

# The Efficacy and Safety of Norethisterone in the Management of Menorrhagia of Dysfunctional Uterine Bleeding

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## Abstract

*Introduction:* Dysfunctional uterine bleeding (DUB) usually presents as heavy menstrual bleeding without any underlying cause. Norethisterone is the most frequently prescribed drug for dysfunctional uterine bleeding serving 38% of the patient population the reason being cost effectiveness and absence of side effects. *Aim and Objectives:* To study the efficacy and safety of Norethisterone in the management of Dysfunctional uterine bleeding. *Material and Methods:* A total of 50 women between 20 to 50 years of age presenting with abnormal or dysfunctional uterine bleeding during a period of one year included in the study. During each visit a detailed menstrual history was taken and Pictorial Blood Assessment Chart (PBAC) score was calculated. All patients of Dysfunctional uterine bleeding under study treated with Norethisterone and the treatment outcome measured. *Results:* Among a total of 50 patients, there were 24 (48%) patients belonged to 31-40 years age group with 35.40 years to be a mean of all ages. The mean Haemoglobin level recorded was 7.5gm%. The mean Pictorial Blood Assessment Chart (PBAC) score prior to treatment was 274 which was found to be decreased upto 188 after treatment of 3 months with Norethisterone. A total of 32% patients suffered from side effects out of which 20% had nausea as most common. *Conclusions:* Norethisterone when used in patients with Dysfunctional uterine bleeding (DUB), it suppresses endometrial development, re-establishes predictable bleeding patterns, decreases menstrual flow and lowers the risk of iron deficiency anaemia.

**Keywords:** Dysfunctional Uterine Bleeding (DUB); Pictorial Blood Assessment Chart (PBAC).

## Introduction

Dysfunctional uterine bleeding (DUB) is a condition that affects nearly every woman at some point in her life, it causes vaginal bleeding to occur outside of the regular menstrual cycle. According to the American Society for Reproductive Medicine, it is most common during puberty and menopause, but can occur anytime when hormones are imbalanced [1].

Dysfunctional uterine bleeding (DUB) may be ovulatory or anovulatory. In 80-90% of DUB, bleeding results from dysfunction of hypothalamo-pituitary-

ovarian axis which leads to anovulation. As anovulatory cycles produces no progesterone to stabilize the cyclic withdrawal of the estrogen prepared endometrium, bleeding episodes becomes irregular and therefore amenorrhoea, metrorrhagia and menorrhagia are common. In other 10-20% women with DUB, ovulation occurs cyclically and menorrhagia is thought to originate from defects in the control mechanism of menstruation [2].

The treatment options for dysfunctional uterine bleeding are diverse, which can be finally tailored to cater the needs of patients of different socioeconomic background, different age groups and different reproductive needs [3]. Treatment options range from

offering medical measures such as cyclooxygenase inhibitors, tranexamic acid, hormonal agents and in cases not managed by medical therapy offering surgical management [4]. Norethisterone (a conventional progesterone) is the most frequently prescribed drug for dysfunctional uterine bleeding serving 38% of the patient population, the reason being cost effectiveness and absence of side effects. It suppresses endometrial development, re-establishes predictable bleeding patterns, decreases menstrual flow and lowers the risk of iron deficiency anaemia [5].

#### *Aim and Objectives*

To study the efficacy and safety of Norethisterone in the management of dysfunctional uterine bleeding.

#### **Material and Methods**

In the present study, patients presenting with dysfunctional uterine bleeding (DUB) to Department of Obstetrics and Gynaecology, Sardar Patel Medical College, Bikaner during the specified period from September 2015 to August 2016 were taken up for study. We included 50 women between 20 to 50 years presenting with abnormal or dysfunctional uterine bleeding without any organic, systemic or iatrogenic cause.

#### *Inclusion Criteria*

- All patients with dysfunctional uterine bleeding (DUB) of 20-50 years of age were included in the study.
- All patients who were ready for follow up.

#### *Exclusion Criteria*

- Patients who were pregnant, lactating, with history of heart disease, hypertension, migraine, Polycystic ovarian disease, liver and kidney impairment and thyroid dysfunction were excluded.
- Patients with fibroid uterus, adenomyosis, atypical endometrial hyperplasia, bleeding disorders were also excluded.

Informed consent was taken from all the patients. After obtaining an approval from institutional ethics committee, a detailed history and clinical examination was done. As dysfunctional uterine bleeding (DUB) is a diagnosis of exclusion, investigations were done

to rule out any other possible cause for abnormal uterine bleeding. These included complete blood cell count including hemoglobin (Hb) level, thyroid stimulating hormone, coagulation profile, PAP smear, pelvic ultrasound to measure endometrial thickness and rule out any pelvic pathology and endometrial sampling.

