

Results of Surgical Treatment of Ovarian Endometrioma

Munkhbayar Choijiljav^{1,2}, Munkhbayarlakh Sonomjamts³, Yanjinsuren Darmaa¹

¹Department of Obstetrics and Gynecology, School of Medicine, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia; ²Department of Gynecology, National Center for Maternal and Child Health, Ulaanbaatar, Mongolia; ³Department of Pulmonology and Allergology, School of Medicine, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia

Submitted: August 14, 2021

Revised: August 21, 2021

Accepted: September 17, 2021

Corresponding Author

Munkhbayar Choijiljav, MD
Department of Obstetrics and
Gynecology, School of Medicine,
Mongolian National University
of Medical Sciences, Ulaanbaatar
14210, Mongolia
Tel: +976-9902-0032
E-mail: doc.munkhuu@gmail.com

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/bync/4.0/>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited. Copyright© 2021 Mongolian National University of Medical Sciences

Objective: Diagnosing and treating ovarian endometrioma at the clinical stage and making a comparative study of the treatment results. **Methods:** In 2018-2019, 63 women aged 20-45 years diagnosed with ovarian endometriosis in the gynecology department of the Obstetrics and Gynecology Hospital of the National Center for Maternal and Child Health were included in the study. A hospital-based clinical prospective case-control study was used. **Results:** The first group of women received dienogest after surgery for 3 months during which pain during menstruation ($p < 0.001$), pain during intercourse ($p < 0.001$), and chronic pelvic pain ($p < 0.016$) was assessed. The second group of women received dienogest before surgery for 3 months during which pain during menstruation ($p < 0.001$), pain during intercourse ($p < 0.001$), and chronic pelvic pain ($p < 0.001$) was assessed. In this comparative surgical study, in the first group 14 (43.8) had trouble having the endometrioma removed, and in the second group, 23 (74.2%) had no trouble having the endometrioma removed. **Conclusion:** The use of synthetic progestin before surgical removal of moderate to severe endometriosis with laparoscopy decreases the blood loss during surgery ($p < 0.021$) and facilitate the removal of the endometrium from the ovary.

Keywords: Dienogest, Laparoscopy, Remove Endometrioma

Introduction

Endometriosis is a common inflammatory condition affecting women, mostly during their reproductive years [1]. It has been defined as the presence of endometrial tissues such as glands and stroma outside the womb and causes pain in the pelvic area and infertility [1-4]. Endometriosis can be asymptomatic, but associated symptoms include abdominal pain, painful periods,

dyspareunia, dyschezia, and infertility. As such, endometriosis not only has a significant impact on the lives of millions of women and their families, but also is associated with an enormous socioeconomic burden [2, 3]. Nowadays, approximately 1 in 10 reproductive-aged individuals (estimated 176 million women worldwide) are affected with endometriosis, among whom 44% are diagnosed with ovarian endometriosis [5]. In Mongolia, 56% (28) of patients who underwent laparoscopic ovarian cystectomy

were diagnosed with endometriosis [6].

The diagnosis of the endometriosis is quite complicated due to its variable presentations as well as the symptoms which are not unique thus leading to misdiagnosis with other conditions including adenomyosis. The gold standard for the diagnosis is a laparoscopy, however this technique is still new in Mongolia compared with developed countries. It is generally accepted that endometriosis presents in three different entities, which are frequently found together: peritoneal lesions, deep endometriosis, and ovarian endometriotic cysts (endometriomas) [4]. Endometriomas are probably the most commonly diagnosed form of endometriosis because of the relative ease and accuracy of ultrasound diagnosis. Although their exact prevalence and incidence are not known, they have been reported in 17–44% of women with endometriosis [5]. The presence of ovarian endometriomas has been reported as being a marker for deep endometriosis and multifocal deep vaginal, intestinal and ureteric lesions [6].

