Original Article

Intrauterine Progesterone Versus Oral Progesterone in the Treatment of Dysfunctional Uterine Bleeding

Sarwat Ara[1], Rashda Shahid[2], Ahmad Khan[3]

[1]Associate Professor, Gynecology & Obstetrics Department, PMC Allied Hospital, Faisalabad
[2]Senior Registrar, Gynecology & Obstetrics Department, PMC Allied/DHQ Hospital, Faisalabad
[3]Ex.House Officer, I.H.U, Faisalabad

Correspondence: *Dr. Sarwat Ara*
Associate Professor, Gynecology & Obstetrics Department, PMC Allied Hospital, Faisalabad
sarwatara_fcps@hotmail.com

Abstract

Objective: To compare the effect of intrauterine progesterone with oral progesterone in treatment of DUB.

Study Design: Randomized Control Trial.

Place and Duration: Outdoor & indoor patients in obstetrics & gynecology department Allied Hospital Faisalabad, from 1st Jan 2014 to first Jan 2015.

Methodology: Seventy-four (74) patients from outdoor and indoor with dysfunctional uterine bleeding fulfilling the inclusion and exclusion criteria were assessed for effect of both therapies. To each Group (A and B) 37 patients randomly allocated and then effects of both therapies were compared. All the variables of study were recorded and results were calculated.

Results: Decrease of menstrual blood loss was more in group A than group B assessed in the form of reduced number of pads used per day 59.4% in group A versus (vs) 32.43% in group B. Menstrual bleeding stopped 3 days earlier than usual 29.7% in group A vs 13.5% in group B. Clots were absent in 73% in group A vs 45.9% in group B. Improvement in Hemoglobin(Hb) was 59.46% in group A vs 16.22% in group B.

Conclusion: Intrauterine progesterone is more effective than oral progesterone in the treatment of DUB.

Key Words: Dysfunctional uterine bleeding(DUB), Heavy menstrual bleeding (HMB). Menorrhagia, Intrauterine progesterone, Oral progesterone(OP), Intrauterine levonorgestrel releasing system (LNG- IUS).

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Introduction

Dysfunctional uterine bleeding (DUB) or heavy menstrual bleeding (HMB) is defined as heavy and/or irregular menstruation in the absence of recognizable pelvic pathology, pregnancy or general bleeding disorders and commonly occurs at the extremes of reproductive life. It is simply called menorrhagia without an underlying cause. It may be anovulatory or ovulatory DUB.

Clinically, it is defined as a total blood loss of more than 80 ml per cycle or duration of menses lasting for more than 7 days.[2] Menorrhagia interferes with the woman's physical, emotional, social and material quality of life.[3] Medical therapy is a principal treatment for dysfunctional uterine bleeding.[4] First line treatment prostaglandin inhibitors, antifibrinolytic agents, oral contraceptive pill, oral high dose progestogens and intrauterine progesterone system

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reduce menstrual blood loss.[5,6] Cyclical 21 days treatment therapy is third line option for management of menorrhagia.[7] Oral medication suits a minority of women in the long term, and the Progesterone (levonorgestrel) releasing intrauterine system (LNG-IUS) device provides a better alternative to medical therapy and surgery in majority of cases though hysterectomy is a definitive treatment for heavy menstrual bleeding.[8] LNG-IUS was originally developed as a contraceptive device but has also been shown to be more effective in achieving a significant reduction in menstrual blood loss than any other medical treatment.[9,10]

Marked endometrial suppression with scanty menstrual bleeding are major health benefits, making its use ideal in iron deficiency anemia in woman with heavy menstrual blood loss as elevating hemoglobin levels within 3 months of LNG-IUS use and increase of in hemoglobin level up to1.5 g/dl after one year.[10,11]

Studies in Pakistan showed oral progesterone to be effective in 87.8% patients with heavy menstrual bleeding.[12] While according to an Indian study intrauterine progesterone was found to be effective in 57.7%.[13]

The main challenge of gynecologists is to select the most effective method of treatment of DUB.[14]

Methodology

It was randomized controlled trial. Observing Non probability consecutive sampling technique.

