

Levonorgestrel intrauterine system (Mirena): An emerging tool for conservative treatment of abnormal uterine bleeding

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ABSTRACT

Introduction: To study the efficacy of levonorgestrel intrauterine system (LNG-IUS; Mirena) in conservative management of abnormal uterine bleeding (AUB).

Materials and Methods: Seventy women between 30 and 55 years with AUB were included in a study conducted over a period of 3 years. Response was assessed monthly for first 4 months and then yearly for maximum 2 years.

Results: Mirena caused a 80% decrease in median menstrual blood loss (MBL) at 4 months, 95% decrease in MBL by 1 year, and 100% decrease (amenorrhoea) by 2 years. Mean hemoglobin (Hb) % showed a significant rise of 7.8% from baseline 4 months post Mirena insertion. Mirena acted as an effective contraceptive in women not using any other form of contraception. Hysterectomy could be avoided in most of the women.

Conclusion: Mirena provides an incredible nonsurgical alternative in treatment of menorrhagia. Its effects are reversible and it is an excellent fertility-sparing device. It is also an effective contraceptive.

Key Words: Abnormal uterine bleeding, mirena, contraceptive

INTRODUCTION

Heavy menstrual bleeding is one of the most common gynecologic complaint in contemporary gynecology. Excessive menstruation is often incapacitating and expensive to treat and can severely affect a woman's quality of life both personal as well as social. Nearly 30% of all hysterectomies are performed to alleviate heavy menstrual bleeding.^[1] Historically, definitive surgical correction has been the mainstay of treatment for menorrhagia. But today modern gynecology has trended toward conservative therapy both for controlling costs and the desire of many women to preserve their uterus. Mirena is a hormonal intrauterine device classified as a long-acting reversible contraceptive method. T-shaped polyethylene frame (T-body) with a steroid reservoir (hormone elastomer core) made of a mixture of levonorgestrel and silicone (polydimethylsiloxane), containing a total of 52 mg levonorgestrel around the vertical stem. The device releases the hormone at an initial rate of 20 µg/day and declines to a rate of 14 µg after 5 years, which is still in the range

of clinical effectiveness.^[2,3] It causes a local foreign body reaction characterized by an increase in inflammatory cells including neutrophils, lymphocytes, plasma cells, and macrophages is seen. These changes are finalized within 3 months of insertion of levonorgestrel intrauterine system (LNG-IUS). Hormonal actions are caused by the levonorgestrel component.

MATERIALS AND METHODS

After the approval by the ethics committee of the hospital, 70 women aged between 30 and 55 years with at least one issue with abnormal uterine bleeding (AUB) were included in the study after taking written and informed consent over a period of 3 years. These patients came to the outpatient department (OPD) with various menstrual complaints like menorrhagia in 70% patients (49/70), polymenorrhagia in

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21.4% patients (15/70), menometrorrhagia in 4.2% patients (3/70), while some patients presented with dysmenorrhea in 4.2% patients (3/70).

The study included women with uterine size <12 weeks with no cervical, vaginal pathology and a negative pap smear. Premenstrual dilatation and curettage (D & C) hysteroscopy was done in women above 40 years of age and in women with histopathology report negative for malignancy were also included. Women with congenital or acquired uterine anomaly, intramural and subserous fibroids more than 3 cm and submucous fibroids distorting the uterine cavity, acute pelvic inflammatory disease, genital bleeding of unknown etiology, liver disease, and known or suspected carcinoma of the breast were excluded. A detailed history and examination (general, systemic, pelvic, and breasts) was done. Transvaginal ultrasound was done using a 7.5 MHz transducer probe on day 4, 5, or 6 of menses. Any obvious pathologies like fibroids, adenomyosis, endometriosis, endometrial polyps, ovarian cysts, or any other adnexal pathology were diagnosed. The patient was called for follow-up in OPD and the histopathology report was reviewed, whether it was proliferative phase, proliferative phase with cystic dilatation, secretory phase, endometrial hyperplasia, or carcinoma. Patients with endometrial cancer were excluded. In case of proliferative phase, patients were started on tab. norethisterone acetate (5 mg) twice a day from day 5 to day 25 and in case of secretory phase from day 20 to day 25 for a total of three cycles and response was noted. In case of no contraindications and a good response to norethisterone, Mirena was inserted post-menstrually on day 5,6, or 7 when bleeding had stopped. Prior to insertion, the patient was counseled regarding the altered bleeding pattern known to occur with Mirena for 3-6 months. She was counseled regarding amenorrhea post insertion. It was inserted on OPD basis except for a few patients where cervix could not be properly visualized or in cases where cervix was pulled up as in previous cesarean section or in anxious patients where it was inserted in operation theater (OT) under minimal sedation. Post insertion, the patient was asked to maintain a menstrual calendar for 4 months, wherein she would mark the days when she has spotting or bleeding. The women were called for follow-up after 1 month, then 4 months, and then yearly (for maximum 2 years); and asked regarding the relief they have obtained from the antecedent menstrual complaints. A detailed general, systemic, pelvic (to see for Mirena threads), and breasts examination was done at every visit. Follow-up ultrasound was done at every visit to see for Mirena location and if there were any changes in the original pelvic pathology or development of a new pathology like ovarian cysts. Hemoglobin (Hb) estimation was done after 4 months. The efficacy of Mirena was measured in

the form of subjective symptomatic improvement along with improvement in quality of life.

