



## Therapeutic use of LNG intrauterine system (Mirena) for menorrhagia due to benign lesions – An alternative to hysterectomy ?

Kumar Sushil, Antony ZK, Mohindra V, Kapur A

INHS Asvini, Naval Hospital, Colaba, Mumbai 400 005.

**OBJECTIVE(S)** : To evaluate the efficacy of an intrauterine system releasing levonorgestrel (LNG-IUS, Mirena) in the treatment of women with menorrhagia .

**METHOD(S)** : This was a prospective, non-comparative study. Twenty patients who had menorrhagia due to non-malignant causes were included in the study (age range 20-42 years). However patients of fibroid uterus with uterine size more than 12 weeks and those with submucous fibroid were excluded. A LNG-releasing-intrauterine system was inserted on any day during bleeding or within a week of cessation of bleeding. Menstrual blood loss was assessed, before LNG-IUS was inserted, and after 3, 6, and 12 months of use.

**RESULTS** : The most common bleeding pattern at 3 months after insertion was spotting and after 6 and 12 months the majority of women presented with amenorrhea or oligomenorrhea. One woman requested removal of the LNG-IUS because of continuous spotting even after 4 months of insertion. The remaining women continued the use of LNG-IUS beyond 1 year.

**CONCLUSION(S)**: LNG-IUS is an effective treatment for menorrhagia due to benign causes and could be an alternative to hysterectomy.

**Key words** : LNG-IUS, menorrhagia, fibroid, endometriosis, adenomyosis

### Introduction

Abnormal uterine bleeding is a common reason for consulting a gynecologist and menorrhagia the commonest reason for performing hysterectomy. Until recently, conservative medical treatment has been disappointing, and surgical alternatives like endometrial ablation and endometrial resection have now been developed. The role of these surgical alternatives in the treatment of menorrhagia is not currently clear. One minimally invasive procedure for control of menorrhagia is insertion of progesterone releasing intra-uterine device (LNG-IUS; Mirena, German Remedies). Levonorgestrel (LNG) is released from this intrauterine system at a rate of 20 µg / 24

hours. It suppresses endometrial growth. The glands of the endometrium become atrophic and the epithelium becomes inactive. This system, originally developed for contraception, has been shown to decrease the amount and duration of normal menstrual flow. Its utility in idiopathic menorrhagia is well documented but its efficacy in fibroids, adenomyosis and endometriosis needs careful evaluation. If LNG-IUS can control the blood loss in all cases of menorrhagia, it may become a simpler alternative to hysterectomy in times to come. The present study was under taken to assess the therapeutic utility of LNG-IUS for idiopathic menorrhagia and menorrhagia caused by benign lesions of the uterus.

### Methods

Twenty volunteers who had menorrhagia with or without dysmenorrhoea were recruited for the study. Women were excluded from the study if they had a fibroid larger than 5 cm in diameter as assessed by ultrasonography, a history of malignancy, clinical suspicion of malignancy, active liver disease, adnexal tumor or cyst, and pelvic inflammatory

Paper received on 14/03/2005 ; accepted on 30/08/2005

Correspondence :

Dr. Sushil Kumar

Senior Advisor and HOD

Department of Obstetrics and Gynecology

INHS Asvini, Colaba, Mumbai - 400 005.

Tel. 022 22177049 Email : cdrsushilkumar@rediffmail.com

disease. Malignancy was excluded by clinical examination, Pap smears, and endometrial thickness of less than 8 mm on postmenstrual ultrasonography. The study was conducted at our postgraduate teaching hospital and tertiary care center from 1st June, 2003 to 31st December, 2004. The LNG-IUS was inserted in the uterine cavity during menstruation according to the instructions for insertion given by the manufacturer but in those unwilling for insertion during menstruation it was inserted within a week of cessation of menstruation. The degree of disturbance caused by their menstrual bleeding, pain, or both, on the general well being and physical activity was assessed by using a visual analogue scale at inclusion in the study, after 6 months and after 12 months of use, and at discontinuation. The visual analogue scale consisted of a horizontal line of 10 cm. The left end was indicated as *not disturbing* the right end as *very disturbing*. Patients were asked to mark with a cross the point on the line that most closely indicated the effects of uterine bleeding or menstrual pain on normal life, without distinguishing between these two. The women were asked to mark in a menstrual diary their days of menstrual bleeding and spotting.

