

Ormeloxifene an Effective Alternative for Surgery for Abnormal Uterine Bleeding of Ovulatory Disorders.

Received: 14 February 2023, **Revised:** 16 March 2023, **Accepted:** 18 April 2023

Priyanka Karumuri¹, Shailaja R Bidri¹, Sangamesh Mathapati^{1*}

¹Department of Obstetrics and Gynecology, Shri B M Patil Medical College, Hospital and Research Centre, BLDE (Deemed to be University), Vijayapura-586103, Karnataka, India.

Corresponding Author -Dr. Sangamesh Mathapati

Email Id: Sangamesh.mathapati@gmail.com

Phone Number: 9686266326

Keywords:

AUB-O, Ormeloxifene, HMBL, Hysterectomy.

Abstract

Introduction: Abnormal uterine bleeding is a significant debilitating clinical condition and effect 14-25% of women. We sought to determine the effectiveness and potency of Ormeloxifene in the treatment of AUB-O in this longitudinal investigation.

Objectives: To study the efficacy and acceptability of Ormeloxifene in management of AUB.

Methodology: The study was conducted in Department of Obstetrics and Gynecology of BLDE(DU) Shri B M Patil medical college. In this study 52 patients aged 30-55 years, presenting with heavy menstrual bleeding were enrolled. Patients with any structural pelvic cause, liver dysfunctions, who are using IUCDs or oral contraceptives, were excluded from the study. All the participants were subjected for complete menstrual history, medical history, clinical examination and laboratory evaluation done. All cases received Ormeloxifene 60mg twice weekly for the first 12 weeks, followed by once weekly for next 12 weeks. The participants were followed every three months and six months for subjective and objective improvement in menstrual blood loss by history, measuring PBAC score, endometrial thickness, hemoglobin concentration.

Results: 50 out of 52 study participants completed the treatment and all 50 had improvement in symptoms of HMBL after using Ormeloxifene for 6 months. They had minimal and minor side effects. There was improvement in hemoglobin concentration, PBAC score, TVS-ET score in all the participants.

Conclusion: Ormeloxifene is effective and safe in patients with AUB-O and this can reduce the burden of surgery in patients suffering from AUB-O.

1. Introduction

AUB can be caused by ovulatory abnormalities like oligovulation, anovulation, polycystic ovarian alterations, and corpus luteal dysfunction which results in severe, extensive bleeding. One of the most typical gynecological symptoms encountered on a daily basis is AUB, which can afflict one-third of women of childbearing age.¹ All civilizations experience significant social and physical morbidity as a result of the vast range of AUB disturbances, which may also be indicative of a serious underlying disease. 10%–30% of menstrual women experience menorrhagia at any given moment, and up to 50% of women may experience it during the perimenopausal transit phase. According to studies, menstrual blood loss averages 60 to 80 ml per month and is linked to iron deficiency anaemia. Any irregularity in the

regularity, frequency, duration, or volume of menstrual flow is referred to as AUB, and its underlying cause could be pharmacological, pathological, or physiological.²

Even while research into less invasive surgical procedures like endometrial ablation has increased, hysterectomy is still the only viable long-term solution for women who have no further fertility issues. The need for non-surgical methods of lowering menstrual blood loss is still present. The Royal College of Obstetricians and Gynaecologists (RCOG) advises starting therapy with medicinal management before turning to surgical procedures in order to reduce the morbidity associated with hysterectomy.³

It is undoubtedly a difficult assignment when there is no general agreement on the drugs that should be

Journal of Coastal Life Medicine

provided in this situation. Their main downsides, despite being efficient in lowering blood loss, are their expense and unfavorable side effects when used frequently.⁴

The most recent designer medicine for the treatment of AUB is ormeloxifene. It is a third-generation selective oestrogen receptor (ER) modulator that has a high affinity for ERs. In some tissues, like the vagina, bone, and central nervous system (CNS), cardiovascular system (CVS), it acts like an oestrogen, whereas in the uterus and breasts, it has an antiestrogenic action. Its pharmacological role in AUB is based on this. The discovery of two distinct types of ER α and ER β as well as knowledge of the intricate nature of ER structure and function provide a significant therapeutic opportunity for discovering a substance with favourable bone, cardiovascular, and neurological profiles without having a negative impact on uterine and breast reproductive tissues. Two receptor isoforms with varying ligand affinities coexist in many tissues, there are at least two activating factors present, and there are an increasing number of coactivators and corepressors. These factors all contribute to the selective ER regulation.⁵

Many studies have been done on Ormeloxifene for abnormal uterine bleeding with ovulatory dysfunction but still there is a lacunae in this research field. Hence the present study has been undertaken to study an efficacy of Ormeloxifene in the treatment of AUB-O.

