

# Clinical efficacy of levonorgestrel releasing intrauterine system for the treatment of adenomyosis in perimenopausal women

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## Summary

**Background:** The aim of this study was to evaluate the efficacy of levonorgestrel-releasing intrauterine system (LNG-IUS) in the treatment of menorrhagia, dysmenorrhea, and poor quality of life caused by adenomyosis in perimenopausal women. **Materials and Methods:** Ninety-six women with menorrhagia, dysmenorrhea, and poor quality of life with adenomyosis in perimenopausal women were included and were invited to complete a SF-36 Health Survey. Excluded were cervical and endometrial lesions that underwent a Pap smear, transvaginal sonography, and endometrial biopsy. LNG-IUS was inserted in the postmenstrual phase. Blood loss was assessed by pictorial blood loss assessment chart (PBAC), and dysmenorrhea intensity was assessed by a visual analogue scale (VAS). The patients were followed up after one, three, six, 12, and after 18 months. The participations are asked to complete the short form 36 (SF-36) health survey questionnaires. **Results:** The menstrual blood size was ( $60.287 \pm 21.832$ ) ( $41.186 \pm 16.153$ ), ( $30.988 \pm 15.670$ ), ( $19.238 \pm 13.649$ ), ( $16 \pm 11.464$ ) after treatment one, three, six, 12, and after 18 months, respectively, which reduced significantly compare with before treatment ( $88.691 \pm 33.775$ ,  $p < 0.05$ ). The VAS of dysmenorrhea dropped continuously and significantly from the baseline score of ( $74.968 \pm 15.889$ ) to ( $38.797 \pm 16.781$ ), ( $24.857 \pm 16.595$ ), ( $15.840 \pm 14.305$ ), ( $10.784 \pm 13.593$ ), and ( $8.196 \pm 12.919$ ), respectively, after treatment one, three, six, 12, and after 18 months of the LNG-IUS insertion ( $p < 0.05$ ). The results of SF-36 Health Survey shown the quality of life was significantly improved. **Conclusion:** These data suggest that LNG-IUS is a safe and effective option for reduces menorrhagia, relieve dysmenorrhea, and improve the quality of life in patients with adenomyosis from perimenopausal women.

**Key words:** Levonorgestrel intrauterine system; Menorrhagia; Dysmenorrhea; Adenomyosis; Perimenopause; SF-36 Health Survey.

## Introduction

Adenomyosis is a common gynecological condition that is characterized by the presence of endometrial glands and stroma deep within the myometrium layer of the uterus associated with myometrial hypertrophy and scattered hyperplasia, which is often responsible for menorrhagia, dysmenorrhea, dysgraphia, non-cyclic pelvic pain, anemia, and infertility [1]. The incidence of adenomyosis reached to 8%~27% in women of reproductive age [2]. Medical treatment for adenomyosis includes non-hormonal or hormonal oral medications for prolonged period of time, which have some serious side-effects, while others are unpopular because they are ineffective and temporary in nature. Although hysterectomy has always been advocated as an effective treatment, less invasive procedures, such as endometrial resection, have been proposed as an alternative; however, these procedures may be associated with lower success rates [3]. Women, therefore, need some therapy to tide over this difficult time. Levonorgestrel intrauterine system (LNG-IUS) is a non-surgical, long-acting, alternative to the traditional medical and surgical treatments that is one such feasible option in these women [4-6].

The LNG-IUS is a T-shaped device composed of a cylinder

containing 52 mg of LNG covered by a rate controlling membrane. Initially, 20 mcg of levonorgestrel is released every 24 hours, which later decreases to 11 mcg every 24 h by the end of five years [7, 8]. The LNG-IUS has increasingly been used not only for contraception but also for treatment of heavy menstrual bleeding, dysmenorrhea, leiomyomata, endometriosis, and adenomyosis, due to the main role of LNG-IUS on the endometrium by suppressing the endometrial glands and causing decidualization of the stroma, mucosal thinning, and an inactive endometrium [9-11]. The most common side effects of LNG-IUS are amenorrhea, spotting, and pelvic inflammatory disease [12-13]. Compared with the studies on menorrhagia and dysmenorrhea, there has been limited literature regarding the effects of the LNG-IUS on quality of life caused by adenomyosis in perimenopausal women, especially a long-term follow-up study.

