

Comparative Trial of Levonorgestrel Intrauterine System and Norethisterone for Treatment of Idiopathic Menorrhagia

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ABSTRACT

Objective: To compare efficacy and acceptability of the levonorgestrel releasing intrauterine system and norethisterone for treatment of idiopathic menorrhagia.

Study Design: Randomized control trial.

Place and Duration of Study: Department of Obstetrics and Gynaecology Department, Pakistan Ordinance Factory Hospital, Wah Cantt from 1st July 2009 30th June 2010.

Methodology: Seventy six patients with regular and heavy menstrual bleeding with decrease hemoglobin levels, age ranging between 35-45 years were selected. These patients were having anemia and the other general physical examinations were normal. The pelvic examination was also normal. The cervical smear cytology was unremarkable. They were divided into two groups; Group A, levonorgestrel releasing intrauterine system (Mirena) was inserted into the uterus and group B, Norethisterone tablet was prescribed at a dose of 5 mg three times a day. Haemoglobin, number of days of menstruation per month and number of pads soaked per day were noted.

Results: The mean age in group A was 39.89±3.24 years and mean age in group B was 40.58±3.42 years and number of parity in group A was 4.53±1.08 and in group B 4.26±1.31. The mean haemoglobin in group A was 10.89±0.30 and in group B was 10.82±0.32. Statistically there was no significant ($P>0.05$) difference between two groups. The mean number of days in group A was 2.00±0.81 and in group B was 3.63±0.75. Statistically there was significant ($P<0.05$) difference between two groups. The mean number of pads used in group A was 1.63±0.67 and in group B was 2.68±0.62. Statistically there was significant ($P<0.05$) difference between two groups. When compared the patient's acceptability, 30 (78.9%) women have acceptability in group A while in group B, 28 (73.6%). Statistically there is no significant ($P>0.05$) difference between the two groups.

Conclusion: The norethisterone and levonoregestrel releasing intrauterine system are effective treatments for menorrhagia. The subsequent is very effective treatment of idiopathic menorrhagia and is associated with higher rates of satisfaction as compared to norethisterone therapy.

Key Words: Trial, Levonorgestrel releasing intrauterine system, Norethisterone, Idiopathic menorrhagia

INTRODUCTION

The origin of term menorrhagia is Greek language the term "men or meno" meaning the month and the "rrhagia" meaning to rush out/burst forth. By definition menorrhagia is defined as blood loss of more than 80 mL/cycle or menstrual bleeding lasting more than 7 days per cycle. It persists for several consecutive cycles without any postcoital or intermenstrual bleeding.¹ It is characterized heavy menses or prolonged menstrual flow. The patients present with acute distress due to blood loss, fatigue or light-headedness, orthostasis, tachycardia and pallor.²

The main causes of menorrhagia are dysfunctional uterine bleeding (DUB), fibroids, endometrial or cervical polyps, endometrial hyperplasia, endometrial or cervical cancer, adenomyosis, pelvic inflammatory disease (PID), coagulation disorders, hypothyroidism, drugs such as warfarin and intrauterine devices (IUD).^{3,4}

Idiopathic menorrhagia (IM) is common condition which presents with heavy regular menstrual bleeding without any recognized cause such as no pelvic pathology or nor a bleeding disorder and patient is not taking antiplatelets, anticoagulants and thrombolytics.³ It is necessary for diagnosis of idiopathic menorrhagia to exclude all the causes of menorrhagia. The woman's suffering from IM, are mostly diagnosed as dysfunctional uterine bleeding (DUB).^{1,5}

There are various mechanisms, which demonstrate the pathogenesis of dysfunctional uterine bleeding, such as increased female genital tract fibrinolytic activity and variation in prostaglandin levels and.¹ Due to this inhibitors of fibrinolysis and prostaglandin synthetase inhibitors are prescribed in the treatment of IM, which are effective and they reduce menstrual blood loss by about 50% and 25% respectively.⁴ The other medical treatments consist of combined oral contraceptive pill, the norethisterone, gonadotrophin releasing hormone analogues, danazol and levonorgestrel releasing intrauterine system.^{6,7}