2. Methodology

Study Setting: The study was conducted Department of Obstetrics and Gynecology, Shri B.M. Patil Medical College, Hospital and Research Centre B.L.D.E. (Deemed to be University) from 1st January 2021 and 30th June 2022. All women in the age group 30-55 years with HMBL were screened and total of 52 participants were enrolled after considering inclusion and exclusion criteria. Patients with Pelvic diseases including Adenomyosis, Endometrial hyperplasia with atypia, Uterine fibroids, Cancers of the uterus, cervix, ovary, vagina, and uterus, Illnesses like coagulopathy, hepatic dysfunction, heart disease, stroke, renal ailments, and platelet abnormalities, Previous thrombosis history, Thyroid disorders, Pregnancy related bleeding, Using oral contraceptives or IUCDs, and participants with Ormeloxifene hypersensitivity were excluded from the study. Participants were

educated about PBAC ask to keep record of bloodloss by PBAC. Informed written consent were taken according to the declaration of Helsinki. Then the participants were subjected for complete menstrual history, medical history, clinical examination and laboratory evaluation which include Complete Blood Count, Bleeding Time, Clotting Time, TSH, T3, T4, Transvaginal Scan, Endometrial Thickness. All participants received ormeloxifene 60mg twice weekly for the first 12 weeks, followed by once weekly for the next 12 weeks. Every three months, every six months, or earlier if necessary, follow-up was conducted. During the follow up the participants were evaluated for Menstrual blood loss by history, haemoglobin concentration and proliferative endometrial thickness by transvaginal sonography were the main outcome indicators (TVS). Ormeloxifene's acceptance and side effects were the secondary outcome indicators. At each appointment, a thorough menstrual history was taken, including information on the number of sanitary napkins used, the passage of clots, and dysmenorrhea. Any negative impacts were supposed to be highlighted. Ormeloxifene's acceptability and subjective symptom improvement were evaluated. Any side effects of the drug ormiloxifen were noted

Statistical analysis: The data obtained was entered in a Microsoft Excel sheet, and statistical analysis was performed using SPSS (Version20). Results were depicted in Mean \pm SD, counts and percentages, and diagrams. The Wilcoxon signed-rank test was used to compare two groups' differences in continuously distributed continuous data that were normally distributed. We compared categorical variables using the Mac Nemer's chi-square test. Statistical significance was set at $p < 0.05$. Two-tailed statistical tests were used for each test.

3. Results

The descriptive analysis of the present study is shown in Table 1. The comparison of Haemoglobin concentration, PBAC, TVS-ET between pre and post-treatment with Ormeloxifene is shown in Figure 1, Figure 2, and Figure 3 respectively where it is shown that there is a significant improvement seen in these parameters post-treatment with Ormeloxifene. The Wilcoxon signed-rank test of the PBAC score, Hemoglobin concentration, TVS-ET at 0 month, 3 month, and 6 month is shown in Table 2 showing a

Journal of Coastal Life Medicine

significant difference in which normality was checked using Shapiro-Wilk test as shown in Table 3. $p < 0.05$ was considered as statistically significant. Less than

4% of study participants showed hypomenorrhea after treatment with Ormeloxifene.

Table 1: Descriptive Analysis of the current study

	Minimum	Max	Mean	Std. Dev.
Age (Years)	30	50	37.19	5.901
Parity	1	6	2.83	0.985
No. of Days of flow	4	24	9.77	4.626
Cycle Length (Days)	15	60	25.58	7.209
Duration of Symptoms (Months)	1	24	4.81	5.022

