ORIGINAL RESEARCH PAPER
Volume - 11 | Issue - 10 | October - 2022 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

STUDY OF EFFICACY AND SAFETY OF ORMELOXIFENE IN MANAGEMENT OF ABNORMAL UTERINE BLEEDING

Obstetrics & Gynaecology

Dr. Anushree Senior Resident , Department of Obstetrics &Gynaecology ,Nalanda Medical College and Hospital ,Patna

Dr. Priya Ranjan Junior resident , Department of Obstetrics &Gynaecology , Nalanda Medical College and Hospital ,Patna

Dr. Vinita Singh Associate Professor, Department of Obstetrics &Gynaecology , Nalanda Medical College and Hospital, Patna

ABSTRACT

Background: Ormeloxifene, also known as centchroman, is one of the selective estrogen receptor modulators, or SERMs, a class of medication which acts on the estrogen receptor . In some parts of the body, its action is estrogenic (e.g., bones), in other parts of the body, its action is antiestrogenic (e.g., uterus, breasts. **Methodology:** This prospective study was done for 6 months taking 100 patients with complaint of abnormal uterine bleeding. Ormeloxifene 60 mg was prescribed twice a week for 3 months and then 60 mg once a week for next 3 months . During follow-up endometrial thickness by usg, haemoglobin level , PBAC score and side-effects of the drugs were assessed. **Results:** A total 100 patients of age 20-45 years were enrolled , in which 94 patients completed the follow up. There was statistically significant decrease in endometrial thickness, PBAC score and increase in haemoglobin level. **Conclusion:** Thus Ormeloxifene , a non- steroidal and non- hormonal agent with its convenient dose schedule provides effective and favourable medical treatment.

KEYWORDS

Abnormal uterine bleeding, PBAC score, Ormeloxifene.

INTRODUCTION

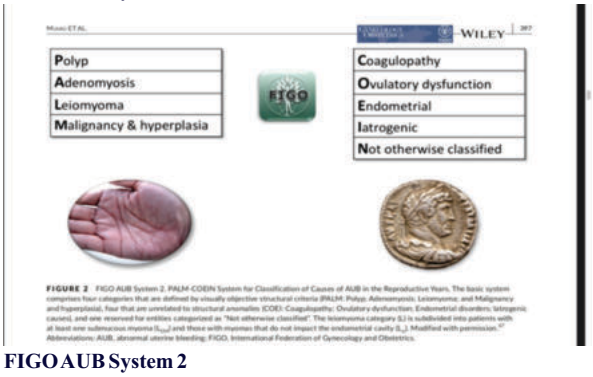
Chronic nongestational AUB in the reproductive years is defined as bleeding from the uterine corpus that is abnormal in duration, volume, frequency, and/or regularity, and has been present for the majority of the preceding 6 months. Acute AUB, is defined as an episode of heavy bleeding that, in the opinion of the clinician, is of sufficient quantity to require immediate intervention to minimize or prevent further blood loss. May present in the context of existing chronic AUB or in its absence.(FIGO 2018)

FIGO- AUB two system classification

- AUB System 1: to define the types of AUB symptoms.
- AUB System 2: PALM-COEIN

Parameter	Normal	Abnormal	☑
Frequency	Absent (no bleeding) = amenorrhea		☐
	Infrequent (>38 days)		☐
	Normal (≥24 to ≤38 days)		☐
	Frequent (<24 days)		☐
Duration	Normal (≤8 days)		☐
	Prolonged (>8 days)		☐
Regularity	Normal or "Regular" (shortest to longest cycle variation: ≤7-9 days)*		☐
	Irregular (shortest to longest cycle variation: ≥8-10 days)*		☐
Flow Volume (patient determined)	Light		☐
	Normal		☐
	Heavy		☐

FIGO AUB System 1



FIGO AUB System 2

INCIDENCE: About 10–15% of women experience episodes of abnormal uterine bleeding (AUB) at sometime during the reproductive years of their lives. It is common during the extremes of reproductive life, following pregnancy and during lactation. It has been shown that 55.7% of adolescents experience abnormal menstrual bleeding in the first year or so after the onset of menarche because of the immaturity of the hypothalamic–pituitary–ovarian axis leading to anovulatory cycles. Evaluation

- History and clinical exam
- Pelvic imaging - USG pelvis
- CBC, UPT
- Coagulopathy screen – specific indications
- Endometrial biopsy – specific indications
- TSH - when clinically indicated

MANAGEMENT OF ABNORMAL UTERINE BLEEDING:

- Combined Oral Contraceptives
- Progestogens
- GnRH agonists
- Androgenic drugs
- Tranexamic acid