The pathogenesis of endometriomas remains contentious, with a variety of theories proffered, including: invagination and subsequent collection of menstrual debris from endometriotic implants which are located on the ovarian surface and adherent peritoneum, colonization of functional ovarian cysts by endometriotic cells, and coelomic metaplasia of invaginated epithelial inclusions [7]. Endometriomas frequently present a clinical dilemma as to whether and how to treat them when found during imaging. Overall, currently available treatment options for all types of endometrioses include oestrogen suppression, progestins, surgery, or a combination of these [8]. Surgical treatment is the mainstay of endometrioma management when treatment is required and is aimed at the elimination of endometriotic tissue, provision for sufficient tissue for histological assessment, and preservation of maximum normal ovarian tissue where fertility is desired and/or risk of menopause is to be avoided. It has been shown that surgical treatment of endometriotic cysts is associated with the unintentional removal or destruction of ovarian follicles, which can be objectified by a measurable post-operative reduction in serum antimüllerian hormone (AMH) levels or antral follicle count (AFC) on ultrasound [9]. Ozaki et al. compared preoperative administration of dienogest and gonadotropin-releasing hormone agonist (GnRH) on the improvement of surgical outcomes in patients who underwent laparoscopic cystectomy and showed that dienogest

makes a significant improvement on endometriosis compared to the administration of GnRH agonist alone [10]. Yap et al. has reported, on the other hand, that there was no significant difference between pre-surgery hormonal suppression and post-surgery hormonal suppression for the outcome of pain [11].

Currently, depending on the pathological state, the treatment for endometriosis is based on laparoscopic surgery, medications such as non-steroidal anti-inflammatory drugs (ibuprofen, naproxen), gonadotropin releasing hormone analogs, and antagonists (leuprolide, goserelin) [7, 8]. However, there is still insufficient evidence to conclude that pre and post-surgical treatments with medicine as well as hormonal suppression are beneficial for surgical outcomes. Thus, in the present study, we aimed to diagnose and treat ovarian endometrioma at the clinical stage and make a comparative study of the treatment results.

Materials and Methods

Study design and sampling

This was a hospital-based pre-post study of 129 women, ages 20 - 46, diagnosed with ovarian endometriosis at the National Center for Maternal and Child Health in Ulaanbaatar, Mongolia, between 2018 and 2019. All women were seen by obstetricians or gynecologists, and 117 of them completed a specific questionnaire. Before the treatment, AMH and CA - 125 were measured in 5 ml of blood taken the 2nd and 3rd day of their menstrual cycle using a Cobas E411 Analyzer immunoassay apparatus (Hitachi, Japan). CA - 125 measurements between 0 - 35 unit/ml and AMH measurements between 2.0 - 12.0 ng/ml were the normal ranges. Transvaginal ultrasonography (NeuEcho-10, 7.5 MHz Neusoft Medical Systems, China) was performed between the 3rd and 5th day of the menstrual cycle. The International Federation of Gynecology and Obstetrics (FIGO) 5B and 5M international classification was used to determine the endometrioma's stage [10] and include 4 stages: minimal (1 - 5 score) and mild (6 - 15 score), moderate (16 - 40), and severe (> 40).

The decision regarding the type of treatment was based on the physicians' recommendation. Patients with minimal and mild endometriosis were typically treated with synthetic progesterone (dienogest) or a nonsteroidal anti-inflammatory drug (ibuprofen). When prescribed, dienogest 2 mg orally daily was started after 3

- 5 days of menses and was taken for 28 days, and ibuprofen 400 mg orally every 12 hours was started on day 1 of menses and was taken for 5 days. Patients with minimal and mild stages who failed 3 ~ 6 months of nonoperative treatment and those with moderate and severe endometriosis underwent laparoscopic excision. The patients were stratified into the following groups: Group I received only oral dienogest, Group II received only oral ibuprofen, Group III received dienogest for 3 months after surgery, and Group IV received dienogest for 2 months before surgery.

After obtaining informed consent, laparoscopy was performed. All laparoscopic cystectomy operations were performed under the general anesthesia between the 5th to 9th day of the patient's menstrual cycle using routine laparoscopic equipment (Olympus, Japan). The endometriosis stage was defined according to the American Society of Reproductive Medicine's guidelines, using 2 extra trocars [11].

Mild endometriosis was removed by electrocoagulation. Endometriomas larger than 4 cm were carefully removed from the cyst wall. Hemostasis was achieved with atraumatic forceps and bipolar forceps electrocoagulation. All endometrioma removed during the surgery were sent for pathologic analysis.