## Results

Etiological distribution of patients is given in Table 1. General anesthesia was requested by one (5%) woman. Insertion without anesthesia was described as easy in 15 of the remaining 19 women (78%). At 12 months, the IUD remained in situ in 19 women (95% percent), of whom 15 (78%) reported amenorrhea and 4 (22%) reported intermenstrual bleeding. At 12 months health-related quality of life had improved significantly. Sexual function scores changed little. No pregnancies were noted during the study. At the end of the study period, 17 of the total 20 women (85%) chose to continue using the LNG-IUS. Discontinuations were due to oligomenorrhea after 13 months in one (5%), dysmenorrhea after 12 months in one (5%), and irregular bleeding after 4 months in one (5%). There were three cases of menorrhagia due to fibroids in the study. The fibroids ranged from 1 cm to 4 cm in size and one to three in number. There was considerable reduction in menstrual bleeding in all of them. After 12 weeks two out of these three women with intramural fibroids developed amenorrhea while the remaining one had scanty menstrual bleeding. Post-treatment sonography revealed endometrial thickness of no more than 4 mm, but no appreciable change in the volume of the fibroids. There were two cases of endometriosis, confirmed by laparoscopy. In one case there was reduction in dysmenorrhea as well as in the bleeding but in the other inter-menstrual spotting continued for 3 months and she also had a weight gain of 3 kg in 3 months though there was reduction in frequency and intensity of pain. In the one case of adenomyosis there was

a reduction in size of the uterus as well as in menstrual bleeding. Five patients gave a history of heavy bleeding associated with previous copper intrauterine device (IUD). All these five patients had considerable improvement with LNG-IUS and chose to continue the device even after 1 year.

**Table 1. Etiology (n=20).**

Etiology	Number	Percentage	Age range (years)
Fibroid uterus	3	15	30-40
Endometriosis	2	10	30-35
Adenomyosis	1	05	30
Previous history of menorrhagia due to Cu intrauterine device	5	25	25-35
Idiopathic	9	45	30-40

## Discussion

This small, uncontrolled, prospective study provides further evidence of the high effectiveness of the LNG-IUS in patients having menorrhagia. Though we found insertion easy in four women the insertion was considered difficult, without anesthesia. Difficult insertion as compared to standard copper IUD insertion and vasovagal symptoms are reported by other workers also <sup>1</sup>. This is because the procedure of insertion of the device is quite different than that of standard IUD and its size is larger. Continuation rate of 85% after one year shows high patient acceptance.

Comparative trials from various studies suggest that use of the LNG-IUS can be a therapeutic alternative to endometrial ablation or hysterectomy in women with menorrhagia <sup>2-4</sup>.

In idiopathic menorrhagia the use of LNG-IUS is associated with a significant reduction in the number of days of bleeding and menstrual blood loss <sup>5</sup>. This effect is based on the marked local action of the intrauterine release of LNG on the endometrium. In suppressed endometrium the production of many highly active compounds ceases. Reduction of excessive blood loss is seen as early as the first menstruation after insertion, and at 1 year the reduction is more than 90%. Complications and side effects are rare, fertility is preserved, and invasive procedures such as endometrial ablation, hysterectomy, and hospitalization are avoided.

The role of LNG-IUS in the management of fibroids has been poorly studied. Anecdotal reports of management of small fibroids, especially intramural ones, appear in the literature. The decrease in menorrhagia may be more due to atrophy of the endometrium than due to a decrease in the

size of the fibroid itself. In one of the studies <sup>6</sup> 12 women with uterine fibroids and severe menorrhagia were treated with LNG-IUS and 11 had considerable reduction in menorrhagia.

There is no ideal treatment for endometriosis. Though oral progestogens are effective, they have poor compliance due to systemic side effects. LNG-IUS, which releases considerably lower doses of progesterone, may reduce the systemic side effects. Lockhat et al <sup>7</sup> found significant improvement ( $P < 0.05$ ) in severity and frequency of pain and menstrual symptoms in 85% of patients. Five patients discontinued because of side effects like acne, pelvic pain and excessive weight gain. Both the patients in our study are still continuing with the device though one had prolonged intermenstrual bleeding and excessive weight gain in the initial months. In spite of low levels of serum progesterone in these patients the systemic side effects of progesterone like bloating sensation, edema, and breast tenderness have been reported <sup>8</sup>. It is because progesterone in LNG-IUS is derived from C19 group of progestogens, which is more active than C21 group.