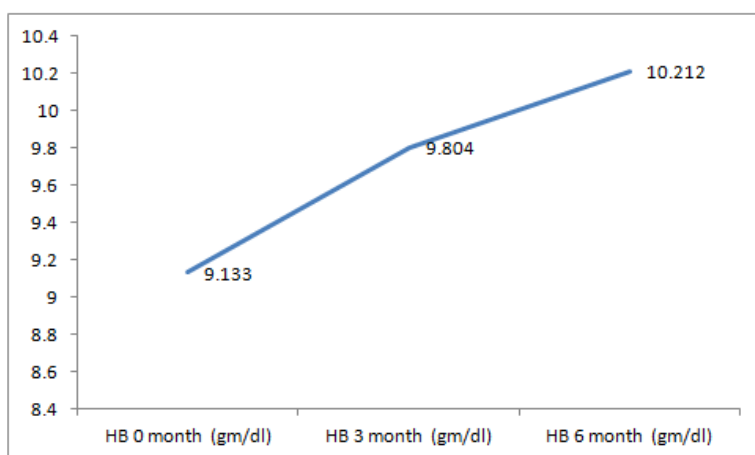


Figure 1: Comparison of Hemoglobin Pre-Treatment and Post-Treatment

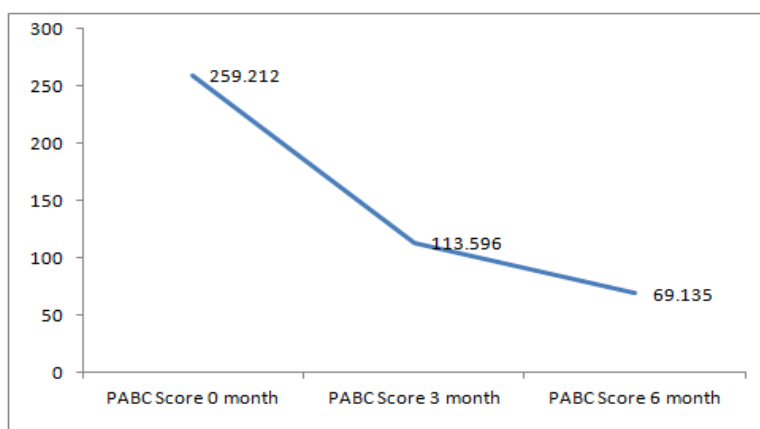


Figure 2: Comparison of PBAC Pre-Treatment and Post-Treatment

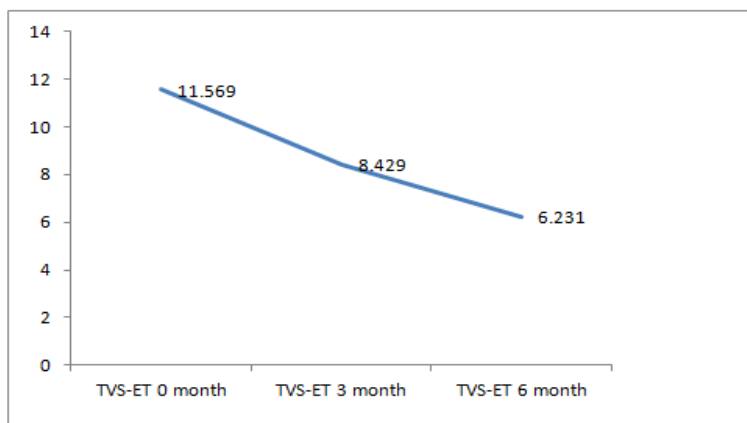


Figure 3: Comparison of TVS-ET Pre-Treatment and Post-Treatment

Table 2: Wilcoxon Signed-rank test

Measure 1	Measure 2	W-value	Z	P
PBAC Score 0 month	PBAC Score 3 month	1378.000	6.275	<0.001
PBAC Score 0 month	PBAC Score 6 month	1378.000	6.275	<0.001
Hb 0 month (gm/dl)	Hb 3 month (gm/dl)	52.000	-5.801	<0.001
Hb 0 month (gm/dl)	Hb 6 month (gm/dl)	103.000	-5.337	<0.001
TVS-ET 0 month	TVS-ET 3 month	1378.000	6.275	<0.001
TVS-ET 0 month	TVS-ET 6 month	1378.000	6.275	<0.001

Table 3: Test for Normality (Shapiro-Wilk)

		W	P
PBAC Score 0 month	PBAC Score 3 month	0.902	<0.001
PBAC Score 0 month	PBAC Score 6 month	0.924	0.003
Hb 0 month (gm/dl)	Hb 3 month (gm/dl)	0.503	<0.001
Hb 0 month (gm/dl)	Hb 6 month (gm/dl)	0.583	<0.001
TVS-ET 0 month	TVS-ET 3 month	0.782	<0.001
TVS-ET 0 month	TVS-ET 6 month	0.816	<0.001