Inclusion criteria

Women were included in the study if they were diagnosed with endometriosis as proven by signs, symptoms, examination, lab finding, and ultrasonography and provided informed consent.

Exclusion criteria

Women were excluded from the study if they 1) chose not to obtain the labs or ultrasound exam, 2) had any cancer signs detected by the international classification [12], 3) had a drug allergy, 4) had a contraindication to receiving luteinizing hormone, 5) had an endocrinology disorder, 6) had a history of chemo and radiation therapy, 7) had acute inflammation in pelvic cavity, 8) had ovarian cyst which is not caused by endometriosis, and 9) infertility not caused by endometriosis.

Statistical analysis

Chi-square and Fisher's exact tests were used to compare frequencies between two different treatment groups. The paired t-test was used to compare the variables between before and after treatment. Multiple logistic regression was performed to

identify the risk factors for abnormal anti-müllerian hormone levels. Statistical analysis were performed using Excel and SPSS-20.0 version. A p-value of < 0.05 was considered statistically significant.

Ethical statement

The study protocol was approved by the Research Ethics Committee of Mongolian National University of Medical Sciences on the 23rd of February 2018 (No.2018/3-06). All participants were informed about the study and provided written informed consent.

Results

In the present study, a total of 66 women were diagnosed with endometriosis by medical examination and ultrasonography, however, three participants were eliminated from the study due to the misdiagnosis. The mean age of the study group was 31.6 ± 6.8 (minimum 20 years and maximum 45 years). The majority was 25-29 years. The mean height of the participants in the present study was 159.3 ± 18.6 cm with mean weight of 60.6 ± 9.8 kg.

The mean age at menarche was 14.1 ± 1.2 (86.4% at 10-15 years and 13.6% after 16 years of age). Also, 86.4% of the participants defined their menstrual cycle as normal or regular, while 13.6% had irregular menstruation.

The most common symptoms of the participants were pelvic pain during menstruation (98.4%), pelvic pain during sexual intercourse (82.5%), abdominal pain continuing more than 6 months (90.6%), urinary symptoms (36.7%), pain during constipation (58.9%), other abdominal symptoms (95.3%), and most of the participants had 3-4 of the above-mentioned symptoms. Of the 6 endometriosis related symptoms, according to the self-reports of the participants, 31.3% experienced severe pain during the menstruation, 34% reported severe pain during sexual intercourse or constipation, 65% had primary infertility, and 31.7% had secondary infertility. We have used American Society for Reproductive Medicine revised classification system for endometriosis in order to evaluate endometriosis by laparoscopy. Furthermore, 79.3% of the participants had mild adhesions while 50.7% had severe tissue adhesions, and 77.7% had abdominal liquid formation during laparoscopy. The location of the endometrioma was: 19% in left ovary, 23.8% in right

Table 1. Endometrioma and laparoscopy.

Variables	Mean ± SD
Age, years	31.5 ± 8.9
Length of endometrioma	
Right ovary (cm)	3.2 ± 2.27
Left ovary (cm)	3.0 ± 2.6
Location of endometrioma	
N (%)	
In left ovary	12 (19.4)
In right ovary	15 (23.8)
Bilateral	32 (50.6)
Adhesion for both ovaries	4 (6.3)
Number of endometrioma	1-2
Location of endometrioma	
Upper	10 (15.8)
Lower	45 (71.4)
Upper and lower	8 (12.7)

Table 2. Before laparoscopy surgery with and without Progesterin pills.

Location	Before surgery Without progestin (Group I) (n = 32)	Before surgery With progestin (Group II) (n = 32)	Total (n = 64)	p-value
	N (%)	N (%)		
Stripping adhesion in left ovary	10 (15.9)	5 (16.1)	12 (19.0)	0.042
Stripping adhesion in right ovary	5 (7.9)	7 (22.5)	15 (23.8)	
Stripping adhesion in both ovaries	17 (27.0)	19 (61.4)	36 (57.1)	

Table 3. Laparoscopic ovarian cystectomy.