The menorrhagia is a common complaint in indoor and outdoor patients of obstetrics and gynecology department patients.⁸ These patients are mostly referred by general practitioners. In these patients suffering from IM, hysterectomy was reported in 60% of patients. The hysterectomy is an effective treatment in those women who have completed their family or not require conception or further conception, but keep it in mind that hysterectomy is major operation.^{3,4}

MATERIALS AND METHODS

This randomized control trial was conducted in Obstetrics and Gynaecology Department, Pakistan Ordinance Factory Hospital, Wah Cantt from 1st July 2009 30th June 2010. Seventy six patients with regular and heavy menstrual bleeding with decrease hemoglobin levels, age ranging

between 35-45 years were selected for this study. These patients were having anemia and other general physical examination was normal. The pelvic examination was also normal. The cervical smear cytology was unremarkable. Women with fibroid uterus, endometrial polyp, endometriosis, pelvic inflammatory disease, coagulation disorders and hypothyroidism were excluded. They patients were placed into two groups. The Group A consist of intrauterine system containing levonorgestrel (Mirena) was placed into the uterus and group B was prescribed Norethisterone tablet 5 mg 3 times a day for 6 months. Hemoglobin level was measured before starting treatment and then once every 3 months after start of treatment for six months. Number of days of menstruation per month before start of treatment and then once every 3 months after treatment for 6 months was noted down. Number of pads (Always Super Plus) soaked per day before treatment and then once every 3 months were noted. The data entered and analyzed through SPSS-22. Student's 't' test was used for comparison of quantitative variables like number of days, number of pads and haemoglobin. For patient's acceptability, Chi square test was used. P value <0.05 was considered statistically significant.

RESULTS

The mean age in group A was 39.89 ± 3.24 years and mean age in group B was 40.58 ± 3.42 years. The majority of women were in the age range of 35-40 years, 23 (60.5%) women in group A and 20 (52.6%) women in group B. Maximum number of parity, 3-4, 20 (52.6%) in group A and (n = 25) 65.7% in group B and minimum number of parity was recorded between 5-7 (n = 18) 47.4% in group A and (n = 13) 34.3% in group B. The mean number of parity in group A was 4.53 ± 1.08 and in group B 4.26 ± 1.31 (Table 1).

There were 23 (60.5%) in group A and 24 (63.1%) in group B having maximum level of haemoglobin between 10-10.9 [g/dl] and 15 (39.5%) in group A while in group B, 14 (36.9%) having minimum level haemoglobin between 11-11.6 [g/dl]. The mean haemoglobin in group A was 10.89 ± 0.30 and in group B was 10.82 ± 0.32 . Statistically there was no significant ($P > 0.05$) difference between two groups (Table 2).

The maximum women between 1-2 days (n = 26) 68.4% in group A and 37 (97.4%) women between 3-5 days in group B were noted. The minimum number of women recorded between 3-5 days (n = 12) 31.6% in group A and 1 (2.6%) woman in group B. The mean number of days in group A was 2.00 ± 0.81 and in group B was 3.63 ± 0.75 . Statistically there was significant ($P < 0.05$) difference between two groups (Table 3).

In group A, 34 (78.4%) women were used 1-2 pads and 3-4 pads used 4 women in group A. While in group B, 15 (39.5%) women were 1-2 pads and 23 (60.5%) used 3-4 pads. The mean number of pads used in group A was 1.63 ± 0.67 and in group B was 2.68 ± 0.62 . Statistically there was significant ($P < 0.05$) difference between two groups (Table 4).

When compared the patient's acceptability, 30 (78.9%) women have acceptability in group A while in group B, 28 (73.6%). Statistically there is no significant ($P = 0.589$) difference between the two groups (Table 5).

Table 1: Demographic information of the patients in both groups

Variable	Levonorgestrel releasing intrauterine system (n = 38)		Norethisterone (n = 38)	
	No.	%	No.	%
Age (years)				
35-40	23	60.5	20	52.6
41-45	15	39.5	18	47.4
Parity				
3 - 4	20	52.6	25	65.7
5 - 7	18	47.4	13	34.3

Table 2: Distribution of patients by haemoglobin in both groups

Haemoglobin (g/dl)	Levonorgestrel releasing intrauterine system (n = 38)		Norethisterone (n = 38)	
	No.	%	No.	%
10.0 – 10.9	23	60.5	24	63.1
11.0 – 11.6	15	39.5	14	36.9
Mean±SD	10.89±0.30		10.82±0.32	
P value	>0.05			