Note: Significant results suggest a deviation from normality

4. Discussion

Abnormal Uterine Bleeding owing to Ovulatory Dysfunction (AUB-O), the most prevalent monthly illness in women of reproductive age, is characterized by abnormal uterine bleeding without a clinically discernible organic, systemic, or iatrogenic cause. As in our study, maximum participants belongs to middle age group (30-35 years), indicates ovulatory dysfunction is common mostly in middle age group. So, the conventional treatment option like hysterectomy might not be suitable for these patients. In our study, we observed the flow rate is more than 10 days for most of the participants indicating towards the altered hemodynamic status of the patients suffering from AUB-O. This might be due to increase in demand of red cells resulting into alteration of the homeostatic mechanisms of the body, which may precipitate if hormonal mechanisms are not providing the required optimal feedback. We also observed the presentations of complaints of our participants are almost within 6 months which shows the awareness of the disease in society. We also found that almost all participants showed improvement after receiving treatment with Ormeloxifene after 6 months of usage, resulting in increase in hemoglobin concentration (9.13 to 10.21), decrease in PBAC score (259.21 to 69.13), decrease in TVS-ET score (11.57 to 6.23), whereas the side effects like hypomenorrhea, amenorrhea, headache, etc. were almost negligible in most of the participants.

Annu M et al (2008) in their study found that Ormeloxifene significantly reduced endometrial thickness.⁶ Which is similar to our study finding.

Neha Agarwal.et.al. (2013) in their study found Ormeloxifene effective, quick-acting and, promising option for medical management of AUB-O. They also found the drug protective against endometrium carcinoma.⁷ Our study showed improvement in the HMBL symptoms.

A study by Nandhini G. M., (2022) also corroborate our findings, showing that ormeloxifene improves haemoglobin, the pictorial blood loss assessment chart score, and endometrial thickness.⁸

Dhananjay BS et al (2012) found Ormeloxifene effective in increase in the hemoglobin concentration and decrease in the endometrial thickness in AUB-O

patients.⁹ These findings are also similar with our results of present study.

These results of Ormeloxifene therapy state toward the efficacy and potency of the drug in management of AUB-O.

5. Conclusion

- We conclude that Ormeloxifene, a drug having efficacy to reduce the heavy menstrual bleeding significantly in patients with AUB-O.
- Can be a drug of choice for the perimenopausal women specifically suffering from predisposed anaemia and other associated diseases.
- Ormeloxifene clearly has an advantage over other treatment alternatives like progesterones, combined oral contraceptive tablets, etc. in the pharmacological management due to its outstanding safety profile, simple dose schedule, and demonstrated efficacy in the treatment of AUB-O.
- This can reduce the burden of surgery in the patients suffering from AUB-O.
- Ormeloxifene can be used in patients who are suffering from AUB-O as it is having negligible side effects.

References

- [1] Munro MG, Critchley HOD, Fraser IS., FIGO Menstrual Disorders Committee. The two FIGO systems for normal and abnormal uterine bleeding symptoms and classification of causes of abnormal uterine bleeding in the reproductive years: 2018 revisions. *Int J Gynaecol Obstet.* 2018 Dec;143(3): 393-408.
- [2] Singh HO, Singh A, Dhole TN, Nain S. Effect of ormeloxifene for management of dysfunctional uterine bleeding. *Biochem Physiol* 2015;4:174.
- [3] Fraser IS, Sungurtekin U. Defining menstrual disturbances. In: MacLean A, O'Brien PM, editors. *Study Group on Menstrual Disorders.* London: Royal College of Obstetricians and Gynaecologists; 2000. p. 141-52.
- [4] Shelly W, Draper MW, Krishnan V, Wong M, Jaffe RB. Selective estrogen receptor modulators: An update on recent clinical findings. *Obstet Gynecol Surv* 2008;63:163-81

Journal of Coastal Life Medicine

- [5] Dhananjay BS, Sunil Kumar N. The Role of Sevista in the Management of Dysfunctional Uterine Bleeding. *J Clin Diagnostic Res.* 2013;7(1):132134.
- [6] Makker A, Tandon I, Goel MM, Singh M, Singh MM. Effect of ormeloxifene, a selective estrogen receptor modulator, on biomarkers of endometrial receptivity and pinopode development and its relation to fertility and infertility in Indian subjects. *Fertility and sterility.* 2009 Jun 1;91(6):2298-307
- [7] Agarwal N, Singh S, The efficacy and safety of Ormeloxifene in Dysfunctional Uterine Bleeding. *IOSR-JPBS.* 2013; 5(5): 18-21.
- [8] Nandhini G. M., Hiremath P. B., Shameera Banu A A study of efficacy of ormeloxifene in abnormal uterine bleeding of ovulatory disorders. *Int J Reprod Contracept Obstet Gynecol.* 2022 Apr;11(4):1230-1235
- [9] Dhananjay BS, Nanda SK. The role of sevista in the management of dysfunctional uterine bleeding. *Journal of clinical and diagnostic research: JCDR.* 2013 Jan;7(1):132.