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CASE REPORT

The Feasibility of Hysteroscopic Endomyometrium Resection combined with concomitant Insertion of LNG-IUD for Treatment of Symptomatic Adenomyosis; A 36 Case Series with 5-year follow up result.

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ABSTRACT

Background: Treatment for patients with symptomatic adenomyosis has been mainly by hysterectomy. The aim of this 5-year observational study was to assess the feasibility of Hysteroscopic Endomyometrium Resection with concomitant Insertion of Levonorgestrel-Releasing Intrauterine Device for symptomatic adenomyosis.

Methods: From May 2015 and December 2022, a group of 36 women with symptomatic adenomyosis underwent this combined modality treatment at a community hospital. The core outcomes of the study were effective rate of dysmenorrhea, menorrhagia, secondary outcomes as hysterectomy, Intrauterine device expulsion, or premature removal, repeated the procedures.

Results: The study followed the progress of 36 women, aged 42.9±4, over a period of five years. The procedures were performed safely, and no complications were observed. The total successful rate of amenorrhea was 27 of 36 (75%). For the Pain Control, the intervention led to a significant reduction in pain scores, with the mean pain score decreasing by approximately 63.4% (95% CI: -64.3% to -62.5%). For the Blood Loss, with the mean blood loss decreasing by approximately 75.77% (95% CI: 32.93% to 118.61%). The study also showed reduced CA-125 level, reduction in uterine length and volume, about 70% of patients reported being very satisfied and satisfied of this combined treatment.

Conclusion: In this study, we not only confirmed the five-year effectiveness of Transcervical endomyometrium resection combining with Levonorgestrel-Releasing Intrauterine Device in treating symptomatic adenomyosis, achieving a high rate of amenorrhea and patient satisfaction in women wishing to preserve their uterus, but we also identified a need for additional measures to reduce menstrual flow during the initial six months following treatment. We demonstrated this combined modality is feasible and safe for treatment of symptomatic adenomyosis.

Keywords: Symptomatic Adenomyosis, Transcervical endomyometrium resection. Levonorgestrel-Releasing Intrauterine Device.

Introduction

Adenomyosis is a non-cancerous condition of the uterus, characterized by the abnormal presence of endometrial tissue within the muscular layer of the uterus (myometrium). This disorder is believed to be caused by a combination of factors, including hormonal imbalances, inflammation, and fibrosis, although the exact mechanisms behind its development are not completely understood. The prevalence of adenomyosis is not definitively known, with estimates varying widely; it's observed in 9 to 62 percent of women who undergo a hysterectomy. Symptoms of adenomyosis can vary greatly and may include pelvic pain, heavy menstrual bleeding, and fertility problems. However, it's also important to note that some women with adenomyosis may not experience any symptoms at all. This variability is influenced by diverse population groups and reasons for hysterectomy, varying diagnostic criteria, and the quantity of histologic sections analyzed. Approximately two-thirds of cases exhibit symptoms. Adenomyosis is classified into two types: diffuse uniformly and focal, both of which lack a pseudocapsule[1, 2].

The treatment of symptomatic adenomyosis, most reported are hysterectomy, remains a topic of debate. The Levonorgestrel-Releasing Intrauterine Device (LNG-IUD), a hormone-releasing IUDs, in vitro releases 20 mcg of levonorgestrel per day for 5 years, has treating symptomatic adenomyosis but have a high one-year expulsion rates 25.3% and 33% had persisted bleeding that needed further treatment[3].

Transcervical resection of the endomyometrium (TCREM) has demonstrated its safety and significantly superior effectiveness compared to alternative methods of endometrium destruction for managing heavy menstrual bleeding in women[4]. Xia documented the complete resection of adenomyosis using hysteron-resectoscopy; however, this approach requires an experienced surgeon due to safety considerations[5].

The treatment of adenomyosis using TCREM combined with the insertion of a LNG-IUD is a feasible approach. TCREM is a minimally invasive surgical procedure that involves the resection of the endometrial lining and some parts of the myometrium from the uterus, targeting the areas affected by adenomyosis. Following this procedure, the insertion of an LNG-IUD can provide localized hormone therapy. Levonorgestrel, a progestin, is slowly released by the IUD, which can help in reducing uterine bleeding and pain, common symptoms of adenomyosis.