Table 3: Distribution of patients by number of days in both groups

No of days	Levonorgestrel releasing intrauterine system (n = 38)		Norethisterone (n = 38)	
	No.	%	No.	%
1 – 2	26	68.4	1	2.6
3 – 5	12	31.6	37	97.4
Mean±SD	2.00±0.81		3.63±0.75	
P value	<0.05			

Table 4: Distribution of patients by number of pads in both groups

No. of pads	Levonorgestrel releasing intrauterine system (n = 38)		Norethisterone (n = 38)	
	No.	%	No.	%
1 – 2	34	89.4	15	39.5
3 – 4	4	10.6	23	60.5
Mean±SD	1.63±0.67		2.68±0.62	
P value	<0.05			

Table 5: Distribution of patient's acceptability in both groups

Patient's acceptability	Levonorgestrel releasing intrauterine system (n = 38)		Norethisterone (n = 38)	
	No.	%	No.	%
Yes	30	78.9	28	73.6
No	8	21.1	10	26.4

$\chi^2 = 0.291$

$P = 0.589$

DISCUSSION

There are various medical treatments for IM. In this particular study reduction in menstrual blood loss achieved using various first line treatments. This treatment consists of mefenamic acid, tranexamic acid, combined oral contraceptive pill, prostaglandin synthetase inhibitors, gonadotrophin releasing hormone analogues and danazol.⁹⁻¹¹ The above treatment is mostly for short period of time, due to their side effects. In our study the intrauterine system containing levonorgestrel was found having impressive and effective treatment for IM and it reduced the menstrual blood.

According to Barrington and Bowen-Simpkins¹² reported that group of women were treated with levonorgestrel intrauterine releasing system and 80%

reduction is found in menstrual blood loss in patients suffering from IM. Whereas in the present study [mean age 39.89 years, age range 35-45 years] (Table 1) and improvement in 78.9% women (Table 5). The results of the present study are comparable with Barrinton and Bowen-Simpkins.¹²

In idiopathic menorrhagia the use of levonorgestrel intrauterine releasing system is very useful and it was reduced the days of menstrual cycle and decreased the menstrual blood loss.¹³ This is due to effect is local action of the levonorgestrel in the uterus endometrium. It reduces the production of many active compounds in the endometrium and reduces the excessive blood loss immediately after insertion and found in more than 90% of women. The levonorgestrel is having few side effects and complications. Mostly there are no fertility problems. The benefits of levonorgestrel consist of reduction in invasive procedures such as hospitalization, endometrial ablation and hysterectomy. The result of the present study is consistent with Luukkainen.¹³

The heavy menstrual period is a subjective complaint. In many studies, it has been observed, that 50% of women who were presented with complain of heavy periods were having normal menstrual blood loss.¹⁴

The levonorgestrel and norethisterone are the best medical treatment for the IM. In this study, we found that the levonorgestrel was a very effective treatment and it reduced the menstrual blood loss within normal limits in most of the patients. There were no toleration problems within most of the women, who were taking the levonorgestrel. The most of the women were agree to continue long term treatment with levonorgestrel. There were few systemic and local side affects with levonorgestrel. The advantages of this particular drug are that it acts as a very useful contraceptive. The other advantages are that it is easily removable and affects are reversible after removal.^{15,16}

The menorrhagia is a common gynecologic problem often needing hysterectomy. The intrauterine system containing releasing levonorgestrel reduces menstrual blood loss in most of the women, which were having no organic cause. The most of the women tolerate this particular drug and satisfied with results. The intermenstrual bleeding is noted for three months in few women after insertion. The counseling of the patients is very important before insertion. The most of the women are agree for insertion of levonorgestrel releasing intrauterine systems for the treatment of IM. This particular drug was reduced menstrual blood loss in most of the patients and it replaced hysterectomy, which was previously treatment of choice in certain patients with heavy menstrual bleeding.

CONCLUSION

The norethisterone and levonoregestrel releasing intrauterine system are effective treatments for IM. The levonoregestrel is very effective treatment of IM and is associated with higher rates of satisfaction as compared to norethisterone therapy. The levonoregestrel reduced

menstrual blood loss in most of the patients and it replaced hysterectomy, which was previously treatment of choice in certain patients with heavy menstrual bleeding.

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