The present study aimed to evaluate the efficacy of LNG-IUS not only in the treatment of menorrhagia and dysmenorrhea but also to observe the quality of their life using the SF-36 Health Survey questionnaire after 18 months follow-up period, which has been designed to evaluate following these concerns in global health: physical functioning, phys-

Table 1. — Comparison of the menstruation and blood levels before and after LNG-IUS treatment (mean±SD).

	Menstruation (mean ±SD)	<i>p</i>	VAS (mean ±SD)	<i>p</i>
Before treatment	88.691±33.775		74.968±15.889	
After 1 month	60.287±21.832	7.731E-1 <sup>a</sup>	38.797±16.781	1.19E-34 <sup>a</sup>
After 3 months	41.186±16.153	9.35009E-11 <sup>b</sup>	24.857±16.595	2.66E-08 <sup>b</sup>
After 6 months	30.988±15.670	1.40931E-05 <sup>c</sup>	15.840±14.305	6.92E-05 <sup>c</sup>
After 12 months	19.238±13.649	1.58878E-07 <sup>d</sup>	10.784±13.593	0.008639 <sup>d</sup>
After 18 months	16±11.464	0.064786 <sup>e</sup>	8.196±12.919	0.126609 <sup>e</sup>

Note: Continuous variables are expressed as mean ± standard deviation; Paired-samples *t*-test as appropriate;

<sup>a</sup>*p* < 0.001 vs. before treatment. <sup>b</sup>*p* < 0.001 vs. after one month. <sup>c</sup>*p* < 0.001 vs. after three months. <sup>d</sup>*p* < 0.001 vs. after six months. <sup>e</sup>*p* < 0.001 vs. after 12 months.

Table 2. — Changes in mean ± SD scores of SF-36 questionnaire between before and after treatment with LNG-IUS in patients with adenomyosis.

Variables	SF-36 Health Survey(mean ±SD )			
	Before treatment	After 1 month	After 6 months	After 12 months
Physical functioning	36.129±9.949	57.872±10.304 <sup>a</sup>	70.219±10.747 <sup>b</sup>	73.522±7.956 <sup>c</sup>
Role physical	14.095±15.793	48.404±17.888 <sup>a</sup>	59.065±16.880 <sup>b</sup>	63.636±14.635
Bodily pain	12.893±15.323	51.382±20.772 <sup>a</sup>	71.802±19.598 <sup>b</sup>	82.113±17.899 <sup>c</sup>
General health	22.936±17.224	59.702±17.005 <sup>a</sup>	74.296±14.188 <sup>b</sup>	78.715±9.585 <sup>c</sup>
Vitality	39.861±16.664	66.968±11.028 <sup>a</sup>	73.901±9.273 <sup>b</sup>	76.988±6.090 <sup>c</sup>
Social functioning	39.494±22.247	69.547±12.904 <sup>a</sup>	76.510±10.677 <sup>b</sup>	83.096±8.693 <sup>c</sup>
Role emotional	16.148±16.584	39.553±16.640 <sup>a</sup>	69.032±22.157 <sup>b</sup>	83.443±21.380 <sup>c</sup>
Mental health	49.244±10.464	68.212±7.678 <sup>a</sup>	73.318±6.929 <sup>b</sup>	73.5±4.428

Note: Continuous variables are expressed as mean ± standard deviation; Paired-samples *t*-test as appropriate;

<sup>a</sup>*p* < 0.001 vs. before treatment. <sup>b</sup>*p* < 0.001 vs. after one month. <sup>c</sup>*p* < 0.001 vs. after six months.

ical, bodily pain, general health, vitality, social functioning, and emotional and mental health roles [14, 15]. Therefore, this report presents the results of this extension part of the study with regards to menstrual flow, dysmenorrhea, bleeding patterns, effectiveness, and safety.