This combined approach leverages both surgical and hormonal treatments. The surgical component directly removes or reduces the adenomyotic tissue, potentially alleviating symptoms more immediately. The hormonal aspect, provided by the LNG-IUD, can help in managing the condition over the long term by controlling the hormonal environment within the uterus, which is thought to play a role in adenomyosis. Earlier study of TCREM, resect both the endometrium and underlying myometrium layer with concomitant insertion of an LNG-IUD, an effective exposure more dept myometrium to local progesterone from LNG-IUD appears to be safe and to result in a high rate of amenorrhea, but more and longer-term data are called for to evaluate clinical outcome and efficacy[6,7].

This study aimed to assess the feasibility of TCREM combined with LNG-IUS for the treatment of symptomatic adenomyosis over a 5-year follow-up period.

Methods:

From May 2015 to December 2022, a total of 36 women who voluntarily sought to preserve their uterus but had no desire for conception and showed no signs of other pelvic diseases, participated in this study. This study was conducted at a community hospital and focused on hysteroscopic endomyometrium resection, combined with the immediate insertion of LNG-IUD, as a treatment for symptomatic adenomyosis.

All patients were quantified dysmenorrhea pain VAS scale with blood loss at least 100 ml per month for previous 2 months by Magnay Menstrual Pictogram[8]. After obtaining the patient's medical history and conducting a physical examination, the primary imaging modality for diagnosing adenomyosis was a midsagittal transvaginal or abdominal ultrasound (TVUS or TAUS), as previously recommended by Sun et al.[9]. In patients with a large uterus on pelvic examination (>12 weeks size) or combined with other uterine structural abnormalities were excluded from the study.

A total of 36 patients, the average age was 42.95±4.57 years, were subjected to endomyometrium resection under spinal anesthesia, using a 27Fr bipolar resectoscope equipped with a 24 Fr 5x3 mm loop wire. Normal saline served as the distention medium. The histologic diagnosis of adenomyosis was made by at least 2.5 mm invasion. The resection depth of the endomyometrium was limited to 5 mm. Depending on the location of lesion, resection was typically performed on the diseased side of the uterine wall or in diffuse symmetrical type on both anterior and posterior walls. After surgery the LNG-IUD was inserted without difficulty. No operative complication was recorded.

The core primary outcomes of the study were to determine the treatment's effectiveness, included pain reduction, menstrual improving. And the IUD expulsion, IUD premature removal, repeated procedures, or the need for a hysterectomy as a secondary outcome. We also evaluated the blood hemoglobin and CA-125 level, uterine length with volume before and patients' satisfaction after the treatment as a secondary outcome. Premature removal of Mirena was defined as the patient decided to remove it during the study period for reasons other than menorrhagia or dysmenorrhea. Patients were following year 1 and year 5 at our clinic or by telephone interviews, for clinical conditions, and adverse effects after surgery. Five years later, five questions regarding The Assessment of Patient Satisfaction are employed: "Are you satisfied with the procedures you received in the hospital?" The responses, "Very satisfied," "Satisfied," "unsatisfied," "very unsatisfied", are then recorded.

Descriptive statistics for fundamental clinical traits of patients were computed in Microsoft Excel, presenting means SD or frequency count (percentage). All data underwent analysis using Microsoft Excel software. For normally distributed data, paired t-tests were employed to compare treatment outcomes before and after the intervention were

conducted using SPSS version 24, with a significance threshold of $P < 0.05$.

Result.

The baseline characteristics of the study women before after treatment are shown in Table 1. For the Pain Control Improvement, the intervention led to a significant reduction in pain scores, with the mean pain score decreasing by approximately 63.4% (95% CI: -64.3% to -62.5%, for both groups). For the Blood Loss Improvement: there was a notable improvement in blood loss, with the mean blood loss decreasing by approximately 75.77% (95% CI: 32.93% to 118.61%, for both groups).

Table 1. Baseline characteristics of 36 patients with adenomyosis

Parameter	Study data N=36	5-year follow-up N=34
Age, mean ± SD (yrs.)	42.95±4.57. (Range 28 to 51)	
Parity Nulliparous Multiparous	5(13%) 31(87%)	
Symptoms Menorrhagia and dysmenorrhea Dysmenorrhea Menorrhagia	 29(81%) 4(11%) 3(8%)	
Duration of symptoms before treatment(months)	13.4±14.97 (Range 2 to 60)	
Location of lesion Anterior Posterior Diffuse	 3((8%) 24(67%) 9(25%)	Ant. Type, one repeated the procedure. Post-type. Three failed owing to expulsion iud.2 diffuse type underwent hysterectomies
Follow up(months)	76±8.5 (Range 62 to 92)	
Dysmenorrhea VAS scores	6.2±2.2 (Range 9-4)	1.9±2.5 (N=34, range 0-8, p value<0.001)
Blood loss (ml)	205.9±76.8	54.1±85.7(N=34 range minimal to 250, p value <0.001)
Hb (g/dL)	8.69±1.95. (±) 13-6.2	11.0 ±1.6 (N=34, Range 12-6, p value=0.625)
BMI (mean ± SD)	23.3±3.3. Range 32-17.7	24.2 ±3.7(N=34, Range 31.5-18, p value = 0.797)