Drugs used (no identified pathology)

- Tranexamic acid (first-line – FOGSI 2016).
- NSAIDs
- LNG –IUS (first line – NICE 2018, First line for women desiring contraception – FOGSI 2016)
- Combined Oral Contraceptives (Second line for women desiring contraception – FOGSI 2016)
- Cyclic luteal phase oral progestins (from day 5 to 26), are recommended if COCs are contraindicated
- Centchroman (ormeloxifene) is an option when steroidal hormones and other medical options are not suitable. 60 mg 2 days a week at an interval of 3 days. May lead to amenorrhea
- GnRH agonists with add-back hormone therapy are recommended as a last resort when medical treatments for AUB have failed or are contraindicated Other medical management modalities in AUB
- DMPA
- Danazol: Rarely used because of the adverse effects
- Gestrinone: (progesterone receptor ligand) rarely used in acute AUB
- **ACOG recommended drugs (2013) {alphabetic order}**
- Conjugated equine estrogen
- COC
- Medroxyprogesterone
- Tranexamic acid Surgical management
- The indications for surgery for women with AUB include failure to respond to medical therapy, inability to utilize medical therapies (i.e. side effects, contraindications), significant anemia, impact on quality of life, and concomitant uterine pathology (large uterine fibroids, endometrial hyperplasia).
- Surgical options
  - ◇ endometrial ablation
  - ◇ hysterectomy

ROLE OF ORMELOXIFENE: Ormeloxifene is best known as a non-hormonal, non-steroidal oral contraceptive which is taken once

per week. In India, ormeloxifene has been available as a birth control product since the early 1990s (discovered by Central Drug Research Institute (CDRI) in Lucknow)and it is currently marketed here under the trade name, Saheli . Ormeloxifene has also been licensed under the trade names, Novex-DS, Centron and Sevista. The drug has been postulated to have antiestrogenic effect on uterus.

AIM OF STUDY

The aim is to study of efficacy and safety of ormeloxifene in management of abnormal uterine bleeding.

STUDY DESIGN: It is a prospective clinical study.

SELECTION OF CASES: This prospective clinical study was conducted in Nalanda medical college hospital ,Patna from February 2019 to march 2020.A total of hundred women in the age group 20- 45 years diagnosed with abnormal uterine bleeding visiting gynaecological outpatient facility were selected.

SAMPLE SIZE: A total of 100 cases were selected and studied.

Inclusion Criteria: All cases of abnormal uterine bleeding not related to any identifiable pelvic pathology.

Exclusion Criteria: The following were excluded from the study-

1. Presence of any pelvic pathology on ultrasound such as fibroid, adenomyosis, polyp, adnexal mass
2. uterine size > 10 weeks 3.Coagulopathies
4. Use of IUCD and COC
5. Patient not willing to go for the study

MATERIALS AND METHODS

This study is a prospective study. The selected cases were given 60 mg tablet twice weekly (every Monday and Friday) for the first 12 weeks and then once a week (every Monday) for another 12 weeks. During follow-up endometrial thickness by usg, haemoglobin level , PBAC score and side-effects of the drugs were assessed.

RESULTS AND ANALYSIS

Initially we recruited 100 patients for ormeloxifene in which 94 patients completed study while 6 patients lost in follow up. In those 6 patients, 2 patients had gone through hysterectomy. The present study was conducted on 94 patients. The means age of patients were 32.91+/- 6.82 years and most of the patients (71.11%) from rural area. Most of patients in our study were literate (73.33%). Socioeconomic status of most of patients were lower. Maximum number of the cases in the study were housewives. In our study most of the women presenting with complaint of abnormal uterine bleeding were married. It was further observed in this study that as the parity increased, the abnormal uterine bleeding also increased. Effects of Ormeloxifene treatment on Endometrial thickness, Haemoglobin and PBAC Score were seen in patients of Abnormal uterine bleeding.

The treatment effects of Ormeloxifene in patients of abnormal uterine bleeding, it was found that the endometrial thickness (in mm) has decreased to 7.66 ± 1.00 at 3 months and 6.68 ± 1.11 at 6 months (post-treatment), from the basal value (pre-treatment) of 8.86 ± 1.13 (mm). The decrease in endometrial thickness was statistically highly significant in this arm also, on follow up (post treatment) at three months and six months, (p value <0.001, significant) The treatment effects of Ormeloxifene, in patients of abnormal uterine bleeding haemoglobin levels has increased to 8.86 ± 0.79 at 3 months and 9.91 ± 0.80 at 6 months (post-treatment) from the pre-treatment (basal value) of 8.09 ± 0.63 (gm/dl). The increase in mean haemoglobin levels was highly significant statistically, on post treatment.

