Original Article

Effectiveness and safety of Levonorgestrel releasing intrauterine system in treatment of menorrhagia secondary to oral anticoagulations and chronic liver disease

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Objective
To determine whether the levonorgesterol releasing intra-uterine contraceptive device can safely reduce menstrual blood loss and improve quality of life in patients with bleeding disorders and those on oral anticoagulation.

Methods
Patients presenting with menorrhagia, without pelvic pathology and suffering from bleeding disorder or using oral anticoagulants had Mirena inserted at Military Hospital, Rawalpindi. Baseline hemoglobin and menstrual blood loss was evaluated using pictorial blood assessment chart. Follow up hemoglobin and menstrual assessments were performed at 3, 6 and 12 months. At 12 months, patient satisfaction was assessed.

Results
Eighteen patients with bleeding disorders (3 chronic liver disease and 6 on anticoagulation with warfarin) were included in the study. One patient was lost to follow up after 3 months. Remaining were followed for one year. Continuity rate was 91% at one year. Mirena resulted in decrease in menstrual blood loss by 60% at 3 months, 70% at 6 months and 85 % at one year ($p<0.001$ for all). Seven (31%) became amenorrhic and another seven (31%) had intermenstrual spotting. Blood transfusion requirement was completely eliminated. Patient satisfaction was very high.

Conclusion
In patients with bleeding and coagulation disorders, Levonorgesterol releasingintrauterine system provided an efficacious and satisfactory choice in the treatment of menorrhagia and it reduced the need for blood transfusion and surgery. (Rawal Med J 2009;34:187-190)

Key words
LNG-IUS, menorrahagia, bleeding disorders, CLD.

Abbreviations: MBL: Menstrual blood loss, Hb: Haemoglobin, LNG-IUS: Levonorgesterol releasing-intrauterine system, PBAC: Pictorial blood assessment chart, CLD: chronic liver disease.

INTRODUCTION

Idiopathic menorrhagia accounts for 12% of all gynecology referrals[1] and majority have no organic disease.[2] Primary coagulation disorder is found in 20% of adolescent menorrhagia[3] and prevalence of Von Willibrand's disease was 10% in women presenting with menorrhagia, compared to general population where it was 1.3%.[4] These patients are often young and surgery in the form of hysterectomy is unsuitable and unsafe. It is also difficult to remain compliant on drug therapy indefinitely. Furthermore, a reported 25% of gynecologic surgeries involve abnormal uterine bleeding.[5] Modern gynecology dictates the trend toward conservative therapy for cost containment and because many women desire to preserve their uteruses. Levonorgesterol Releasing Intrauterine System (LNG-IUS, Mirena) reduces bleeding in women with menorrhagia due to benign causes.[6] Aim of this study was to determine whether Mirena can safely reduce menstrual blood loss and improve quality of life in such patients.

PATIENTS AND METHODS

This Quasi experimental study was carried out in the out patient department of Military Hospital Rawalpindi from January 2004 to January 2007 and 24 patients were enrolled in the study. Out of these, 18 (75%) were with bleeding disorders (including 3 with CLD due to Hepatitis C) and 6 patients (25%) were on anticoagulants. Amongst those on warfarin, 5 (20.8%) had prosthetic heart valves and 1 (4.1%) had cardiomyopathy. All had severe menorrhagia and no pelvic pathology. MBL was assessed objectively using PBAC as described in Royal College of Obstetricians and Gynecologists

(RCOG) guideline with score of 100 equal to 80 ml blood loss.[7] LNG-IUS was inserted on day 5-8 of period. Hb and menstrual loss were measured at 3, 6 and 12 months. At the conclusion of study, patient satisfaction was assessed on a scale of four, from not satisfied to extremely satisfied. Statistical analysis was done by measuring menstrual blood loss, and change in Hb was analyzed before and after insertion of Mirena by chi square test and paired 't' test respectively using SPSS version 10.

RESULTS

Majority of patients belonged to age group 35-40 (Table 1). Baseline MBL was heavy in these ladies. Most of them were already on norethisterone, tranexamic acid / mefanamic acid for treatment of menorrhagia. It was not possible to get them off treatment to calculate the real base line. One young lady was on continuous high dose norethisterone for the past one year and still had acyclical irregular bleeding

Table 1. Demography of patients (n=24).

Age group	Number	Percentage †
24-30 years	4	16.6
30-35 years	4	16.6
35-40 years	9	37
40-45 years	7	29.8

† Percentages have been rounded off.

Table 2 shows the breakdown of patients with Von Willebrand's topping the list. MBL was heavy on PBAC; (158; range 102-780ml) and decreased to 62 ml (range 10-140ml) at 3 months, 40 ml (range 0-125ml) at 6 months and 25 ml (range 0-110ml) at one year ($p<0.001$) (Table 3).

Table 2. Diseases contributing to bleeding disorder (n=24).

