

**Use of Norethisterone in Management of Dysfunctional Uterine Bleeding**Harvy Nigam Shah<sup>1</sup>, Paramtap Manoj Joshi<sup>2</sup>, Jitendra Shukla<sup>3</sup>, Vivek Patel<sup>4</sup><sup>1</sup>Senior Resident, Department of Obstetrics and Gynaecology, Dhiraj Hospital Sumandeep Vidyapeeth<sup>2</sup>Senior Resident, Department of Obstetrics and Gynaecology, Shardaben Hospital<sup>3</sup>Associate Professor, Department of Obstetrics and Gynaecology, Dhiraj Hospital Sumandeep Vidyapeeth<sup>4</sup>Resident 3<sup>rd</sup>, Department of Obstetrics and Gynaecology, Dhiraj Hospital Sumandeep Vidyapeeth

Received: 25-04-2024 / Revised: 23-05-2024 / Accepted: 16-06-2024

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Conflict of interest: Nil

**Abstract:**

**Objective:** To study effect of Norethisterone in the management of abnormal uterine bleeding. Background: Any variation in the frequency of menstruation, the length of the flow, or the volume of blood lost is referred to as abnormal uterine bleeding (AUB). It is a common disease that impacts the day-to-day life of women of reproductive age. This condition may have a substantial impact on the women's quality of life, including their physical, social, and emotional aspects. AUB is responsible for around 20–30 % of visits to out-patient departments among women of reproductive age.

**Results:** The mean age of study participants in the present study was 28.77 years. 41% of the women were illiterate and 63% were from upper lower socioeconomic class. 56% of the women were suffering from irregular menses. Heavy menstrual bleeding was prevalent among 40% The mean score of pictorial blood assessment among women were 180.80 at the time of starting treatment. It was 116.6 after month of treatment and it was 87.73 after 3 months of treatment. Perceived blood loss was significantly lower among the women after treatment with Norethisterone. Limitation in work and physical activities were also significantly reduced after treatment. Social and leisure activities were enjoyed more among women after three cycles of the treatment with progesterone only pills. Breakthrough bleeding and weight gain was most common side effects of progesterone only pills which were seen among 13% regular menses was seen among 10% of the women

**Keywords:** Abnormal uterine bleeding, Norethisterone.

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**Introduction**

Menstruation is a highly complicated process that involves the hormones estrogen and progesterone as well as their receptors, the endometrial vasculature, the endometrial vasoactive chemicals, the processes of tissue breakdown and remodelling, as well as endometrial repair and regeneration. Between 21 to 35 days is considered to be the average duration of a woman's menstrual cycle. The average length of a regular menstruation is between 5 and 7 days. Abnormal uterine bleeding (AUB) refers to bleeding from the uterus that lasts for a longer period of time than is typical or that takes place at an abnormal time.

The term AUB encompasses both Heavy Menstrual Bleeding (HMB) and Intermenstrual bleeding (IMB). The severity, length, and random recurrence of the DUB may vary. DUB may occur at any stage in a woman's life, from menarche to menopause, may be ovulatory or anovulatory cycles. In underdeveloped nations, the incidence of AUB seems to impact between 5 and 15 % of reproduc-

tive-aged women, with a greater frequency among older women[3] The diagnosis of DUB may be categorized as primary, secondary, or iatrogenic[4,5]. The FIGO released the PALMCOEIN categorization system in 2011 to standardize nomenclature, diagnosis, and tests for women presenting with AUB in which Depending on whether there are structural defects or not, different causes are categorized[6]. By taking a thorough history of the presenting symptoms, doing a thorough physical examination, and requesting laboratory and imaging tests, if necessary, it is possible to identify the most probable cause of acute DUB and make the best therapeutic decision for each patient.

Management can be medical or surgical depending upon the aetiology. Medical management mainly consists of hormonal management and is considered the first line therapy for the management of DUB. Combined oral contraceptive pills, oral progesterone, IV equine estrogen and progesterone intra-uterine systems are the available options. An-

ti-fibrinolytic drugs like tranexamic acid and NSAIDs are effective treatment for chronic AUB, amino-caproic acid and desmopressin also have specific indications.[7][8] Surgical management options include Dilatation and Curettage, endometrial ablation, uterine artery embolization and hysterectomy.[7][8]

Norethisterone are first-line treatment for HMB in an emergency presentation[9,10], they act by stimulating the enzyme (17-hydroxy steroid dehydrogenase), which turns estradiol into estrone (less potent). It Prevents estrogen receptor induction. It also prevents the endometrium from going through mitosis.[11]. Treatment aims to limit blood loss and improve the quality of life of women.[12]

**Materials and Methods**

**Study Setting**

The study was conducted in the Departments of Obstetrics and Gynaecology and Department of Pathology, Dhiraj General Hospital, Pipariya, Waghodia, Vadodara, Gujarat. It was an observational study.