All outdoor and indoor patients in obstetrics and gynecology department, Allied Hospital affiliated with Faisalabad medical university Faisalabad from 1st Jan 2014 to first Jan 2015 including group A (37 patients) were treated by intrauterine progesterone and in group B (37 patients) were treated by oral progesterone cyclically. We kept level of significance 5% and power of test 90% proportions of patients with successful treatment in group A taking intrauterine progesterone releasing system is 57.7% (taken from Indian study, because no recent Pakistani study is available) and proportion in group B with oral progesterone is 87.8% (taken from recent study in Pakistan).

We included all women with heavy and/or irregular menstrual bleeding (in absence of any pelvic/systemic pathology, pregnancy and bleeding disorder). Our exclusion criteria was all women with heavy and/or irregular menstruation in the presence of recognizable pelvic pathology uterine fibroids, endometrial polyps, endometrial hyperplasia (that is endometrial thickness more than12 mm), pregnancy, general bleeding disorders, pelvic inflammatory disease, polycystic ovarian disease, and thyroid disease. Patients with breast cancer and genital tract malignancies.

After taking ethical committee approval and explaining the procedure, informed consent was taken. All the women, fulfilling the above-mentioned inclusion criteria were selected for the study.

Exclusion criteria were strictly followed to limit the confounding variables. Risks (spotting, amenorrhea, expulsion, uterine perforation) benefits (better compliance, reduction in blood loss leading to normal bleeding days, better quality of life, improvement in daily routine work and pain-free menstruation) was explained. A detailed history of general physical, breast, abdominal and complete pelvic examination was done. Haemoglobin was tested before insertion. Then at 3rd and 12th month.

Pelvic ultrasonography and endometrial sampling (if age>40 years) was also done before insertion. After history and examination, 74 cases with DUB were selected from outdoor and indoor. The envelopes after shuffling were distributed randomly. Half were allocated to the prescription of oral progesterone and other half had a prescription of intrauterine progesterone. Effects of both therapies were assessed after every 3 months for 12 months in terms of reduced number of pads she used, reduced number of days she bled, the absence of clots and improvement in hemoglobin level. Data was entered on Performa designed for this purpose. Telephonic contacts and addresses noted for follow up.

Results

In 74 patients minimum age was 13 and maximum 55 years with mean ±SD 32.99 ±11.40

A number of pads used by 37 patients before treatment were in intrauterine progesterone group were in the range of 3 – 10 with mean ±SD 7.03 ±1.86 and in oral progesterone group were in range of 3 – 10 with mean ±SD 5.92 ±1.53 **(Table I)**.

A number of pads used by 37 patients after

treatment in intrauterine group, were in the range of 2 – 8 with mean ±SD 5.24 ±1.38 and in oral progesterone group were in range of 3 – 8 with mean ±SD 4.86 ±1.13 (Table I).

Table I: Baseline Characteristics of Patients in Both Groups

	Variables	n	Min	Max	Mean	Standard Deviation
Intra Uterine Progesterone Group	Age of the patient	37	21	50	36.32	8.55
	Number of pads patient used before treatment	37	3	10	7.03	1.86
	Baseline hemoglobin level of the patient	37	6.8	10.4	8.859	1.13
	Number of days patient bleed before treatment	37	3	16	7.97	3.13
Oral Progesterone Group	Age of the patient	37	13	55	29.65	12.94
	Number of pads patient used before treatment	37	3	10	5.92	1.53
	Baseline hemoglobin level of the patient	37	5.9	10.4	8.757	1.094
	Number of days patient bleed before treatment	37	4	12	6.16	2.23

Table II: Passage of Clots and Duration of Menstrual Bleeding

Passage of clots before treatment	**Intra Uterine Progesterone Group**		**Oral Progesterone Group**	
	Frequency	**Percentage**	**Frequency**	**Percentage**
YES	28	75.7	29	78.4
No	9	24.3	8	21.6
Total	37	100	37	100
Passage of clots after treatment	**Intra Uterine Progesterone Group**		**Oral Progesterone Group**	
	Frequency	**Percentage**	**Frequency**	**Percentage**
Yes	10	27	20	54.1
No	27	73	17	45.9
Total	37	100	37	100
Menstrual bleeding finishing earlier than normal	**Intra Uterine Progesterone Group**		**Oral Progesterone Group**	
	Frequency	**Percentage**	**Frequency**	**Percentage**
Yes	11	29.73	5	13.51
No	26	70.27	32	86.49
Total	37	100	37	100
Decreased number of pads used/day	**Intra Uterine Progesterone Group**		**Oral Progesterone Group**	
	Frequency	**Percentage**	**Frequency**	**Percentage**
Yes	22	59.46	12	32.43
No	15	40.54	25	67.57
Total	37	100	37	100