## Materials and Methods

Ninety-six women with a history of heavy menstrual bleeding due to adenomyosis were included in the study. All patients referred between July 2011 and May 2013 because of adenomyosis were asked to participate in this study during their initial visit to the Department of Gynecology of the First Affiliated Hospital in the Medical University of Xinjiang. Written informed consent was obtained from all patients in this study, and the study was approved by the ethics committee of First Affiliated Hospital of Xinjiang Medical University.

A prospective observational study was conducted to study the efficacy of LNG-IUS in the treatment of menorrhagia, dysmenorrhea, and poor quality of life caused by adenomyosis in perimenopausal women. All the women underwent a Pap smear, transvaginal sonography, and endometrial biopsy to exclude uterine and endometrial lesions. LNG-IUS was inserted in the post-menstrual phase. They were followed up after one, three, six, 12, and after 18 months.

Menstrual blood loss was assessed by pictorial blood loss assessment chart (PBAC) devised by Higham *et al.* [14]. The PBAC score >100 mL is equivalent to blood loss of >80 mL, which defines menorrhagia.

The dysmenorrhea intensity was based on the visual analogue

scale (VAS) in which patients recorded the occurrence and intensity of their pain daily. VAS consists of a subjective evaluation of the pain on a scale of 10; in which 0 indicates no pain and 10 indicates an unbearable pain [15].

Observing the quality of their life was designed to detect a mean difference between before treatment with LNG-IUS and after the LNG-IUS insertion that were followed up after one, six, and 12 months in The Short Form 36 (SF-36) Health Survey. The SF-36 is a generic instrument which assesses “functional health and well-being from the patient’s perspective”. It is a 36-item questionnaire which is used globally to assess changes in health status, as well as to compare the burden of illness in a population. The eight areas of perceived health in SF-36 include: physical functioning, physical role, bodily pain, general health, vitality, social functioning, and emotional and mental health roles. The scores of the eight subscales range from 0 to 100. Higher scores indicate less limitations or distress in the different dimensions [16-17].

All statistical analyses were performed with SPSS Version 17 software. The results are expressed as mean ± SD and intergroup differences were analyzed by paired-samples *t*-test. *P* values were two-sided, and the significance level was *p* < 0.05.

## Results

Of the 96 women who had LNG-IUS inserted were between 44 and 56 years of age, and the mean age was 48.5 ± 4.3 years. The menstrual blood size decreased continuously and significantly after LNG-IUS treatment. The most obvious change in menstrual flow was dropped from (88.691±33.775) to (60.287±21.832) after one month of the

treatment ( $p < 0.05$ ). Changes in menstruation after treatment of LNG-IUS are shown in Table 1. The mean VAS scores decreased continuously and significantly after LNG-IUS insertion. The most remarkable change in VAS was the baseline score dropping from  $74.968 \pm 15.889$  to  $38.797 \pm 16.781$  after one month of the treatment ( $p < 0.001$ ). From then on, the VAS continued to drop to  $10.784 \pm 13.593$  at 12 months, which was the lowest score in the one year ( $p < 0.001$ ). However, it then reduced slightly to  $8.196 \pm 12.919$  at 18 months, and there was no significance compared at 12 months ( $p > 0.05$ ). Changes in dysmenorrheal levels after treatment of LNG-IUS are shown in Table 1.

The SF-36 Health Survey in this study showed that the scores of physical functioning, body pain, general health, vitality, and emotional role increased continuously and significantly after the LNG-IUS insertion from one to 12 months, respectively. The scores of physical and mental health roles were not statistically significant after the LNG-IUS insertion from six to 12 months. The mean  $\pm$  SD scores of SF-36 questionnaire between before and after treatment with LNG-IUS in patients with adenomyosis is shown in Table 2.

