Gynecology & Obstetrics
ISSN: 2161-0932

Ma et al., Gynecol Obstet (Sunnyvale) 2015, 5:8
DOI: 10.4172/2161-0932.1000309

Research Article Open Access

# Clinical Efficacy of Levonorgestrel Releasing Intrauterine System for the Treatment of Adenomyosis in Perimenopausal Women

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**Abstract**

**Background:** The aim of this study was to evaluate the efficacy of levonorgestrel-releasing intrauterine system (LNG-IUS, Mirena) in the treatment of menorrhagia, dysmenorrhea and poor quality of life caused by adenomyosis in perimenopausal women.

**Patients 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. Exclude cervical and endometrial lesions through 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). They were followed up after 1 month, 3 months, 6 months, 12 months, 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 ± 21.832) (41.186 ± 16.153), (30.988 ± 15.670), (19.238 ± 13.649), (16 ± 11.464) after treatment 1, 3, 6, 12, and after 18 months, respectively, which reduced significantly compare with before treatment (88.691 ± 33.775, $P< 0.05$). The VAS of dysmenorrheal dropped continuously and significantly from the baseline score of (74.968 ± 15.889) to (38.797 ± 16.781), (24.857 ± 16.595), (15.840 ± 14.305), (10.784 ± 13.593) and (8.196 ± 12.919), respectively, after treatment 1, 3, 6, 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.

**Keywords:** Levonorgestrel intrauterine system; Mirena; 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 hyperplasia scattered, which is often responsible for menorrhagia, dysmenorrhea, dyspareunia, 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 nonhormonal 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 nonsurgical, 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 ratecontrolling membrane. Initially, 20 mcg of levonorgestrel is released every 24 h, which later decreases to 11 mcg every 24 h by the end of 5 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, 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 (Mirena) not only in the treatment of menorrhagia, dysmenorrheal but also to observed 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, role physical, bodily pain, general health, vitality, social functioning, role emotional and mental health [14,15]. Therefore, this report presents the results of this extension part of the study with regard to menstrual flow, dysmenorrhea, bleeding patterns, effectiveness and safety.

## Materials and Methods

Ninety-six women with history of heavy menstrual bleeding due

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**Received** July 15, 2015; **Accepted** July 27, 2015; **Published** August 03, 2015

**Citation:** Ma JQ, Guo CF, Hasim A (2015) Clinical Efficacy of Levonorgestrel Releasing Intrauterine System for the Treatment of Adenomyosis in Perimenopausal Women. Gynecol Obstet (Sunnyvale) 5: 309. doi:10.4172/2161-0932.1000309

to adenomyosis were included in the study. All adenomyosis patients referred between July 2011 and May 2013 because of adenomyosis were asked to participate in our study during their initial visit to the Department of Gynecology of the First Affiliated Hospital in the Medical University of Xinjiang. The adenomyosis diagnosed based on radiological criteria combined with ultrasound diagnosis. 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 levonorgestrel intrauterine device 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 for excluding uterine and endometrial lesions. LNG-IUS was inserted in the postmenstrual phase. They were followed up after 1 months, 3 months, 6 months, 12 months, 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 indicated no pain and 10 indicated an unbearable pain [15].

Observed 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 1 month, 6 months, 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 comparing the burden of illness in a population. The eight areas of perceived health in SF-36 include: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional and mental health. The scores of the eight subscales range from 0 to 100. Higher scores indicate less limitations or distress in the different dimensions [16,17].

## Statistical Analysis

All statistical analyses were performed with SPSS Version 17 software (SPSS Inc., Chicago, IL, USA). The results are expressed as mean ± SD, 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 Ninety-six 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 was decreased continuously and significantly after the LNG-IUS treatment. The most obvious change in menstrual flow was dropping from (88.691 ± 3.775) to (60.287 ± 21.832) after 1 month of the treatment ($P < 0.05$). Changes in menstruation after treatment of LNG-IUS were shown in Table 1. The mean VAS scores decreased continuously and significantly after the LNG-IUS insertion. The most remarkable change in VAS was the baseline score dropping from 74.968 ± 15.889 to 38.797 ± 16.781 after 1 months of the treatment ($P <0.001$). From then on, the VAS continued to drop to10.784 ± 13.593 at 12 months, which was the lowest score in the 1 year ($P < 0.001$). However, then reduced slightly to 8.196 ± 12.919 at 18 months, there was no significant compared with at 12 months ($P > 0.05$). Changes in dysmenorrheal levels after treatment of LNG-IUS were shown in Table 1.