Parameter	Study data N=36	5-year follow-up N=34
CA-125(mean ± SD)	146.6±142.1 Range 494-20.3	57.5±64.5 (N=34, Range 250-6, P value<0.001)
Uterine size Vol (cm3) length(cm)	260.45.±108.20 9.71±1.35	216.62±179.71 (N=34, p value=0.005) 8.49±1.55(p value=0.002)
Operation time minutes. (mean ± SD) Weight of resection (mean ± S D)	21.14 ±7.6 3.09 ± 4.02g. range 23.5-0.96 g	

*Denote N=34, excluded 2 women who underwent hysterectomy.

Table 2 presents the outcomes of the study, indicating that nine women (25%) experienced treatment failure within a five-year period. Most of these failures occurred during the first year, primarily due to inadequate menstrual control. However, after the second year, most failures were attributed to side effects associated with LNG-IUS itself. These side effects included repeated yeast infections, weight gain, and troublesome bloody discharge, which occurred following combined treatments of 2 years, 3 years, and 4 years, respectively.

Table 2 Core Outcomes Undergoing Combined Treatments of 36 Symptomatic Women with Adenomyosis

Time after treatment year	Amenorrhea N (%)	TAH N (%) Total 2(6%)	Expulsion N (%) 3 (8%)	Premature removal of Mirena N (%) Total 4(11%)	Total success rate
1	32(89%)	1(3%)	3(8%)	0	32(89%)
2	31(86%) #	1(3%)	0	2(Infection, repeat procedures) *	29(81%)
3	31(86%) #	0	0	1(persisted bloody discharge) *	28(77%)
4	31(86%) #	0	0	1(weight gaining) *	27(75%)
5	31(86%) #	0	0	0	27(75%)

TAH: total abdominal hysterectomy. # after the year 2 amenorrhea was not change. Total 5 years successful rate 75%.

Throughout the entire span of five years, the treatment exhibited an overall success rate of 75%. Even one year after the conclusion of the 5-year period, there were 17 instances of patients having the IUD removed, while 10 patients continued to utilize it, and 7 cases were lost to follow-up.

As for The Assessment of Patient Satisfaction, 62% of patients reported being "Very satisfied" (22 patients), 8% were "Satisfied" (3 patients), and 11(30%) expressed being "Dissatisfied" (11 patients) with no women was very dissatisfied. It's worth noting that two additional patients who had successful treatment but reported dissatisfaction due to skin allergies and irregular bleeding respectively.

Discussion

In this 5-year follow-up study demonstrated encouraging results. The successful rate after 1 year was 89% (32/36), with amenorrhea rate was 32 out of 36 (89%), four treatments failed (11%) included 1 hysterectomy and 3 spontaneous expulsions of Mirena. After 5 years successful rate was 75% (29/36). The hysterectomy rate was 2 (6%), expulsion rate was 3 (8%), and premature removal was 4 (11%), all of which were lower than the figures reported in the previous studies[3,4]. This study suggests that the endomyometrium resection to the depth of 5mm and insertion of LNG-IUS treatment is an effective exposure more dept myometrium to local progesterone.

For the sake of programmatic considerations, we restricted the resection of the endomyometrium to a depth of 5 mm. Our reported the median weight of resected tissue was 3.09 ± 1.95g. range 23.5-0.96 g, different from Xia reported 54.4-46.9g, and Wortman et al 12.3-8.6g[4,5].

In this study majority of adverse events came from the LNG-IUS, premature removal in 3 patients with 2 more unsatisfied for the treatment. Table 2. Most common side effect reported by Nidhi et al, was vaginal spotting observed in 50.0% of the patient followed by vaginal discharge (38.1%). [10]. Adverse effects of this combination regimens were issued as a concern. We found that the most failure occurred before 6 months, with these patients experiencing persistent heavy menstrual bleeding, ultimately leading to the expulsion of the IUD, and necessitating a hysterectomy.