## Discussion

Adenomyosis is a poorly understood disease that affects women of reproductive age, causing menorrhagia, dysmenorrhea, and infertility, which occurs when the normal relationship between the basal endometrial layer and the myometrium is disrupted. Adenomyosis is thought to be most prevalent among women aged 30-50 years based on pathologic examination of hysterectomy specimens in women treated surgically for menorrhagia [18]. Traditionally, the hysterectomy is definitive treatment for menorrhagia caused by adenomyosis. However, various studies have reported the LNG-IUS to be an effective treatment for menorrhagia and an alternative to hysterectomy [19-20]. LNG-IUS, designed initially in the mid-1970s, provides highly effective, safe, and long-term reversible contraception. It is also used to treat heavy menstrual bleeding, dysmenorrhea, and offers endometrial protection during estrogen replacement therapy in postmenopausal women [21]. The aim of this paper was to analyze the efficacy of LNG-IUS in the treatment of menorrhagia, dysmenorrhea, and poor quality of life caused by adenomyosis in perimenopausal women.

In the present study, the menstrual blood size decreased continuously and significantly after the LNG-IUS treatment. At 18 months, however, blood loss of the women was not significant compared with 12 months of the adenomyosis patients. It is indicated that most of the patients were asymptomatic after the 12-month treatment with the LNG-IUS. Previous studies have reported that LNG-IUS is a good alternative to surgical management such as hys-

terectomy and endometrial ablation in heavy menstrual bleeding, who conducted a randomized controlled trial involving 571 women with heavy menstrual bleeding who were treated with LNG-IUS or with the usual medical therapy. In both groups, the patient-reported scores on the menorrhagia multi-attributes scale improved from the baseline to six months, though the LNG-IUS group showed significantly better improvement sustainment over a two-year period. Moreover, all of the menorrhagia multi-attributes scale domains showed significantly superior improvements for the LNG-IUS group. Also, at two years, the LNG-IUS group had a higher continuation rate than the usual-medical-treatment group, with no significant differences in the rates of hysterectomy, endometrial ablation or sexual activity scores [22].

Dysmenorrhea is a common problem among patients with adenomyosis. In this study the authors studied the severity of dysmenorrhea using the VAS in which patients recorded the occurrence and intensity of their pain daily. This study found that the mean VAS scores decreased continuously and significantly after LNG-IUS insertion. The most remarkable change in VAS was the baseline score dropping from  $74.968 \pm 15.889$  to  $24.857 \pm 16.595$  after three months of the treatment. Although the changes after 12 months were not as remarkable as those within the first six months, the present authors must emphasize that the changes were constant and continuous, and the lowest VAS score was obtained at 18 months. It has been reported that the lowest VAS score was obtained at 36 months by Sheng *et al.* [8].

One of the strengths of the present study was that it also evaluated quality of life after treatment with the LNG-IUS from scores of SF-36 questionnaire. The major advantage of this survey was its ability to compare the physical and mental status of adenomyosis patients between before and after treatment with the LNG-IUS. The results showed that the scores of physical functioning, body pain, general health, vitality, and emotional role increased continuously and significantly after the LNG-IUS insertion from one to 12 months, respectively. The results indicated that the quality of adenomyosis patients' life was significantly improved after LNG-IUS insertion. The SF-36-based survey has been used among 931 women with endometriosis treated in 12 tertiary care centers in ten countries that investigated the effect of endometriosis on education, work and social well-being, endometriosis-associated symptoms and health-related quality of life [23], and also used in types and frequency of digestive symptoms in patients with different localizations of pelvic endometriosis and which specific symptoms are related to rectal stenosis [24]. To the best of the present authors' knowledge, this study is first using SF-36-based survey to observe the quality of adenomyosis patient's life.

The results provide evidence in support of information that LNG-IUS is an effective device for reduces menor-

rhagia, relieve dysmenorrhea, and improve the quality of life in patients with adenomyosis from perimenopausal women.

### Acknowledgements:

The authors would like to thank all investigators and study personnel involved in the conduct of the study.

The research was funded by the Natural Science Foundation of Xinjiang (2015211C059).

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