The cases were advised to maintain a menstrual diary to record the total number of days of bleeding, number of sanitary pads used, degree of soaking of each pad, number and size of clots passed, and if they have experienced any dysmenorrhoea. The Pictorial Blood loss Assessment Chart (PBAC) Scoring was then done accordingly to assess menstrual blood loss. PBAC is a simple procedure for objective assessment of menstrual blood loss. A PBAC score  $\geq 100$  indicates a menstrual blood loss  $\geq 80$  ml and is considered diagnostic for menorrhagia [6].

All women under study were given Norethisterone tablet 5 mg twice a day for 21 days followed by 7 days withdrawal, for 3 months. Patients were followed for 3 months. During each visit a detailed menstrual history was taken and PBAC score was calculated. Hemoglobin concentration and endometrial thickness were measured after 3 months of the treatment. Any side effects, if experienced, were also noted.

The primary outcome measures were reduction in the amount of menstrual blood loss, which was assessed by fall in PBAC score, rise in hemoglobin level and reduction in endometrial thickness done in proliferative phase by an ultrasound. All outcome measuring parameters were presented as Mean and were analyzed using the Z technique. Statistical significance was taken as  $p \leq 0.05$ .

#### **Results and Observations**

The table 1 shows distribution of patients according to their age, parity, residence and the duration of overall symptoms the patient is suffering from. Among total 50 patients, there were 24 (48%) patients who belonged to 31-40 years age group with a mean of 35.40 years. About parity status, overall mean is 2.8. Maximum patients belonged to rural communities (62%) and more than half number of patients were having less than 09 months duration of symptoms with an average duration of 6.7 months.

Table 2 shows results of various investigations carried out prior to the treatment with Norethisterone. About 70% of patients were having haemoglobin level between 6-8gm%. The mean Haemoglobin level recorded was 7.5gm%. On USG examination, the

mean endometrial thickness found to be 11.7mm with a maximum number of patients (76%) in the range of 10.1mm to 15mm. The PBAC score estimated among the patients with uterine bleeding shows that maximum patients belonged to intermediate group which ranges between 201 to 300 and mean score was found to 274 among the patients studied.

From the table 3, most common side effect with Norethisterone was nausea. A total of 32% patients have side effects out of which 20% had nausea followed by spotting (10%) and headache (6%). The side effects of the given treatment were mild, and they didn't affect the compliance of the patients receiving the treatment. These side effects are insignificant

**Table 1:** Distribution of variables among study subjects

Patient characteristics		Number of patients N=50; (%)	Mean Values
Age Intervals (Years)	20-30	17 (34%)	35.40
	31-40	24 (48%)	
	41-50	9 (18%)	
Parity Status	01	5 (10%)	2.8
	02	16 (32%)	
	03	16 (32%)	
	≥ 04	13 (26%)	
Residence	Urban	19 (38%)	----
	Rural	31 (62%)	
Duration of Symptoms (months)	0-3	10 (20%)	6.7
	4-6	18 (36%)	
	7-9	11 (22%)	
	10-12	10 (20%)	
	>12	01 (02%)	

**Table 2:** Results of various investigations prior to treatment with Norethisterone

Results of Investigations (prior to treatment)		Number of patients N=50; (%)	Mean Values
Hemoglobin (gm%)	<6	02 (04%)	7.5
	6-8	35 (70%)	
	8.1-10	13 (26%)	
Endometrial thickness on USG (mm)	0-5	00 (00%)	11.7
	5.1-10	10 (20%)	
	10.1-15	38 (76%)	
	15.1-20	02 (04%)	
PBAC score	100-200	00 (00%)	274
	201-300	39 (78%)	
	301-400	11 (22%)	

**Table 3:** Side effects of treatment with Norethisterone

Side Effects	Number of patients(N=50)	Percentage
Nausea	10	20%
Headache	3	6%
White discharge	2	4%
Spotting	5	10%
Total	16	32%

**Table 4:** Comparison of results of investigations prior to and after treatment with Norethisterone

Investigations	Mean Values after investigation		P-value
	Pre-Treatment	After 3 months of treatment	
Haemoglobin (gm%)	7.5	8.5	0.0008
Endometrial thickness (mm)	11.7	10.3	0.0006
PBAC score	274	188	0.0009

when compared to the other methods of management for DUB available.

After treating the patients with Norethisterone, they were followed up further for a period of 03 months and again various investigations were performed in order to review the treatment outcome among the patients. The various parameters studied were found to show a favourable outcome with a significant improvements in their clinical status. The mean values estimated, depicted in the above table no. 04 shows a comparative improved condition among overall patients studied.