The study was conducted over one and half year period from 9th January, 2022 to 9th July,2023. All non-pregnant women who came to Dhiraj General Hospital with complaints of bleeding per vaginal were our accessible population.

**Exclusion Criteria**

The following women were excluded from the present study: Pregnant patients

- Women who had any indication for surgical management.
- Women who did not give informed consent.
- Women with co-morbidities like bleeding disorders, hypertension, Immuno-deficient conditions.

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- Women with gynecological malignancies

All the study participants were given Tablet Norethisterone 5 milligram two times a day starting from the 5th day of menstruation cycle to 25th day. The treatment is given for three cycles. Oral iron tablets containing 100mg of Ferrous Ascorbate were also given.

**Study Measurements**

**1. The Pictorial Blood Loss Assessment chart (PBAC)**

The PBAC is a semi-quantitative measurement tool. Women were instructed to count their number of used towels or tampons each day and then divide them by level of soiling.

Also instructed to record clots and incidences of flooding by placing tally mark in the chart.

**For tampons:** 1 for lightly stained, 5 for moderately soiled and 10 for completely saturated tampons.

**For sanitary napkins:** 1 for lightly stained, 5 for moderately soiled and 20 for completely saturated pads.

Clots were given a score of 1 for small and 5 for large clots.

The total score was calculated by adding up the sum of all scores for the tampons or sanitary napkin used in the next menstrual cycle. Possible range of total score is completely dependent on quantitative and qualitative amount of bleeding during menstruation. Abnormal PBAC bleeding score (BS)  $\geq 100$ , which correlates with menorrhagia, defined as  $>80$  mL of menstrual blood loss

DAY	DAY1	DAY2	DAY3	DAY4	DAY5	DAY6	DAY7	DAY8	DAY9	DAY10	TOTAL TALLIES	MULTIPLYING FACTOR	ROW TOTAL
												X1	
												X5	
												X20	
												X1	
												X5	
												X10	
Small blood clots (= Dime)												X1	
Large blood clots (≥ Quarter)												X5	
Menstrual accidents												X5	
<b>Total Score (Sum of rows)</b>													

Figure 1:

**2. Menorrhagia Impact Questionnaire (MIQ)**

The MIQ is made up of six separate measurements or elements. The first four things are graded on a 4-point (item 1) or 5-point (items 2-4) scale.

Item 5 does not have a summative scale since it is

used as a descriptive tool to evaluate limits of certain activities and is seen as supporting information for items 2-4. Item 6 is a worldwide evaluation (impact, etc.). The magnitude and significance) of the change in MBL as compared to the prior period. The impact answer alternatives were 0 ('about

the same,' 1 ('better,' or 2 ('worse')). If a change is documented, a 7- point rating scale is utilized to define the level of improvement (item 6a) or deterioration (item 6b). Finally, item 6c (meaningful-

ness of change in MBL) assesses the subjective impression of the change in MBL and may be regarded as an essential component of the MIQ.

**Table 1:**

MIQ concept	MIQ item	Response scale
Perception of amount of blood loss	MIO 1 'During your most recent menstrual period, your blood loss was'	1. Light 2. Moderate 3. Heavy 4. Very Heavy
Limitations in work outside or inside the home	MIO 2 "During your most recent menstrual period, how much did your bleeding li	1. Not At All 2. Slightly 3. Moderately 4. Quite A Bit 5. Extremely
Limitations in physical activities	MIQ 3 'During your most recent menstrual period, how much did your bleeding limit you in your physical activities	1. Not At All 2. Slightly 3. Moderately 4. Quite A Bit 5. Extremely
Limitations in social or leisure activities	MIQ 4 'During your most recent menstrual period, how much did your bleeding limit you in your social or leisure activities?'	1. Not At All 2. Slightly 3. Moderately 4. Quite A Bit 5. Extremely
Global assessment of change in blood loss	MIO 6/6a/6b 'Compared to your previous menstrual period, would you say your blood loss during this period was':	0. About the same 1. Better (7-item scale): 1. Almost the same, hardly better at all 2. A little better 3. Somewhat better 4. An average amount better 5. A good deal better 6. A great deal better 7. A very great deal better 2. Worse (7-item scale): 1. Almost the same, hardly worse at all 2. A little worse 3. Somewhat worse 4. An average amount worse 5. A good deal worse 6. A great deal worse 7. A very great deal worse
Meaningfulness of perceived change in blood loss	MIQ 6c 'Was this a meaningful or important change for you?'	0. No 1. Yes

