

“Mirena as an Alternative to Hysterectomy in Cases of Dub”

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Abstract

Introduction: Dysfunctional uterine bleeding is the leading cause of hysterectomy due to conventional treatment failure. Levonorgestrel releasing intra uterine device (Mirena) is found to solve this issue by better control of bleeding and thus reducing hysterectomy rate.

Objective: To measure the efficacy of Mirena as compared to OCP's in control of DUB and to determine that it is an alternative to hysterectomy.

Study Design: It was an interventional (experimental) type of study.

Setting: Department of Obstetrics and gynecology Unit 11 Lady Willingdon Hospital, Lahore.

Duration with Dates: In a total of 60 patients presenting with DUB in out patient department from 7th April 2004 to 31st December 2005.

Subjects and Methods: In a total of 60 patients selected were randomly allocated to Group A and B to receive Mirena and OCP's respectively. Both groups were followed at 6 months and 1 year of treatment. Main outcome measures were patient satisfaction with current treatment and their decision to continue or opt for hysterectomy. 80.7% women receiving Mirena

were satisfied with their treatment, while only 30% in the OCP's group (p-value < 0.05) at the end of study. 7.69% was the discontinuation rate of treatment in Mirena group while it was 50% in the control group (p-value < 0.05).

Conclusion: Mirena is a better option in the treatment of DUB and it can prove to be an alternative to hysterectomy, while we want a more conservative type of treatment.

Keywords:

1. Dysfunctional uterine bleeding.
2. Menorrhagia.
3. Abnormal uterine bleeding.
4. Levonorgestrel.
5. Oral contraceptive pills.
6. Tranexamic acid.
7. Estrogens.

Introduction

Dysfunctional uterine bleeding is defined as “excessive bleeding (excessively heavy, prolonged or frequent) of uterine origin which is not due to demonstrable pelvic disease, complication of pregnancy or systemic disease”.¹

Single episodes of DUB generally carry a good prognosis but patients who experience repetitive episodes might experience significant consequences. Frequent and heavy uterine bleeding increases the risk of iron deficiency anemia. Flow can be copious enough to require hospitalization for fluid management, transfusion or intravenous hormone therapy. Chronic unopposed estrogen stimulation of endometrium seen

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in most of cases of DUB increases the risk of endometrial hyperplasia and endometrial carcinoma. Therefore timely and appropriate management will prevent most of these problems. Menorrhagia affects 10 – 30% of menstruating women at any time and may occur at some time during perimenopause in up to 50% of women,² telling how much high incidence of this problem in our patients attending outpatient department. So it is usually the problem of females of 38 – 45 year age group³ and it is the major reason for hysterectomy among these women⁴ as until recently medical treatment has been disappointing.⁵

To date levonorgestrel releasing intrauterine system is one of the most effective, reversible, long-term treatment for menorrhagia.⁶ This new intrauterine system, a T – shaped device made of soft, flexible plastic contains 52 mg of the progestin levonorgestrel in a release controlling membrane with a monofilament removal thread.⁷⁻⁸ It releases levonorgestrel at the rate of 20 micrograms / 24 hours⁹ and is effective for at least 5 years.⁷ The glands of the endometrium become atrophic and epithelium becomes inactive under its effect.¹⁰ It exerts its effect only locally and ovarian function is entirely unaffected with normal estradiol concentrations.¹¹

In a study of 165 women 90 % completed 3 year use of this intrauterine system and marked improvement in menstrual pain was reported. Complete or temporary amenorrhea was generally observed.⁷⁻⁹

The purpose of the study was to determine how effectively Mirena controls bleeding and thus reduced the rate of hysterectomy among these patients. Objectives of the study were:

1. To evaluate the efficacy of Mirena in control of bleeding, dysmenorrhoea and improvement in daily activities of patients as compared to conventional medical treatment.
2. To determine that Mirena is better alternative to hysterectomy with less morbidity, mortality and duration of hospital stay.

Materials and Methods

The study was carried out in the department of Obstetrics and Gynecology Unit II of Lady Willingdon Hospital, Lahore. Study was completed in 2 years from 7th Apr 2004 – 31st Dec 2005. Sixty cases with DUB were enrolled into study. They were randomly distributed in 2 groups by systematic randomization

technique. Women between age 40 – 50 with DUB of at least 6 months duration having normal coagulation and thyroid function tests and with endometrial sampling report negative for malignancy were included in the study. Also any patient with fibroid uterus greater than 3 cm or with active liver disease, adnexal tumor or cyst and pelvic inflammatory disease of more than 12 months duration were excluded to enter the study. This was interventional (experimental) type of study.