To address this issue, we suggest administering a GnRH-Agonist for three months, which would effectively reduce ovarian hormones and lead to transient amenorrhea. The goal of this approach is to alleviate heavy menstruation and, consequently, reduce the expulsion rate of the IUS Mirena.

Common symptoms of adenomyosis include dysmenorrhea and menorrhagia. While some patients may only experience one of these symptoms, others might have both, and some could even have minimal symptoms. Around 19% of our patients exhibited only one symptom. Our study found that patients with adenomyosis who sought treatment at the clinic typically presented symptoms for a duration of 12 months.

Currently, there is no strong evidence to indicate which technique that secures the best clinical performance. In 2014, Grimbizis et al. conducted a systematic literature review which found that different uterine-sparing surgical treatments for symptomatic adenomyosis demonstrated an 81% control rate for menorrhagia,50% for dysmenorrhea, and a 46% pregnancy rate[11]. Adenomyosis is

a common disease, yet there is a dearth of comprehensive information regarding treatment effectiveness. An analysis of different approaches unveiled notable inconsistencies in how the disease is defined and treatment outcomes are assessed. In this study, we exclusively employed 2D ultrasound before initiating treatment. However, it's important to acknowledge that this method might overlook some cases of adenomyosis. Typically, adenomyosis is diagnosed through non-invasive methods, and despite the variable and nonspecific nature of its clinical signs and symptoms, they can lead to a suspicion of the condition. Advanced imaging techniques, such as both 2D and 3D ultrasound, as well as MRI, are crucial in accurately identifying the various forms of adenomyosis, whether they are diffuse or focal. The advancement in diagnostic tools has significantly improved the ability of physicians to accurately diagnose adenomyosis using non-invasive methods. This marks a significant milestone considering the clinical implications of the disease. Moreover, these technological advancements pave the way for a new epidemiological landscape. They enable the identification of diverse groups of women who exhibit varying clinical and imaging characteristics of adenomyosis. Investigating these differences should be a focus of future research. This study adopts the Core Outcome Set in Adenomyosis (COSAR) framework[12]. The fundamental aspects encompass pain levels, menstrual bleeding, anemia presence, patient contentment with the treatment, uterine volume, procedure-related discomfort, hospitalization duration, untimely procedure cessation, and adverse events. From an economic perspective, utilizing this combined approach for treatment proves to be budget friendly. Before 2018, the typical expenses associated with the combined therapy in Taiwan were commonly covered by the national health insurance. Nevertheless, patients were required to personally cover approximately 200 US dollars for the LNG-IUS. Hence, the evaluation of patient satisfaction in our study revealed a significantly high satisfaction rate. It's important to note that adenomyosis treatment decisions should also consider clinical guidelines, patient preferences, and individual variations. A cost-effectiveness analysis provides valuable information, but it's just one piece of the puzzle when making treatment decisions for a complex condition like adenomyosis. Finally, to utilize personalized and conservative therapeutic approaches tailored to the specific conditions of each patient can be a good modality[13].

It is important to note that our study had certain limitations: cases number is small, no control groups, and it did not track detailed yearly changes in outcomes. The recall of menstrual blood loss and dysmenorrhea among women with adenomyosis can be prone to errors.

Conclusion.

Our findings indicate that the highest rate of failure with the IUD, specifically the expulsion of the IUS Mirena, predominantly occurred within the first six months. This was mainly due to persistent heavy menstrual bleeding, which often necessitated a hysterectomy. In response to this challenge, we propose the administration of a GnRH-Agonist for a

duration of three months. This treatment aims to decrease ovarian hormone levels, leading to a temporary cessation of menstruation. The objective of this strategy is to mitigate heavy menstrual flow, thereby potentially lowering the likelihood of IUS Mirena expulsion. In our study, we not only confirmed the five-year effectiveness of combining TCREM with LNG-IUS in treating symptomatic adenomyosis, achieving a high rate of amenorrhea and patient satisfaction in women wishing to preserve their uterus, but we also identified a need for additional measures to reduce menstrual flow during the initial six months following treatment.

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The authors of this article have no conflict of interest to disclose.

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Contribution of authorship:

CSY initiated the idea of the subject. CSY and YLL performed the literatures search on the subject. YLL YSB collect the patient' data. All authors approved the final version of this article. All authors followed The Declaration of Helsinki: ethical principles for medical research involving human subjects. (World Medical Association): The hospital ethics committee approved this study (KNH110-c-1). All patients who undergoing these procedures had a signed informed consent.

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