**Statistical Analysis**

Epi info CDC 7 version was used to enter and analyse data. Mean and standard deviation were used to represent continuous variables. Proportions were used for categorical variables. The t test was

used to evaluate the relationship between continuous variables. The chi square test was used to evaluate the relationship between category variables.

**Results**

**Table 2: Age distribution of study participants**

Age	Mean	SD
Mean Age (in years)	28.77	5.93
Age categories	Number	Percentages
13-21 years	10	10.0
22-34 years	71	71.0
35-45 years	19	19.0

The mean age of study participants in the present study was 28.77 years (SD 5.93 years). The majority of the women (71%) were in the age group of 22 to 34 years. Women in the age group of 13 to 21 was % while more than 35 years women were 19%.

**Table 3: Education status among study participants**

Education	Number	Percentage
Illiterate	41	41.0
Primary education	41	41.0
Secondary education	12	12.0
Higher secondary education	03	3.0
Graduate and above	03	3.0

In this study, 41% of the women were illiterate while 41% women were studied up to primary level. The proportion of women who studied up to secondary and higher secondary level was 12% and 3% respectively. Graduated women were 3%.

**Table 4: Socio-economic class among study participants**

Socio economic class	Number	Percentage
Lower	17	17
Lower middle	20	20
Upper lower	63	63

In present research, 63% of the women were belonged to upper lower socio-economic status while 20% were belonged to lower middle socio-economic status. Women who were belonged to lower class were 17%.

**Table 5: Marital status among study participants**

Marital status	Number	Percentage
Unmarried	13	13.0
Married	87	87.0

In present study, 87% of the women were married while 13% were unmarried.

**Table 6: Place of residence among study participants**

Place residence	Number	Percentage
Rural	66	66.0
Urban	34	34.0

In our study, 66% of the women were from rural area while 34% of the women were from urban area

**Table 7: Occupation among study participants**

Occupation	Number	Percentage
Housewife	49	49.0
House help	23	23.0
Labourer	19	19.0
Office worker	06	6.0
Clerk	03	3.0

As shown in Table 5-6, 49% of the women enrolled in the study were house wives while 23% were doing house help. Proportion of labourer, office worker and clerks were 19%, 6% and 3% respectively.

**Table 8: Menstrual bleeding among study participants**

Presenting complaints	Number	Percentage
Irregular menses	56	56.00
Heavy menstrual bleeding	40	40.0
Continuous menstrual bleeding	04	4.0

In this study, 56% of the women were suffering from irregular menses. Heavy menstrual bleeding was prevalent among 40% of the women while 4% of the women had continuous menstrual flow.

**Table 9: Past Menstrual history among study participants**

Past Menstrual history	Number	Percentage
Irregular, increased flow	77	77.0
Regular, increases flow	19	19.0
Continuous menstrual bleeding	04	04

As per Table 9, 77% of the women had irregular increased menstrual flow in past. Regular but increased flow in the past was reported by 19% of the women while 4% had past history of continuous menstrual flow.

**Table 10: Obstetric history among study participants**

Obstetric history	Number	Percentage
Nullipara	13	13.0
P1L1	20	20.0
P1L1A1	03	3.0
P2L2	33	33.0
P3L3	19	19.0
P4L3	04	4.0
P4L4	04	4.0
P5L5	04	4.0

In this study, 13% of the women were nulliparous while 20% were primi parous with one livingchild. Proportion of women second parity was 33% while 31% of the women had multiparity.