Data Collection Procedure

Patients presenting in out – patient department with abnormal uterine bleeding were evaluated by detailed history, examination and investigations to rule out any organic or medical cause. Sixty patients with DUB fulfilling the inclusion and exclusion criteria were then enrolled in the study after taking informed consent and ensuring confidentiality.

These 60 patients were randomly allocated in two groups by using random number table, 30 patients in each group. Group A received Mirena while Group B received OCP's available by the name of Tab. Famila 28. It contains ethinyl estradiol 0.03 mg and levonorgestrel 0.15 mg. Side effects observed with both types of medicine were explained to both groups. Patients were then followed up after 6 months and 1 year of treatment. Data was then entered in proforma for each patient. End of study was when patient decided for hysterectomy or continued treatment for 1 year follow up duration. Patients who had chosen hysterectomy during 1 – year period were followed up by their histopathology report to determine the cause of treatment failure.

Data Analysis

Data was analyzed using SPSS software version 12.0. The data was entered in the computer system and necessary cleaning was done. The study variable included: types of dysfunctional uterine bleeding, histopathological findings of D&C, and side effects of the treatment, treatment continuation and reasons of treatment discontinuation. The outcome variable included in the study were reduction in the amount of blood loss, relieving of dysmenorrhoea, improvement in daily activities, satisfaction with the treatment, preference for hysterectomy, and level of hemoglobin. The frequency distribution of above-mentioned variables was generated.

In order to compare the treatment efficacy between study group "A" and "B" at six month and one

Table 1: Comparison of treatment efficacy in study groups after 6 months of treatment.

Comparison parameters	Group "A" (n = 29)		Group "B" (n = 30)		Chi-Square Test
	Frequency	Percentage	Frequency	Percentage	
Reduction in the amount of blood loss	21	72.4	12	40.0	Chi-Sq = 6.29 P value = 0.012
Relieving of dysmenorrhoea	18	62.3	15	50.0	Chi-Sq = 0.87 p value = 0.351
Improvement in daily activities	23	79.3	10	33.3	Chi-Sq = 12.65 p value = 0.0004
Satisfaction with current treatment	25	86.2	14	46.6	Chi-Sq = 10.29 p value = 0.0013
Preference for hysterectomy	C 3	10.3	20	66.4	Chi-Sq = 19.67 p value = 0.0000

Table 2: Comparison of treatment efficacy in study groups after 1 year of treatment.

Comparison parameters	Group "A" (n = 26)		Group "B" (n = 10)		Fisher Exact Test
	Frequency	Percentage	Frequency	Percentage	
Reduction in the amount of blood loss	21	80.7	2	20.0	p-value = 0.0014
Relieving of dysmenorrhoea	19	73.1	1	10.0	p-value = 0.0016
Improvement in daily activities	15	57.6	2	20.0	p-value = 0.0652
Satisfaction with current treatment	21	80.7	3	30.0	p-value = 0.0069
Preference for hysterectomy	2	7.69	5	50.0	p-value = 0.0105

Table 3: Comparison of mean hemoglobin level in study groups after 6 months and 1 year of treatment.

Study Group	(n)	Mean	Standard Deviation	Student t Test
After 6 months treatment				
Group A	29	9.59	1.55	t - value = 2.38 p-value = 0.021
Group B	30	8.65	1.48	
After 1 year treatment				
Group A	26	10.03	1.30	t - value = 2.51 p-value = 0.017
Group B	10	8.90	0.91	

year interval, Chi-square test was used for qualitative variables such as reduction in the amount of blood loss, relieving of dysmenorrhoea, improvement in daily activities, satisfaction with current treatment, preference for hysterectomy and t-test was used for quantitative variable such as haemoglobin level. The level of

significance for the statistical test was taken as $p \leq 0.05$.

Results

Evaluation of the response to treatment in each group has shown reduction in blood loss in 21 out of 29

(72.4%) in group A and 12 out of 30 patients (40%) in the control group (P-value < 0.05), after 6 months of treatment. When these results were compared with the results after 1 – year of treatment 80.7% of the patients in group A and 20% in – group B (P-value < 0.05) in case of each group had reduction in blood loss (see table 1 and 2).

Other criteria used for assessment of effectiveness of treatment like relieving of associated symptoms and dysmenorrhoea, improvement in performance of daily activities have shown significant differences between 2 groups at 6 month and 1 year of treatment as shown in tables 1 and 2. It is important to note that with passage of time there is significant improvement in response to treatment as the results are compared at 6th month and at 1 year of treatment (P-values ≤ 0.05). Similarly level of haemoglobin in both groups were compared at 6 months and 1 year of treatment which shows significant improvement in Group A as compared to Group B (see table 3).

Primary measures of efficacy were; patient satisfaction for treatment and patient’s decision to continue with the treatment or to opt for hysterectomy in each group.