Variables	Before Surgery		p-value
	Group I (n = 32)	Group II (n = 32)	
	Without Progesterone	With Progesterone	
Bleeding			
N (%)			
51-100 ml	15 (46.8)	26 (83.8)	
≥ 101 ml	17 (53.2)	6 (16.2)	0.002
Number of remained antral follicles			
≤ 2.0	17 (53.2)	9 (25.8)	0.034
> 2.0	15 (46.8)	23 (74.2)	
Endometrioma with blood clot			
Yes	24 (78.0)	18 (54.8)	0.045
No	8 (2.5)	14 (45.1)	
Stripping condition			
Mild	9 (28.1)	23 (74.2)	*0.071
Moderate	23 (71.9)	9 (15.8)	

*Fisher's exact test

Table 4. The results of laparoscopic surgery.

Variables	Group I (n = 32)	Group II (n = 32)	*p-value
	Dienogest before surgery Mean ± SD	Dienogest after surgery Mean ± SD	
Right ovary			
Mean length	2.54 ± 1.2	2.48 ± 0.6	0.010
Left ovary			
Mean length	2.81 ± 1.2	2.65 ± 1.1	0.033

*Paired t-test.

ovary, 50.7% in bilateral ovaries, and 6.3% with adhesion in both ovaries. 71.4% of all the cases of endometrioma was located in the lower part of the ovaria (Table 1).

Surgical outcome of moderate and severe forms of ovarian endometrioma

A study group of 63 patients who underwent surgery were divided into 2 groups. Group I of 32 participants who had a 12-week synthetic progesterone treatment after endometrioma surgery, while Group II, where 31 women enrolled, the same synthetic progesterone was administered during 12 weeks before the surgery. In a total of 36 cases, adhesion was stripped from both ovaries, while in 15 cases from the right ovary and 12 cases from the left ovary (Table 2). The mean size of the endometrioma in the right ovary was 3.2 ± 2.27 cm, in left ovary was 3.0 ± 2.6 cm, and the average endometrioma size was 3.1 ± 2.7 cm with is the average of the 2 numbers.

Next, we compared the progesterone treatment group before the surgery with the group who were administered progesterone after the surgery (Table 3). Bleeding of less than 100 ml during the surgery in Group II (83.8%) was significantly lower than Group I. The number of remaining antral follicles more than 2 was also significantly higher in Group II. Stripping condition during the surgery was milder (74.2%) in the Group II, while the condition was moderate (43.8%) in Group I participants.

Discussion

Endometriosis is a progressive, chronic condition. The exact pathogenesis and treatment are still questionable due to the variable pathogenesis, population age, risk of cancer, the ovarian condition and treatment before the surgery, and adhesion side and size. There are several surgical techniques to

remove endometriosis. Laparoscopic surgery involves removing endometriosis, washing tissues, and washing bloody fluid. Furthermore, laser ablation and excision is a significantly precise technique that can be used to access difficult areas. There is also electrocoagulation technique, where electrical heat can be used to destroy endometriosis and control bleeding [7, 8]. In addition, ultrasound-guided aspiration of endometriomas has been reported to have the risk of cyst recurrence (90% in a month), however this technique can be used on patients for relief of symptoms as well as preserve the fertility of the patients [12].

In the present study, we have compared the surgical outcome of 2 groups of patients who were diagnosed as moderate or severe endometriosis. Group I was administered synthetic progesterone during 12 weeks after surgery, while Group II had 12-week synthetic progesterone treatment before endometrioma surgery. It was revealed in our results that Group II had less bleeding during the surgery compared to that in Group I, which in turn indicates that this method is useful to shorten the surgical operation. Moreover, we did not observed recurrence of the endometriosis in Group II, and after-surgical symptoms were significantly reduced in this group. This is probably a result of the long-term administration of synthetic progesterone, which decreases the activity of the endometriosis and blood circulation.