### Discussion

In the present study, table No. 01 shows age distribution of the study participants (20-50 years) with mean age of 35.40 years. This study age intervals are comparable with previous studies by Debasmita Mandal et. al. [7], Dhananjayan D et. al. [8] and Neha Agarwal et. al. [9]. The reason could be that in younger years of the reproductive life the heavy menstrual bleeding might not cause much of a trouble to the affected women as most of the times the bleeding is temporarily halted during the pregnancies and the health status of young women is mostly better than the women in their later years of life, so they usually present late to the hospital.

The patients were distributed according to the duration of their symptoms ranging from 2-15 months, with mean duration of 6.7 months. The mean duration of symptoms in our study was more as seen in previous studies also [7,9]. It might be because in our area more than 50% of the patients belong to rural population and are of low socioeconomic strata and literacy rate is negligible, so they present late to the hospital.

Table 2 shows that, mean haemoglobin level of patients prior to treatment was 7.5gm%, also the mean endometrial thickness on USG prior to treatment was 11.7mm. These findings are similar to a previously conducted study [7]. This signifies the hyper-estrogenic state in these women.

PBAC score is not routinely used to assess the menstrual blood loss in patients attending the hospitals, but it should be considered for this purpose. As seen in our study, PBAC score directly correlates to the haemoglobin level in patients where the cause of anaemia was only heavy menstrual blood loss. Table 4 shows the comparison in respect to pre- and post-treatment values of mean PBAC score, mean haemoglobin concentration and mean endometrial thickness and all these were found to be significant

in both the groups (p value <0.05). PBAC score can help in subjective quantification of blood loss during each cycle, and can be used as a helpful guide in patients requiring some kind of intervention, even before the development of anaemia and before any significant effect on their quality of life [10].

### Summary and Conclusions

Dysfunctional uterine bleeding (DUB) usually presents as heavy menstrual bleeding without any underlying cause, and it affects the health of the woman and her quality of life as well. The ideal therapy to treat DUB should be a designer drug which can block the action of estrogen on the endometrium, but not its beneficial actions in the body. PBAC score is a simple tool for assessment of menstrual blood loss. It is quite cost effective as it requires no special equipment or setup and is less time consuming also. There were few minor side effects with Norethisterone treatment groups which did not cause any failure of compliance.

However, our study is on a small scale and is of short duration. A larger multicentric studies and trials are required to recommend Norethisterone as an ideal regime for the treatment of DUB.

### References

1. Dadhich S, Agarwal S, Soni M, Jain R. Role of Ormeloxifene in medical management of dysfunctional uterine bleeding. *Asian J Obstet Gynaecol Practice* 2012;6:28-31.
2. VeenaKhare, Gopa Ghosh, Pooja Patil, Nidhi Nagar. "Ormeloxifen HCL vs. Combined Oral Contraceptive Pill in Treatment of DUB". *Journal of Evolution of Medical and Dental Sciences* 2014 Jan 27;3(4):1026-33, DOI: 10.14260/jemds/2014/1941.
3. Coulter A, Kelland J, Peto V, Rees MC. Treating menorrhagia in primary care: an overview of drug trials and a survey of prescribing practice. *Int J Technol Assess Health Care*. 1995;11:456-471.
4. Lethaby A, Farquhar C, Cooke I. Antifibrinolytics for heavy menstrual bleeding. *Cochrane Database Syst Rev*. 2000;(4):CD000249.
5. Samuel NC, Clark TJ. Future research into abnormal uterine bleeding. *Best Pract Res ClinObstetGynaecol*. 2007;21:1023-40.
6. National Collaborating Centre for Women's and Children's Health. Heavy menstrual bleeding 2013.
7. Mandal Debasmita, Parmanik Sumit, SuranaSima, Hazra Abhijit, Mandal Saroj, MaityTapan Kumar.

- Comparative study of low-dose oral contraceptive pill and ormeloxifene in the treatment of dysfunctional uterine bleeding. *Int J Health Allied Sci.* 2014;3(4):225-31.
8. DeepikaDhananjayan and Mirunalini et. al. Comparative study between ormeloxifene and norethisterone in the improvement of menstrual blood loss (mbL) in abnormal uterine bleeding. *International Journal of Current Medical And Pharmaceutical Research*, 2016 Oct;2(10):758-61.
  9. Neha Agarwal et al. Comparative evaluation of the efficacy and safety of ormeloxifene and norethisterone in dysfunctional uterine bleeding *Int J Reprod Contracept Obstet Gynecol.* 2013;2(2);194-198.
  10. Roach L. Uterine bleeding: ACOG Updates Guidelines. *Medscape medical news* 2013.
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