25 out of 29 (86.2%) in group A and 14 out of 30 (46.6%) in group B were satisfied with their current treatment (P-value ≤ 0.05) at 6th month of study period

(see table 1). When these values are compared at 1 year of treatment 21 out of 26 (80.6%) in group A and 3 out of 10 (30%) in group B were satisfied with the treatment (P-value < 0.05), thus maintaining the high satisfaction rate in group A than group B (see table 2).

An important aspect of the study is that high percentage of patients in – group B was disappointed to their treatment and wanted hysterectomy as their final treatment. It was observed that only 3 patients out of 29 (10.3%) in group A, as compared to, 20 out of 30 (66.6%) patients in group B, (P-value < 0.05) opted hysterectomy as their final treatment. Even more significant is the higher treatment failure rate in group B after 1 year of therapy, when 2 out of 26 (7.69) in group A and 5 out of 10 in group B have chosen hysterectomy (P-value < 0.05) (see tables 1 and 2).

These patients of control group were offered to have an option for Mirena insertion, before they undergo hysterectomy. And 10 out of 25 (40%) were willing to have a trial of Mirena before hysterectomy, while 15 out of 25 (60%) refused and underwent hysterectomy. The reason for discontinuation of treatment is shown in table 4.

Side effects observed with each type of treatment during 1 year are shown in table 5 and 6. This data shows more number of patients had side effects in group B.

Table 4:
Reason for discontinuation of treatment.

Case No.	Month of Discontinuation	Reason for Discontinuation	Histopathology Report after Hysterectomy
1.	3 rd	Expulsion	Adenomyosis
2.	4 th	Irregular bleeding	None
3.	4 th	Irregular bleeding	Adenomyosis
4.	5 th	Vaginal discharge	Chronic endometritis and cervicitis
5.	7 th	Irregular bleeding	None
6.	9 th	Pain	Endometriosis

Table 5: Side effects observed after 6 months of treatment.

	Group A (n = 29)		Group B (n = 26)	
	No. of Patients	%	No. of Patients	%
Infection	2	6.6	–	–
Irregular bleeding	16	55	20	66.6
Pain	5	16.6	–	–

Side effects	Group A (n=26)		Group B (n=10)	
	No. of patients	%	No. of patients	%
Headache weight gain	19	73.1	–	–
Nausea vomiting	24	92.3	–	–
Infection	–	–	–	–
Irregular bleeding	6	23	6	60.0
Pain	9	34.6	–	–
Headache weight gain	–	–	5	56
Nausea vomiting	–	–	1	10

Table 6: Side effects observed after one year of treatment.

In order to find out the cause of failure of Mirena, histopathology reports of the 6 patients undergoing hysterectomy were followed. Adenomyosis was found in 2 cases (a case of expulsion and the other one with irregular bleeding), endometritis and chronic cervicitis in 1 patient (one with abnormal vaginal discharge), endometriosis in another 1 case (a case with lower abdominal pain and backache). No significant histopathology finding was observed in 2 cases (each one of these had irregular bleeding) see table 4.

Discussion

Heavy menstrual bleeding is a common cause of iron deficiency anemia and may affect woman's quality of life. In at least half of women who undergo hysterectomies, heavy bleeding is the main presenting complaint.

Concerns have been expressed that unnecessary surgery is being performed and treatment for this common condition is not appropriate.

One difficulty with the variable research is that the focus has been on trying to measure blood loss accurately as a response to treatment. There are problems with this approach. First there is a large discrepancy between women's perception of blood loss and accurate measurement of blood loss. Secondly, the current gold standard for measuring blood loss is a modification of alkaline hematin technique, but this method is impractical clinically. Also, the pictorial blood loss assessment chart is a semi-quantitative method with a scoring system, but its accuracy as a diagnostic test has been questioned. Other outcomes may better reflect improvement in blood loss such as quality of life, patient satisfaction, and acceptability of treatment. That's why I have used these in my study.

The currently available treatments for DUB include NSAID's, anti-fibrinolytics and hormones and

their effectiveness, side effects profile and acceptability to women show considerable variation. A recent decision analysis showed that LNG-IUS ranks much higher than all other medical treatments when effectiveness, length of treatment and acceptability are all taken into account.

In addition LNG – IUS offers comparable improvements in quality of life and psychosocial well being to hysterectomy. But it is a major surgical procedure with considerable morbidity and mortality rate. Also it has greater costs and longer recovery time. In many studies 38 – 50% is the incidence of hysterectomies for DUB. If a more conservative treatment like LNG-IUS is used, the rate of this invasive technique can be decreased.

This was the initiative which has led me to carry out this study to assess that Mirena is a better alternative to hysterectomy in patients with DUB. I tested this new medical treatment as an alternative to hysterectomy, as hysterectomy rate is found to be higher in the conventional medical treatment group. My data suggest that it is a good alternative. 80% of the patients with the LNG-IUS decided to continue the treatment while only 17% of patients in the control group decided to continue the treatment. Thus majority of patients in the control group choose hysterectomy at the end of study.