Numerous studies have reported the treatment of endometriosis involving medication or surgery [12-14]. The use of hormone therapy for endometriosis is important to decrease the recurrence, relieve the pelvic pain as well as to increase the natural pregnancy rate [14-19]. Usually, the endometrioma wall is tightly adherent to the ovarian tissue, thus making it extremely difficult to surgically remove endometriotic areas from the ovarian tissue. In most cases, remaining antral follicles after stripping could be the reason for the cyst recurrence. Moreover, heating the tissue in order to stop bleeding during the surgery

can damage the ovarian tissue and create another adhesion site. There are several reports demonstrated ovarian deficiency after stripping endometrioma from both ovaries [20]. In the present study, we have confirmed 2 cases of endometrioma recurrence in Group I patients who were administered progesterone after surgery, while there was not any cyst recurrence in the patients who had the same progesterone treatment before the surgery. Furthermore, six-month and nine-month follow up of excision of endometriosis revealed that the rate of natural pregnancy was higher (8 cases) in Group II compared with Group I (5 cases). This is consistent with the results of Moore et al. [19-23]. Cochrane reviews by Brown et al. also indicated that there is no evidence of benefit with hormone treatment after endometrioma surgery [18-20].

The present study is the first time we report endometrioma excision surgery based on common clinical diagnosis, ultrasound imaging, and laparoscopy in Mongolia. According to the self-report of the participants, we have checked the 6 main symptoms of endometriosis. A total of 31.3% of participants experienced severe pain (8-10 points) during the menstruation, and 34% reported severe pain during sexual intercourse or constipation. Moreover, the most common symptoms of the participants were pelvic pain during menstruation (98.4%), pelvic pain during sexual intercourse (82.5%), abdominal pain continuing more than 6 months (90.6%), urinary symptoms (36.7%), pain during the constipation (58.9%), and other abdominal symptoms (95.3%). After endometriosis stripping surgery, pelvic and other pain decreased by 80%-90% by the self-report of the participants. This result was consistent with research of Simone et al and Kitawaki et al. [24, 25].

This study has some limitations. First, it was difficult to compare our results with other studies due to the different terms that were used to expressing the pain. Second, our study was done with a relatively small sample size, thus in the future, it would be preferable to increase the sample size in order to strengthen the study.

Conclusions

Accurate and timely diagnosis of endometriosis is quite problematic because of the variable symptoms of the disease. Transabdominal and/or transvaginal basic pelvic ultrasound is a extremely efficient technique to diagnose ovarian endometriosis. On the other hand, to diagnose endometrioma adherence to

the ovarian tissue or abdominal wall, laparoscopy is a powerful technique. In the present study, we conducted moderate and severe endometriosis excision surgery in Mongolian patients. We have concluded that synthetic progesterone treatment before surgery significantly decreased ($p = 0.002$) bleeding during surgery and eased the removal of endometriosis from the ovary.

Conflict of Interest

The authors state no conflict of interest.

Acknowledgment

The authors provided no information regarding financial or institutional support or who contributed to their study.

References

1. Ata B, Uncu G. Impact of endometriomas and their removal on ovarian reserve. *Curr Opin Obstet Gynecol* 2015; 27: 235–41.
2. Brosens IA, Puttemans PJ, Deprest J. The endoscopic localization of endometrial implants in the ovarian chocolate cyst. *Fertil Steril* 1994; 61: 1034–8.
3. Burney RO, Giudice LC. Pathogenesis and pathophysiology of endometriosis. *Fertil Steril* 2012; 98: 511–9.
4. Busacca M, Vignali M. Ovarian endometriosis: from pathogenesis to surgical treatment. *Curr Opin Obstet Gynecol* 2003; 15: 321–6.
5. Chapron C, Pietin-Vialle C, Borghese B, Davy C, Foulot H, Chopin N. Associated ovarian endometrioma is a marker for greater severity of deeply infiltrating endometriosis. *Fertil Steril* 2009; 92: 453–7.
6. Donnez J, Nisolle M, Gillet N, Smets M, Bassil S, Casanas-Roux F. Large ovarian endometriomas. *Hum Reprod* 1996; 11: 641–6.
7. Dunselman GA, Vermeulen N, Becker C, Calhaz-Jorge C, D'Hooghe T, De Bie B, et al. ESHRE guideline: management of women with endometriosis. *Hum Reprod* 2014; 29: 400–12.
8. Giudice LC. Clinical practice. Endometriosis. *N Engl J Med* 2010; 362: 2389–98.
9. Hoo WL, Stavroulis A, Pateman K, Saridogan E, Cutner