RESULTS

In our study, the average age of the cases was 43.39 years (34-53 years). Among the patients who came to the OPD; 15.7% were primipara, 81.4% were multipara, while 2.9% patients were unmarried. 28.6% patients were not sterilized, while 71.4% patients had undergone tubal sterilization. The incidence of prevalent comorbidities is given in Table 1. 18.6% of the participants had some other comorbidities like bronchial asthma, human immunodeficiency virus (HIV), hepatitis B, ischemic heart disease, valvular heart disease, epilepsy, and triple vessel disease.

Mirena was inserted on an out patient basis in most of the patients. Insertion in the operation room under sedation was done in 11 patients, including seven patients with previous cesarean section (one or two), appendicectomies, operations for renal calculus, exploration for prior ectopic pregnancy, and four uncooperative patients, out of which two were unmarried. The number of patients with previous lower segment cesarean section (LSCS) have been given in Table 2.

The various uterine sizes have been tabulated in Table 3. 37.1% of the patients had normal uterine size, followed by 25.7% who had uterine size of 8-10 weeks and 18.6% with

Table 1: Profile of comorbidities

Comorbidities	Number (n = 70)	Percentage
Diabetes	06	08.6
Hypertension	15	21.4
Thyroid	05	7.1
Malignancy	—	—
Others	13	18.6
Diabetes and hypertension	06	08.6

Table 2: Profile of LSCS

LSCS	Number (n = 70)	Percentage
1	07	10.0
2	03	04.3

LSCS: Lower segment cesarean section

Table 3: Profile of uterine size

Uterine size	Number (n = 70)	Percentage
Normal	26	37.1
Bulky-6 weeks	13	18.6
6-8 weeks	09	12.9
8-10 weeks	18	25.7
10-12 weeks	4	5.7

uterine size of 6 weeks. 12.9% of the subjects had uterine size of 6-8 weeks and 5.7% had uterine size of 10-12 wks. Out of these patients, six patients (8.6%) had uterus with restricted mobility.

The profile of ultrasound findings have been shown in Table 4. 44.3% of the population had normal ultrasound findings followed by 37.1% with findings of adenomyosis. 18.6% of the patients had fibroid. Three patients (4.3%) had associated bilateral adnexal endometriotic cysts measuring 2-2.5 cm.

The bleeding patterns in all patients along with those patients with adenomyosis fibroid uterus have been tabulated in Tables 5-7. A reduction in menstrual blood loss (MBL) is seen progressively over a period of 1 month, 4 months, 1 year, and 2 years. In the first follow-up itself, 77% women had only spotting and 64% became amenorrheic by the end of 1 year. All women (100%) became amenorrheic at the end of 2 years. Mean duration from insertion to amenorrhea was 8 months. After insertion, the mean Hb% showed a significant rise of 7.8% from baseline.

Out of the 70 patients, four patients failed to respond to Mirena in the first 1 year. Mirena was subsequently removed and they underwent hysterectomy. Mirena was removed in one patient due to persistent leukorrhea, while Mirena was removed in three patients after 1.5-2 years as they attained menopause (as confirmed by follicle-stimulating hormone (FSH) levels). Mirena was spontaneously expelled in one patient within 1 month of insertion.

Fifty-seven percent of women had no side effects. Others had minor side effects for which assurance was enough. Mirena had to be removed only in one patient because of persistent leukorrhea. Ovarian cysts (simple) were seen in two patients which disappeared in 4 months.

Mirena had a satisfaction rate of 91.42%. Mirena failed to control menorrhagia in four women. These women subsequently underwent hysterectomy. Mirena was expelled in one woman, while it had to be removed in one woman because of persistent leukorrhea.

DISCUSSION

Excessive menstruation is often incapacitating and expensive to treat and can severely affect a woman's quality of life both personal as well as social. Two-thirds of women with menorrhagia show evidence of iron deficiency anemia beyond 80 ml of blood loss.^[4] Heavy menstrual bleeding is a subjective finding, making the exact problem difficult to define. Treatment regimens must address the specific facet of the menstrual cycle which the patient perceives to

Table 4: Profile of ultrasound findings

Ultrasound findings	Number (n = 70)	Percentage
Fibroid	13	18.6
Subserous fibroid	05	33.3
Intramural fibroid	06	40.0
Anterior wall fibroid	01	06.7
Multiple small fibroids	02	13.3
Submucous fibroid	01	06.7
Adenomyosis	26	37.1
Adenomyoma	01	01.4
Normal	31	44.3
Associated endometriotic cysts	03	04.3