LNG – IUS is licensed in many countries for relief of menorrhagia. It has been in the market in Finland since 1990, and its reputation has spread worldwide. It leads to reduction in bleeding by more than 80% after 3 – 6 months and more than 90% at 12 months.¹²

A study carried out by Shahnaz Hassan Siddique, response rate of OCP's on treatment of DUB was 50 – 60%.¹³ In a more recent open randomized study, reduction in menstrual blood loss by 87% was observed in patients using norethisterone treatment and only 22% wanted to carry on the regimen, while LNG – IUS created reduction in menstrual blood loss by 94% and

76% wanted to continue with it. It was observed that this system has cut the hysterectomy rate by up to 50%.¹⁴ In my study, 80.7% cases observed reduction in blood loss and 80% wished to continue the same treatment as compared to conventional treatment group in which only 20% reduction in blood loss was observed and only 16.7% wished to continue the treatment.

The quality of life of women suffering from menorrhagia is impaired in many aspects. Excessive bleeding or pain, or both may impose severe constraints on their professional, social and family activities. In a study published in British Medical Journal¹⁵ comparing Mirena with the other medical treatment group showed no improvement in the control group, while it significantly improved in patients with LNG – IUS in all aspects evaluated. Patients had gradually reduced days of spotting along with improvement in other symptoms. A reduction in dysmenorrhoea has been reported by a number of authors. Perhaps most interestingly there was a 56% reduction in premenstrual syndrome along with improvement in dysmenorrhoea in one study, which was maintained even after 5 years.¹⁶ Similarly in my study group 62% of the patients had relieve of associated symptoms and 75% had improvement in daily activities as compare to 50% and 33.3% in the control group in each aspect respectively.

In Australian and New Zealand journal of Obs. & Gyn., a study was published in which 120 patients using LNG – IUS had to fill a patient satisfaction questionnaire. Results showed 87% continuation rate and 76% satisfaction rate.¹⁷ In my study 80% is the satisfaction rate in LNG – IUS group. In the same study no women removed Mirena for hormonal side effects except for irregular bleeding. In another study carried out in 1998, for three months duration, which compared Mirena with oral hormonal treatment for menorrhagia, there was reduction to normal blood loss in both groups but due to side effects and reluctance to take the pill daily, only 20% of patients wished to continue the pills as opposed to 80% of patients in LNG – IUS who wished to continue the system.¹⁸ In my study hormonal symptoms like acne, hirsutism, weight gain, nausea, vomiting and also poor compliance has led to only 16.7% of patients to continue the OCP's as compare to 80% in the Mirena group. Also it is important to note that no patient in Mirena group experienced hormonal symptoms.

The short – term results with the current study design also subject to bias because of the potential dis-

appointment of control group as regards continuing with their current treatment. This however has not affected the overall conclusion.

Although it has been observed that hysterectomy has the highest satisfaction rate in treatment of menorrhagia than all other medical and surgical measures, it is also an invasive procedure with high morbidity and mortality rate. In a study carried out in Pakistan 285 patients who have undergone hysterectomy were analyzed regarding morbidity. The commonest indication was found to be DUB. Common complications were hemorrhage 9.3%, urinary tract infection 6.3%, and wound infection 5.8%. The mean postoperative hospital stay was 5 – 7 days.¹⁹ Another important aspect is that it is quite costly procedure. The cost is about double than LNG – IUS after 5 years of follow up while improvement in quality of life being comparable.¹¹

Keeping in view this high mortality and morbidity of this invasive procedure, different options, the most suitable one Mirena should be tried first if we really want to reduce or avoid to face the complications of major surgery. A reduction in the number of hysterectomies, even by less than half would be a considerable achievement. Even greater reduction in rate of hysterectomies could be achieved if medical treatment with LNG – IUS could be started at an earlier stage.

Since the main reason for discontinuation of Mirena is menstrual dysfunction in early months of treatment, it is important that patients receive appropriate counseling prior to insertion of this device. It is seen that women who were adequately counseled about the possibility of irregular bleeding or spotting appear to be more satisfied with their choice of treatment, less concerned about changes in menstrual function.

Conclusion

Until recently DUB has been treated by OCP's and other medical treatments, which have a high failure rate and leading to hysterectomy in most of the cases. As it has been seen in this study that Mirena is better than conventional medical treatment in controlling bleeding and other symptoms associated with it, it must be a first option before taking a final decision for hysterectomy in these cases. It has good compliance and easy for the patient, as no need to take medicine daily and at fixed time, also it is an outdoor procedure requiring no hospital admission.

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