- A, Pandis G, et al. Does ovarian suspension following laparoscopic surgery for endometriosis reduce postoperative adhesions? An RCT. *Hum Reprod* 2014; 29: 670–6.
10. Hughesdon PE. The structure of endometrial cysts of the ovary. *J Obstet Gynaecol Br Emp* 1957; 64: 481–7.
 11. Johnson NP, Hummelshoj L, World endometriosis society montpellier C. Consensus on current management of endometriosis. *Hum Reprod* 2013; 28: 1552–68.
 12. Nezhat F, Nezhat C, Allan CJ, Metzger DA, Sears DL. Clinical and histologic classification of endometriomas. Implications for a mechanism of pathogenesis. *J Reprod Med* 1992; 37: 771–6.
 13. Nisenblat V, Bossuyt PM, Shaikh R, Farquhar C, Jordan V, Scheffers CS, et al. Blood biomarkers for the non-invasive diagnosis of endometriosis. *Cochrane Database Syst Rev* 2016; 5: CD012179. doi: 10.1002/14651858.CD012179.
 14. Shaltout MF, Elsheikhah A, Maged AM, Elsherbini MM, Zaki SS, Dahab S, et al. A randomized controlled trial of a new technique for laparoscopic management of ovarian endometriosis preventing recurrence and keeping ovarian reserve. *J Ovarian Res* 2019; 12: 66-9.
 15. Simone F, Pier L, Nicola R, Giovanni C, Remorgida V. Pharmacological treatment of endometriosis: *Drugs* 2009; 69: 943-52.
 16. Bulun SE. Endometriosis. *N Engl J Med* 2009; 360: 268-79.
 17. Muzii L, Di Tucci C, Di Felicianantonio M, Galati G, Verrelli L, Donato VD, et al. Management of endometriomas. *Semin Reprod Med* 2017; 35: 25-30.
 18. Urman B. Pearls and pitfalls in surgery for endometrioma. *Womens Health (Lond)* 2015; 11: 677-83.
 19. Zhu W, Tan Z, Fu Z, Li X, Chen X, Zhou Y. Repeat transvaginal ultrasound- guided aspiration of ovarian endometrioma in infertile women with endometriosis. *Am J Obstet Gynecol* 2011; 204: 61-6.
 20. Unlu C, Yildirim G. Ovarian cystectomy in endometriomas: combined approach. *J Turk Ger Gynecol Assoc* 2014; 15: 177-89.
 21. Carmona F, Martinez-Zamora MA, Rabanal A, Martinez-Roman S, Balasch J. Ovarian cystectomy versus laser vaporization in the treatment of ovarian endometriomas: a randomized clinical trial with a five-year follow-up. *Fertil Steril* 2011; 96: 251-4.
 22. Hayasaka S, Ugajin T, Fujii O, Nabeshima H, Utsunomiya H, Yokomizo R, et al. Risk factors for recurrence and re-recurrence of ovarian endometriomas after laparoscopic excision. *J Obstet Gynaecol Res* 2011; 37: 581-5.
 23. Porpora MG, Pallante D, Ferro A, Crisafi B, Bellati F, Benedetti PP. Pain and ovarian endometrioma recurrence after laparoscopic treatment of endometriosis: a long-term prospective study. *Fertil Steril* 2010; 93: 716-21.
 24. Busacca M, Riparini J, Somigliana E, Oggioni G, Izzo S, Vignali M, et al. Postsurgical ovarian failure after laparoscopic excision of bilateral endometriomas. *Am J Obstet Gynecol* 2006; 195: 421-5.
 25. Brown J, Farquhar C. Endometriosis: an overview of *Cochrane Reviews*. *Cochrane Database Syst Rev* 2014: Cd009590.
 26. Ozaki R, Kumakiri J, Jinushi M, Ikuma S, Murakami K, Kawasaki Y, Kitade M. Comparison of effect of preoperative dienogest and gonadotropin-releasing hormone agonist administration on laparoscopic cystectomy for ovarian endometriomas. *Arch Gynecol Obstet* 2020; 302: 969-76.
 27. Yap C, Furness S, Farquhar C. Pre and post operative medical therapy for endometriosis surgery. *Cochrane Database Syst Rev* 2004; 2004: CD003678.