The SF-36 health survey is a multipurpose, short-form health survey with only 36 questions. It yields an 8-scale profile of scores, as well as summary measures. The SF-36 health survey has been designed to evaluate following these concerns in global health: Physical Functioning, Role Physical, Bodily Pain, General Health, Vitality, Social Functioning, Role Emotional and Mental Health. In this study, the scores of physical Functioning, body pain, general health, vitality, emotional role were increased continuously and significantly after the LNG-IUS insertion from I month to 12 months, respectively. The scores of Role Physical and mental health were not statistically after the LNG-IUS insertion from 6 months to 12 months. The mean ± SD scores of SF-36 questionnaire between before and after treatment with LNG-IUS in patients with adenomyosis shown in Table 2.

## Discussion

Adenomyosis is poorly understood diseases that affect 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 upon 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 levonorgestrel-releasing intrauterine system (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 treatment of heavy menstrual bleeding, treatment of dysmenorrhea, and endometrial protection during estrogen replacement therapy in postmenopausal women [21]. The aim of this paper was to analyze the efficacy of LNG-IUS (Mirena) 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 was decreased continuously and significantly after the LNG-IUS treatment. At 18

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

Note: Continuous variables are expressed as mean ± standard deviation; Paired-samples *t* test as appropriate;
[a]$P < 0.001$ vs before treatment, [b]$P < 0.001$ vs after 1 month, [c]$P < 0.001$ vs after 3 months, [d]$P < 0.001$ vs after 6 months, [e]$P < 0.001$ vs after 12 months.

**Table 1:** Comparison of the menstruation and blood levels before and after LNG-IUS treatment (Mean+SD).

| 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[a] | 70.219 ± 10.747[b] | 73.522 ± 7.956[c] |
| Role Physical | 14.095 ± 15.793 | 48.404 ± 17.888[a] | 59.065 ± 16.880[b] | 63.636 ± 14.635 |
| Bodily Pain | 12.893 ± 15.323 | 51.382 ± 20.772[a] | 71.802 ± 19.598[b] | 82.113 ± 17.899[c] |
| General Health | 22.936 ± 17.224 | 59.702 ± 17.005[a] | 74.296 ± 14.188[b] | 78.715 ± 9.585[c] |
| Vitality | 39.861 ± 16.664 | 66.968 ± 11.028[a] | 73.901 ± 9.273[b] | 76.988 ± 6.090[c] |
| Social Functioning | 39.494 ± 22.247 | 69.547 ± 12.904[a] | 76.510 ± 10.677[b] | 83.096 ± 8.693[c] |
| Role Emotional | 16.148 ± 16.584 | 39.553 ± 16.640[a] | 69.032 ± 22.157[b] | 83.443 ± 21.380[c] |
| Mental Health | 49.244 ± 10.464 | 68.212 ± 7.678[a] | 73.318 ± 6.929[b] | 73.5 ± 4.428 |

Note: Continuous variables are expressed as mean ± standard deviation; Paired-samples *t* test as appropriate;
[a]$P < 0.001$ vs before treatment, [b]$P < 0.001$ vs after 1 month, [c]$P < 0.001$ vs after 6 months.

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

months, however, blood loss of the women was no significant compared with 12 months of the adenomyosis patients. It is indicated that most of the patients were asymptomatic after the 12 months treatment with the LNG-IUS. Previous studies have reported that LNG-IUS is a good alternative to surgical management such as hysterectomy 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 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 2-year period. Moreover, all of the menorrhagia multi-attributes scale domains showed significantly superior improvements for the LNG-IUS group. Also, at 2 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 we studied the severity of dysmenorrhea using visual analogue scale (VAS) in which patients recorded the occurrence and intensity of their pain daily. Our study found that the mean VAS scores decreased continuously and significantly after the LNG-IUS insertion. The most remarkable change in VAS was the baseline score dropping from 74.968 ± 15.889 to 24.857 ± 16.595 after 3months of the treatment. Although the changes after 12 months were not as remarkable as those within the first 6 months, we must emphasize that the changes were constant and continuous, and the lowest VAS score was obtained at18 months. It has been reported that the lowest VAS score was obtained at 36 months by Jie Sheng [8].

One of the strengths of our study is also evaluated quality of life after treatment with the LNG-IUS from scores of SF-36 questionnaire. The major advantage of this survey is 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, emotional role were increased continuously and significantly after the LNG-IUS insertion from 1 month to 12 months, respectively. The results indicated that the quality of adenomyosis patient's 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 10 countries that investigated the effect of endometriosis on education, work and social wellbeing, endometriosis -associated symptoms and health-related quality of life [23], and also used to 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 our knowledge, this study is first time using SF-36-based survey to observe the quality of adenomyosis patient's life.

Our results provide evidence in support of information for LNG-IUS is an effective device for reduces menorrhagia, 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.

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