In intrauterine progesterone group out of 37 patients before treatment passage of clots were present in 28 patients (75.7%) and absent in 9 patients (24.3%) while in oral progesterone group clots were present in 29 patients (78.4%) and absent in 8 patients (21.6%) (Table II)

In intrauterine progesterone group out of 37 patients after treatment passage of clots were present in 10 patients (27%) and absent in 27 patients (73%) while in oral progesterone group clots were present in 20 patients (54.1%) and absent in 17 patients (45.9%) p-value 0.009 (Table II).

In intrauterine progesterone group out of 37 patients haemoglobin levels were improved in 22 patients (59.46%) and no change in 15 patients (40.54%)

while in oral progesterone group out of 37 patients haemoglobin levels were improved in 06 patients (16.22%) and no change in 31 patients (83.78%) p-value 0.0005 (Table III)

Table III: Improvement of Hb level in Both groups

Improvement of Hb level after treatment	Intra-Uterine Progesterone Group		Oral Progesterone Group	
	Frequency	%	Frequency	%
Yes	22	59.46	6	16.22
No	15	40.54	31	83.78
Total	37	100	37	100

Haemoglobin levels after treatment in intra uterine progesterone group were in the range of 6.9-10.9 g/dl with mean ±SD 9.262 ±1.11. And oral progesterone group were in the range of 6.3 – 10.8 g/dl with mean ±SD 9.005 ±1.10. (Table IV)

Table IV: Characteristics of Patients After Treatment in Both Groups

	Variables	n	Min	Max	Mean	Standard Deviation
Intra Uterine Progesterone Group	Number of pads Patient used after treatment	37	2	8	5.24	1.38
	Hemoglobin level of the patient after treatment	37	6.9	10.9	9.262	1.11
	Number of days patient bleed after treatment	37	2	10	4.97	1.94
Oral Progesterone Group	Number of pads patient used after treatment	3	3	8	4.86	1.13
	Hemoglobin level of the patient after treatment	37	6.3	10.8	9.005	1.10
	Number of days patient bleed after treatment	37	3	12	5.73	2.31

Discussion

DUB or Heavy menstrual bleeding (HMB) is an important cause of ill health in women and it accounts for 12% of all gynaecology referrals in the UK[15] and 20% females in Australia are affected by DUB while in Swedish study32% were sufferer and 10 % of working females found to be absent from work due to excessive bleeding. [16]

0ne Pakistani study, gave HMB prevalence of 25% per 100 gynaecological cases.[17] Medical therapy with avoidance of unnecessary surgery is an attractive treatment option for HMB

Oral progestogens (OP) and LNG IUS offer similar endometrial protection for women with Endometrial hyperplasia while LNG IUS offers convenience, least undesirable effects, reversibility, and long-term endometrial protection as concluded by study in 2017.[14] The results of another recent study showed that LNG-IUD is more effective than MPA in treatment of simple endometrial hyperplasia .[24]

It was stressed that women with menorrhagia who presented to primary care providers, the LNG-IUS was more effective than usual medical treatment in reducing the effect of heavy menstrual bleeding on quality of life. [18,19]

As Intrauterine progesterone induces endometrial atrophy more than oral progesterone by local release o f progesterone.[20] That is why the objective of our study to demonstrate the better effect of intrauterine progesterone than oral progesterone in treatment of HMB.

The mentioned study revealed age range of 13-55 years. Mean age was 36.32 ± 8.55 in group A and 29.65 ± 12.94 in group B respectively which is in accordance with study carried in a cochrane database systemic review.[22,30]

Different studies showed comparable reduction in menstrual blood loss by the use of intrauterine progesterone similar to our study [18,21] but contrary to Gupta hp et al. [26]

Studies revealed the efficacy of LNG-IUS very well, which was also appeared accepted alternative with least side effects further superior to both oral and intramuscular progesterone in the treatment and medical management of menorrhagia.[23, ,24.25]