Adenomyosis is an important cause of menorrhagia. Apart from hysterectomy, the treatment options for adenomyosis are limited. In this study we had only one case of menorrhagia due to adenomyosis. The diagnosis of adenomyosis was confirmed by sonography as well as by MRI. The decrease in uterine size occurred within 12 months of insertion of LNG-IUS and was accompanied by resolution of menorrhagia and dysmenorrhoea. Thus, the LNG-IUS is a viable option and represents a real advance in the treatment of adenomyosis. Regular menstruation without pain has been reported after 3 months of treatment with a 27% decrease in uterine size after 9 months <sup>9</sup>. The effectiveness of the LNG-IUS was hypothesized to be due to decidualization and subsequent atrophy of the endometrium besides the direct action of the hormone on the foci of adenomyosis.

In bleeding associated with previous copper IUDs the principal side effects are amenorrhea (which occurs in one quarter of users) and reduced flow, in the form of spotting or oligomenorrhea. Zalel et al <sup>10</sup>, found complete cessation of menstrual bleeding in 5% after 2 months and in 66% after 4-6 months following insertion. Not surprisingly, women presenting with heavy menstrual flow whether or not it was associated with copper-IUD use, found the LNG-IUS with its contraceptive action to be an attractive option. Reduction of menstrual blood loss also results in improvement of the body iron balance and an increase in hemoglobin

concentration. No pregnancy occurred in our patients. However significantly lower pregnancy rates ( $P < 0.0004$ ) have been reported in comparison with other IUDs <sup>11</sup>.

Menorrhagia is a common gynecologic problem often needing hysterectomy. The LNG-IUS reduces bleeding in women with menorrhagia due to benign causes. The patient acceptance and satisfaction is high. Main problem is intermenstrual bleeding especially for the first 3 months after insertion. If the patients can be counseled before insertion, continuation rates for LNG-IUS are high. It has the potential to replace hysterectomy as treatment of choice in certain patients.

#### References

1. Harrison – Woolrych M, Zhou L, Coulter D. Insertion of intrauterine devices: a comparison of experience with Mirena and multiload Cu375 during post marketing monitoring in New Zealand. *N Z Med J* 2003;8:116-7.
2. Nagrani R, Bowen-Simpkins P, Barrington JW. Can the levonorgestrel system replace surgical treatment for the management of menorrhagia? *BJOG* 2002;109:345-7.
3. Latheenmaki P, Haukkamaa M, Paullaka J. Open randomized study of LNG intrauterine system as alternative to hysterectomy. *BMJ* 1998;316:122-5.
4. Hurskainen R, Teperi J, Rissanen P et al. Clinical outcomes and the costs with the levonorgestrel releasing interuterine system or hysterectomy for treatment of menorrhagia *JAMA* 2004;291:1456-63.
5. Luukkainen T. The levonorgestrel intrauterine system: therapeutic aspects. *Steroids*. 2000;65:699-702.
6. Starczewski A, Iwanicki M. Intrauterine therapy with levonorgestrel releasing IUD of women with hypermenorrhea secondary to uterine fibroids. *Ginekol Pol* 2000;71:1221-5.
7. Lockhat FB, Emembolu JO, Konje JC. The evaluation of the effectiveness of an intrauterine administered progestogen levonorgestrel in the symptomatic treatment of endometriosis and in the staging of disease. *Hum Reprod* 2004;19:179-84.
8. Panay N, Studd J. Non-contraceptive uses of hormone releasing intra-uterine systems. In: Studd JW. (ed). *Progress in Obstetrics and gynecology*. Vol 13. Edinburgh: Churchill Livingstone. 1998:379-95.
9. Fong YF, Singh K. Medical treatment of grossly enlarged adenomyotic uterus with the levonorgestrel releasing intrauterine system. *Contraception* 1999;60:173-5.
10. Zalel Y, Gamzu R, Shulman A et al. The progestative effect of the levonorgestrel-releasing intrauterine system-when does it manifest? *Contraception* 2003;67:473-6.
11. Pakarinen P, Toivonen J, Luukkainen T. Randomized comparison of levonorgestrel and copper releasing intrauterine systems immediately after abortion with 5 years follow-up. *Contraception*. 2003;68:31-4.