Disease	Number	percentage
Von Willebrand's	6	25
Thrombocytopenia	5	21
Bernard soulier syndrome	2	8.3
Factor V11deficiency	1	4.5
Factor 1X deficiency	1	4.5
Cardiac patients on warfarin	6	25
Chronic liver disease	3	12

Mean Hb level before and at 3, 6 and 9 months showed a dramatic increase ($p=0.001$) and at one year, mean Hb levels in the 22 patients that were continuing with Mirena were 10.8±0.4815 (Table 4).

Table 3. MBL reduction.

Time scale	Median MBL in ml	MBL difference	P value
Baseline	158 ± 32.4		
3 month	62.4 ± 24.5	96	<0.001
6 month	40 ± 14.5	118	<0.001
12 months	25 ± 1.29	133	<0.001

Values have been rounded off. n=24 baseline; 3 month onwards n = 22 (Dropout/loss to follow up =2).

Some of these patients had received blood transfusions pre insertion, 1-3 times per year (e.g. 2 with ITP, one each with Bernard Soulier and CLD). None required any transfusions following insertion. After one month, patients also discontinued mefanamic and tranexamic acid.

Table 4. Mean Hb levels.

Time scale	Hb level (g/dl)	P value
Pre insertion	8.1 ± 0.4995	
3 months	8.7 ± 0.4987	0.001
6 months	9.1 ± 0.4972	0.001
12 months	10.2 ± 0.4815	0.001

n=24pre insertion; 3 months onward n=22

The rate of amenorrhea at one year was 3/22 (13%). The incidence of inter menstrual spotting was 7/22 (31 %) at one year which reduced patient satisfaction in some patients. The discontinuation rate was low. One patient expelled the device after one month and one was lost to follow up. Remaining 22 patients continued with Mirena.

Satisfaction status	number	percentage
Not satisfied	3	13.6
satisfied	4	18.2
Very satisfied	6	27
Extremely satisfied	9	41

Table 5. Patient satisfaction at one year n=22.*

*Percentages have been rounded off.

Majority of patients were extremely satisfied or satisfied and would recommend the treatment to a friend. Three (13%) unsatisfied patients were still more than willing to continue LNG-IUS (Table 5).Two had mild continuous bleeding and one had migraine with levonorgesterol.

DISCUSSION

The levonorgesterol-Releasing Intrauterine System has been advocated for the treatment of menorrhagia as an alternative to surgery.[7] The LNG-IUS was developed during the 1980s and licensed first for contraception in Finland in 1990.[8] The estimated number of current LNG-IUS users worldwide in approximately 100 countries is more than four million.[9] The LNG-IUS has been shown to reduce MBL more than tranexamic acid, non steroidal anti-inflammatory drugs, danazol, oral progestogens, combined oral contraceptives, or long-term norethisterone in these patients.[10] LNG-IUS cuts down the exorbitant cost significantly in patients with idiopathic menorrhagia.[11] The cost of Mirena in our study was around Rs7000/- and monthly cost of looking after menorrhagia was < Rs100/- due to long duration of use.

We showed that use of LNG-IUS was associated with a significant reduction in the number of days of bleeding and MBL in patients with menorrhagia. Reduction of excessive blood loss was seen as early as 1st month. Afterwards, the trend of reduced menstrual bleeding was sustainable, culminating in amenorrhea or oligomenorrhea in many women. The amenorrhea rate of 30% in our study was much lower than 60-70% at one year reported.[9] Commensurately, an increasingly significant rise in the mean Hb level was also recorded, which was most pronounced after one year of insertion of LNG-IUS. The decrease in MBL was as dramatic as in other studies where Mirena was used for idiopathic menorrhagia but the rate of intrmenstrual spotting was much higher;31% at one year compared to 4-8 % in other studies.[12] Despite high rate of spotting, drop out rate was insignificant. Though 13% of patients were dissatisfied with treatment, they wanted to continue the device to avoid surgical intervention.

A study from Sweden showed that LNG-IUS was an effective non-surgical option for the management of menorrhagia and dysmenorrhoea that has additional benefit as a contraceptive and in relieving premenstrual syndrome.[8] Same has been observed in other studies with less cost.[13,14] In our study, continuance rate was higher (91%) than 65-79% reported by others.[15] According to the Cochrane Review (1966 to 2005), LNG-IUS was more effective than cyclical norethisterone (for 21 days) as a treatment for heavy menstrual bleeding.[16] In our study, women with an LNG IUS were more satisfied and willing to continue with treatment despite side effects. It's cost was less than hysterectomy and there has been no evidence of a difference in quality of life measures between these groups.[17,18.]

CONCLUSION

LNG-IUS reduced bleeding in women with menorrhagia due to bleeding and coagulation disorders. The patient acceptance and satisfaction was high. Main problem was intermenstrual bleeding. If patients can be counseled before insertion, continuation rates can be high. This treatment is cheaper and more effective than current medical therapy for women with menorrhagia who want to retain their fertility and avoid high risk surgery.

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Received: April 12, 2009 Accepted: July 27, 2009

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