Results of our efforts are comparable to a study

regarding the improvement in mean hemoglobin percentage of more than 0.4g /dl within 3 months of LNG-IUS use and an increase of hemoglobin level up to1.5 g/dl after one year. [10.11,27]

LNG-IUS reduces menstrual loss by 97% in 12 months in our observation, which is comparable to studies.[27,29] It also concluded that LNG-IUS provides an implausible nonsurgical alternative in treatment of menorrhagia.[27]

Regarding menorrhagia in late reproductive years, our work supported by a study which claimed that intrauterine progesterone is an effective and overall well accepted option for the medical management of menorrhagia and offered a convenient and bleeding free transition into menopause.[9 23,28]

Our findings the better role of intrauterine progesterone in improving DUB than oral progesterone are in agreement with the results of above quoted studies. [27 28,29,30]

Patients should be educated and made aware of the mortality and morbidity associated with surgery so that compliance for medical therapy should be enhanced

Conclusion

In the context of Pakistani population with significant prevalence of HMB and illiteracy, there is need of awareness about easy and effective medical therapy like LNG-IUS which is cost effective and is outdoor procedure. It has good compliance as compared to oral progesterone therapy which has poor compliance due to regularity and punctuality. Intrauterine progestogens have no systemic side effects than OP

It is also useful in high-risk patient like Diabetes Mellitus, Cardiac patients, patients with history of thromboembolism in which oral progesterone is relatively contraindicated in high doses.

References

1. Munro MG, Critchley HO, Broder MS, Fraser IS; FIGO Working Group on Menstrual Disorders. FIGO classification system (PALM-COEIN) for causes of abnormal uterine bleeding in nongravid women of reproductive age. Int J Gynaecol Obstet. 2011;113:3–13.
2. Magon N, Chauhan M, Goel P, Malik S, Kapur K, Kriplani A, et al..Levonorgestrel intrauterine system: current role in management of heavy menstrual bleeding. J Midlife Helth. 2013;4: 8–15.
3. Kavitha T. A random survey of menstrual problems in Allithurai and Lalgudi areas of Tiruchirapalli district. J Health Edu Res Dev. 2015;3:134.
4. Casablanca Y. Management of dysfunctional uterine bleeding. Obstet Gynecol Clin North Am. 2008;35:219-34.
5. Butler WJ, Carnovale DE. Normal and abnormal uterine bleeding. In: Rock JA, Jones HW, editors. TeLinde's operative gynecology. 10th ed. Philadelphia: Lippincott Williams & Wilkins; 2008. p. 585-608.
6. Desai RM. Efficacy of levonorgestrel releasing intrauterine system for the treatment of menorrhagia due to benign uterine lesions in perimenopausal women. J Midlife Health. 2012; 3: 20–3.
7. Kadir RA. Menorrhagia: treatment options. Thromb Res. 2009;123 Suppl 2:S21-9.
8. 8-Marjoribanks J , Lethaby A, Farquhar C. Surgery versus medical therapy for heavy menstrual bleeding. Cochrane Database Syst Rev. 2016 ;(1):CD003855.
9. Kucuk T, Ertan K. Contineous oral intramuscular medroxyprogesterone acetate versus the levonogrestrel releasing intrauterine system in the treatment of perimenopausal menorrhagia: a randomized prospective, controlled clinical trial in female smokers. Clin Exp Obstet Gynecol. 2008;35:57-60.
10. Mawet M, Nollevaux F, Nizet D, Wijzen F, Gordenne V, Tasev N, et al. Impact of a new levonorgestrel intrauterine system, Levosert on heavy menstrual bleeding: results of a one-year randomized controlled trial. Eur J Contracept Reprod Health Care. 2014;19:169-79.
11. Gemzell-Danielsson K, Pirjo Inki P, Heikinheimo O..Safety and efficacy of the levonorgestrel-releasing Intrauterine system: recent insights. Expert Rev Obstet Gynecol. 2013;8:235-47.
12. Akram H, Nasir A, Rana T. The levonorgestrel intrauterine system in the management of menorrhagia. J Fatima Jinnah Med Coll Lahore. 2008;2:49-51.
13. Kriplani A, Kulshrestha V, Agarwal N, Diwakar S. Role of tranaxamic acid in management of dysfunctional uterine bleeding in comparison with medroxyprogesterone acetate. J Obstet Gynaecol. 2006;26:673-8.
14. Marnach ML, Butler KA , Henry MR , Hutz CE , Langstraat CL, Lohse CM, et al. Oral progestogens versus levonorgestrel-releasing intrauterine system for treatment of endometrial intraepithelial neoplasia. J Womens Health (Larchmt). 2017; 26: 368-73.
15. Lethaby A, Hussain M, Rishworth JR, Rees MC. Progesterone or progestogen-releasing intrauterine systems for heavy menstrual bleeding. Cochrane Database Syst Rev. 2015; 30;(4):CD002126 .
16. Farrell E. Dysfunctional uterine bleeding. Aust Fam Physician. 2004;33:906-8.
17. Abid M, Hashmi AA, Malik B, Haroon S, Faridi N, Edhi MM, et al. Clinical pattern and spectrum of endometrial pathologies in patients with abnormal uterine bleeding in Pakistan: need to adopt a more conservative approach to treatment. BMC Womens Health. **2014** 14:132.
18. Tariq N, Ayub R, Jaffery T, Rahim F, Naseem F, Kamal M. Efficacy of levonorgestrel intrauterine system (LNG-IUS) for abnormal uterine bleeding and contraception. J Coll Physicians Surg Pak. 2011; 21:210-3.
19. Gupta J, Kai J, Middleton L, Pattison H, Gray R, Daniels J, et al.Levonorgestrel intrauterine system versus medical therapy for menorrhagia. N Engl J Med. 2013;368:128-37.
20. Gallos ID, Shehmar M, Thangaratinam S, Papapostolou TK, Coomarasamy A, Gupta JK. Oral progestogens vs levonorgestrel-