Table 1 : Assessment Of Blood Loss By Pbac Score

S. no.	PBAC Score	Menstrual Blood Flow	Pretreatment N=100	1 Month (N=94) 6 Lost To Follow- Up	3 Months (N=94)	6 Months (N=-94)
1.	0	Nil	0 (0%)	0(0%)	10 (10.63%)	20 (21.2%)
2.	0-10	Scanty	0 (0%)	0(0%)	4 (4.25%)	16 (17.02%)
3.	10-100	Moderate	10 (10%)	32(34.04%)	28 (29.7%)	20 (21.2%)
4.	100-300	Heavy	20 (20%)	40(42.5.%)	32 (34.04%)	28 (29.7%)
5.	>300	Very Heavy	70 (70%)	22(23.4%)	20 (21.2%)	10 (10.6%)

Table 2 : Comparison Of Mean Endometrial Thickness (mm) Between Pretreatment Level And Post Treatment At 24 Week.

S.no.	Duration	Ormeloxifene Effect
1.	Pretreatment {basal}	8.86 ± 1.13
2.	Post-treatment At 3 Months	7.66 ±1.00
3.	Post-treatment At 6 Months	6.68 ± 1.11

P VALUE ≤ 0.001

Table 3: Comparison Of Mean Hb Between Pre-treatment Level And Post Treatment At 24 Weeks.

S.no.	Duration	Ormeloxifene Effect
1.	Pretreatment {basal}	8.09 ± 0.63
2.	Post-treatment At 3 Months	8.86 ±0.79
3.	Post-treatment At 6 Months	9.91 ± 0.80

P VALUE ≤ 0.001

Serious side effects which warrant discontinuation of drug were not seen with ormeloxifene, but few side effects like headache was seen in1 patient, weight gain in 1 patient, spotting in 2 patients, and amenorrhoea in 5 patients. None of the patients in this study group developed any significant side effect.

DISCUSSION

A substantial impact on the gynaecological symptoms were seen. Endometrial thickness (in mm) has decreased to 7.66 ± 1.00 at 3 months and 6.68 ± 1.11 at 6 months (post- treatment),from basal value (pre-treatment) of 8.86 ± 1.13(mm).Haemoglobin levels has increased to 8.86 ± 0.79 at 3 months and 9.91 ± 0.80 at 6 months (post-treatment) from basal value of 8.09 ± 0.63(gm/dl). The decrease in endometrial thickness and increase in haemoglobin levels were highly significant on post-treatment.

CONCLUSION

Abnormal uterine bleeding is one of the major gynecological problems affecting women's wellbeing for which women seek health personnel. Medical management should be tried first than surgical interventions. Ormeloxifene is safe nonsteroidal and nonhormonal drug with good compliance and effective in treatment of abnormal uterine bleeding.

REFERENCES

1. Fraser IS, Inceboz US. Defining disturbances of the menstrual cycle. In: O'Brien PNS, Cameron IT, MacLean AB, Eds. Disorders of the menstrual cycle. London, UK: RCOG Press; 2000:151-152 Schorge,Schaffer et.al. Abnormal uterine bleeding. In: Williams Gynaecology. 1stEd.New York,McGraw-Hill;2008:174-96.
2. Devi LT et al. Ormeloxifene in management of dysfunctional uterine bleeding Int J Preod contracept obstet gynecol. 2018;7(5):1885-1892
3. Marret H, Fauconnier A, Chabbert -Buffet N et al; clinical practice guidelines on menorrhagia: management of abnormal uterine bleeding before menopause. Eur J Obstet Gynecol Reprod Biol. 2010; 152: 133-7.
4. Rajan R. Ormeloxifene in management of dysfunctional uterine bleeding DUB today 2008; 1:1-20.
5. Munro MG, Critchley HO, Broder MS, et al. FIGO classification system for causes of abnormal uterine bleeding in nongravid women of reproductive age. FIGO Working Group on Menstrual Disorders. Int j Gynecol Obstet.2011;113: doi:10.1016/j.ijgo.2010.11.011.
6. Komaram R, et al, A study of ormeloxifene in the pharmacological management of dysfunctional Uterine bleeding. J Clin Diagn Res. 2013;7:2534-6.
7. Kamboj VP, Ray S , Dhawan BN. Centchroman .Drugs Today 1992;28:227-32.
8. Soniya P, Verma A. role of ormeloxifene in management of AUB. SJAMS 2017;5(3B):796-99.