of nitric oxide. These actions lead to increased receptivity for the embryo in the uterus and endometrium, thereby improving fertility. However, we found that surgery combined with drug therapy had little effect on pregnancy. The difference was not statistically significant compared with the cumulative pregnancy rate in the medication group and no-medication group ($P>0.05$) [10].

Our data suggested a different type of disease to be present in younger patients. Their symptoms were not severe and they showed good response to treatment. Hence, the recurrence rate was low. This study showed that the recurrence rate of <25 years old was lower. So young endometriosis patients should be active treatment.

Disclosure of conflict of interest

None.

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