releasing intrauterine system for endometrial hyperplasia ;a systematic review and metaanalysi . Am J Obstet Gynecol. 2010; 203:547.e1-10.

21. Mayo Clinic. Mirena (hormonal IUD). [on line].. 10 January 2015. .Availabe from: www.mayoclinic.org/tests-procedures/mirena/basics/definition/prc-20012867.
22. Benagiano G, Carrara S, Filippi V. Safety, efficacy and patient satisfaction with continuous daily administration of levonorgestrel, ethinylesradiol oral contraceptives. Patient Prefer Adherence. 2009;3:131-43.
23. Gallos ID , Krishan P, Shehmar M, Ganesan R, Gupta JK. LNG-IUS versus oral progestogen treatment for endometrial hyperplasia: a long-term comparative cohort study. Hum Reprod. 2013;28:2966-71.
24. Karimi-Zarchi M, Dehghani-Firoozabadi R, Tabatabaie A, Dehghani-Firoozabadi Z, Teimoori S, Chiti Z, et al. A comparison of the effect of levonorgestrel IUD with oral medroxyprogesterone acetate on abnormal uterine bleeding with simple endometrial hyperplasia and fertility preservation. Clin Exp Obstet Gynecol. 2013;40:421–4.
25. Gupta HP, Singh U, Sinha S. Levonorgestrel intra- uterine system-- a revolutionary intra-uterine device. J India Med Assoc. 2007;105:382-5.
26. Kriplani A, Singh BM, Lal S, Agarwal N. Efficacy, acceptability and side effects of the levonorgestrel intrauterine system for menorrhagia. Int J Gynaecol Obstet. 2007;97:190-4.
27. Dhamangaonkar PC, Anuradha K, Saxena A. Levonorgestrel intrauterine system (Mirena): an emerging tool for conservative treatment of abnormal uterine bleeding. J Midlife Health. 2015; 6: 26–30.
28. Hashim H, Zayed A, Ghayaty E, El Rakhawy M. LNG-IUS treatment of non-atypical endometrial hyperplasia in perimenopausal women: a randomized controlled trial. J Gynecol Oncol. 2013;24:128-34.
29. Begum R. Treatment of dysfunctional uterine bleeding with levonorgestrel releasing system (mirena). Oral presentation at the 35th AGM & national scientific conference of OGBS; 2008 June 19-20; Dhaka, Bangladesh.
30. Kai J, Middleton L, Daniels J, Pattison H, Tryposkiadis K, Gupta J. Usual medical treatments or levonorgestrel-IUS for women with heavy menstrual bleeding: long-term randomised pragmatic trial in primary care .Br J Gen Pract. 2016;66:e861-70.