**Table 11: BMI among study participants**

Body mass index (kg/m <sup>2</sup> )	Number	Percentage
18.5-24.9	40	40
25-29.9	43	43
≥30	17	17

In our study, 40% of the women had BMI between 15.5-24.9 kg/m<sup>2</sup> while 43% had BMI 25- 29 kg/m<sup>2</sup>. Proportion of women who had BMI more than or equal to 30 kg/m<sup>2</sup> was 17%

**Table 12: Examination finding among study participants**

Examination finding	Number	Percentage
UT NS/AV FX CLEAR	48	48
UT NS/RV FX CLEAR	41	41
UT BULKY/RV FX CLEAR	08	8.0
UT BULKY/AV FX CLEAR	03	3.0

As per Table 12, uterus was NS/AV FX clear was seen among 48% of the women during examination. UT NS/RV FX CLEAR was observed among 41% of the women. Bulky uterus with RV and AV Fx clear was seen among 8% and 3% of the women respectively.

**Table 13: Pictorial blood assessment among study participants**

PBAC	Mean	Std. Deviation	p-value
Before treatment	180.80	14.95	<0.001
After month of treatment	116.60	14.46	
After 3 months of treatment.	87.73	14.14	

As shown in Table 13, the mean score of pictorial blood assessment among women were 180.80 at the time of starting treatment. It was 116.6 after month of treatment and it was 87.73 after 3 months of treatment. The decrement over the period in the PBAC score was statistically significant.

**Table 14: Menorrhagia impact questionnaire among study participants**

MIQ		Mean	SD	Q1	Q2	Q3	p-value
Item 1: Perceived blood loss	Pre	3.7	0.75	3	4	4	<0.001
	Post	1.63	0.49	1	2	2	
Item 2: Limitations in work outside or inside the home	Pre	3.8	0.61	3	4	4	<0.001
	Post	1.57	0.504	1	2	2	
Item 3: Limitations in physical Activities	Pre	3.63	0.809	3	4	4	<0.001
	Post	1.7	0.466	1	2	2	
Item 4: Limitations in social/leisure Activities	Pre	3.83	0.747	3	4	4	<0.001
	Post	1.5	0.509	1	1.5	2	

Table 14, shows item wise analysis of Menorrhagia impact questionnaire among study participants. Perceived blood loss was significantly lower among the women after treatment with progesterone only pills. Limitation in work and physical activities were also significantly reduced after treatment. Social and leisure activities were enjoyed more among women after three cycles of the treatment with progesterone only pills

**Table 15: Hemoglobin improvement among study participants**

Hemoglobin (gm%)	Mean	Std. Deviation	p-value
Before treatment	7.93	0.84	<0.001
After treatment	10.0	0.74	

The mean hemoglobin level before treatment was 7.93 gm/dl while after treatment with progesterone only pills, it was 10.0 gm/dl.

**Table 16: Side effects due to treatment among study participants**

Side effects	Number	Percentage
Nausea	06	6.0
Headache	03	3.0
Irregular menses	10	10.0
Breakthrough bleeding	13	13.0
Weight gain	13	13.0
Acne	03	3.0

As shown in table 16, breakthrough bleeding and weight gain was most common side effects of progesterone only pills which were seen among 13% each. Irregular menses was seen among 10% of the women. Nausea and headache were seen among 6% and 3% of the women respectively. Acne was occurred among 3% of the women after starting of treatment

### Conclusion

#### Following inferences are drawn from the present study:

The mean age of study participants in the present study was 28.77 years (SD 5.93 years). The majority of the women were less than 35 years. Around one fifth of the women were illiterate and two third of the women were belonged to upper lower socio-economic status. One fifth of the women were primiparous. Around half of the women were suffering from irregular menses.

Heavy menstrual bleeding was prevalent among two fifth of the women. Almost 3 /4th of the women had irregular increased menstrual flow in past.

The mean score of pictorial blood assessment showed significant decrease after three cycles of the treatment with the Norethisterone pills. Perceived blood loss was significantly lower among the women after treatment with Norethisterone. Limitation in work and physical activities were also significantly reduced after treatment. Social and leisure activities were enjoyed more among women after three cycles of the treatment with Norethisterone. Breakthrough bleeding and weight gain was most common side effects of progesterone only pills which were seen among 13% each. Irregular menses was seen among 10% of the women. Nausea and headache were seen among 6% and 3% of the women respectively. Acne occurred among 3% of the women after starting of treatment.

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