Table 5: Profile of bleeding patterns

Bleeding patterns	1 month (n = 70)		4 month (n = 70)		1 year (n = 60)		2 years (n = 36)	
	No.	%	No.	%	No.	%	No.	%
Amenorrhea	04	05.7	14	20.0	44	73.3	36	100
Heavy bleeding	—	—	02	02.9	02	02.2	—	—
Moderate flow	08	11.4	03	04.3	—	—	—	—
Potting	56	80.0	48	68.6	15	25.0	—	—

Table 6: Bleeding pattern in adenomyosis

Bleeding pattern	1 month (n = 26)		4 months (n = 26)		1 year (n = 22)		2 years (n = 14)	
	No.	%	No.	%	No.	%	No.	%
Spotting	20	77.0	20	77.0	11	50.0	00	00
Moderate flow	05	19.2	02	07.7	00	00	00	00
Amenorrhea	00	00	01	03.8	11	50.0	14	100
Menorrhagia	01	03.8	03	11.5	00	00	00	00

Table 7: Bleeding pattern in uterine myomas

Bleeding pattern	1 month (n = 13)		4 months (n = 13)		1 year (n = 13)		2 years (n = 09)	
	No.	%	No.	%	No.	%	No.	%
Spotting	10	76.9	10	76.9	03	23.0	00	00
Moderate flow	03	23	01	07.7	00	00	00	00
Amenorrhea	00	00	02	15.4	09	69.2	13	100
Menorrhagia	00	00	00	00	01	07.7	00	00

be abnormal (i. e., cycle length and quantity of bleeding). There are various methods available for treatment of menorrhagia which includes medical management and surgical management. Many women are not happy with medical treatment and end up undergoing surgery. Nearly 30% of all hysterectomies are performed to alleviate heavy menstrual bleeding.^[1]

Mirena is a hormonal intrauterine device classified as a long-acting reversible contraceptive method. The device

releases levonorgestrel at an initial rate of 20 µg/day and declines to a rate of 14 µg after 5 years, which is still in the range of clinical effectiveness.^[2,3] Most of the hormone stays inside the uterus, and only a small amount is absorbed into the rest of the body.^[5,6]

In our study, Mirena caused a 80% decrease in median MBL at 4 months, 95% decrease in MBL by 1 year, and 100% decrease (amenorrhea) by 2 years. Results of this study are similar to other studies done in the past.^[7-15] Hysterectomy was done only in four patients (5.7%). Hence, our study has proved that Mirena is an excellent alternative to hysterectomy. It is associated with improved psychological well-being and has proved to be very cost-effective. This has also been proved in various other studies done in the past.^[16-18]

The efficacy of Mirena was tested by subjective improvement and improvement in quality of life as told by patient as well as by Hb estimation after 4 months post insertion.

Various studies have shown Mirena to be more effective in heavy menstrual bleeding than antifibrinolytics, oral progestogens, and oral contraceptive pills.^[19-21]

In our study, mean Hb% showed a significant rise of 7.8% form baseline. Significant increase in Hb was also seen in other studies.^[7,22]

91.42% patients were satisfied with Mirena insertion, while 8.58% were not. Reasons for disliking were minor side effects, threads being felt by partner, and intermittent spotting. But none of them required removal except in one patient in whom Mirena was removed due to persistent leukorrhea.

We have also used Mirena in patients with various comorbidities, 21.4% of the women had hypertension, 8.6% had diabetes, 8.6% had both hypertension and diabetes, and 7.1% had thyroid disorders. 18.6% of the participants had some other comorbidities like bronchial asthma, HIV, hepatitis B, ischemic heart disease, valvular heart disease, epilepsy, and triple vessel disease. One patient had family history of breast cancer. Mirena was also inserted in high risk patients like unmarried patient with rheumatic mitral stenosis with balloon mitral valvotomy done 20 years ago, previous two LSCS with an incisional hernia repair, and previous LSCS with a prior abdominal exploration done for ectopic pregnancy. This has also been proven in other studies done in the past.^[23-30]

CONCLUSION

Mirena has been found to be superior to medical treatment and hysterectomy. Mirena had an good efficacy of 80% by

4 months, 95% by 1 year, and 100% by 2 years. It provides excellent patient satisfaction and compliance. LNG-IUS can reduce the MBL and help to improve anemia. It can be safely used in obese patients. It is also a very good alternative for women who have AUB and desire contraception. It is safe in women who have undergone prior abdominal surgeries such as cesarean or myomectomy. LNG-IUS is beneficial in the treatment of uterine fibroid, endometriosis, adenomyosis, and endometrial hyperplasia. Side effects are generally mild and most of the times assurance is enough to ensure continuation of device. Health-related quality of life outcomes and cost effectiveness with LNG-IUS was found to be better than hysterectomy or endometrial ablation. Thus the study concluded that Mirena, the levonorgestrel-releasing intrauterine system, provides an incredible nonsurgical alternative in treatment of menorrhagia which is reversible and spares fertility.

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