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Original research article

Comparative study between ormeloxifene and norethisterone for management of dysfunctional uterine bleeding (HMB)

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Abstract
Dysfunctional uterine bleeding (HMB) is a common gynaecological disorder where patients usually end up in hysterectomy. Menorrhagia is a symptom of abnormal vaginal bleeding. Medical management with NSAIDS and hormones have their inherent side effects. Ormeloxifene (also known as centchroman) is one of the selective oestrogen receptor modulators or SERMs, a class of medications that acts on the oestrogen receptor. It is best known as a non-hormonal, non-steroidal oral contraceptive, which is taken once per week. Ormeloxifene is anti-proliferative drugs, which reduce production of various endometrial derived local factors, and corrects menorrhagia with decrease menstrual blood loss (MBL) and clots. This is a prospective observational study done during April 2023 to June 2023. 100 patients between the age group 25-45 years, clinically diagnosed with DUB were taken into study. 50 patients were treated with Ormeloxifene and 50 with Norethisterone. Ormeloxifene 60 mg was administered orally twice a week for first 12 weeks and then once in a week for next 12 weeks. Norethisterone 5 mg twice a day from day 15-25 of cycle was administered. MBL was measured using pictorial blood loss assessment chart (PBAC), blood hemoglobin. The median difference between pretreatment and post-treatment PBAC score and Hemoglobin was found to be significant in Ormeloxifene group. Ormeloxifene is a cost-effective effect therapy.
Keywords: Dysfunctional Uterine Bleeding [DUB], Menorrhagia, Ormeloxifene, Norethisterone

Introduction

Menorrhagia is an abnormal vaginal bleeding from the genital tract in reproductive age group woman it occurs due to disturbance in the menstrual cycle by regular and irregular uterine bleeding and alteration in the amount and duration of blood loss [1]. It can cause anaemia (iron deficiency), haemorrhagic shock and decrease in the quality of life [2]. It affects 10 to 20% of women in at some stage in their life there is no definitive at hysterectomy in approximately 50% of cases [3]. The pathophysiology of DUB is largely unknown but occurs both in ovulatory and anovulatory menstrual cycles [4]. A number of local factors are thought to be involved in the local control of menstrual blood loss and abnormality in these may cause menorrhagia [5].

Ormeloxifene (also known as centchroman) is one of the selective oestrogen receptor modulator [6] or SERMs, a class of medications which acts on the oestrogen receptor. It 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, and it is currently marketed here under the trade name, Saheli [6]. Ormeloxifene has also been licensed under the trade names, Novex-DS, Centron and Sevista. Ormeloxifene is primarily used as a contraceptive, but it may also be effective for dysfunctional uterine bleeding and advanced breast cancer. Ormeloxifene may be used as a weekly oral contraceptive [7]. Ormiloxifene binds with high afnity of estrogen receptors and mimics the effect of estrogen in some tissue. However, Ormeloxifene acts as estrogen antagonist in uterus (endometruim), which lead to endometrial atrophy hence the decrease menstrual blood loss [8]. Therefore, the aim of present study to evaluate the effect of ormeloxifene drug in women with dysfunctional uterine bleeding. For the first twelve weeks of use it is advised to take ormiloxifene 60 mg twice per week. From the thirteenth week, it is taken once per week [9].

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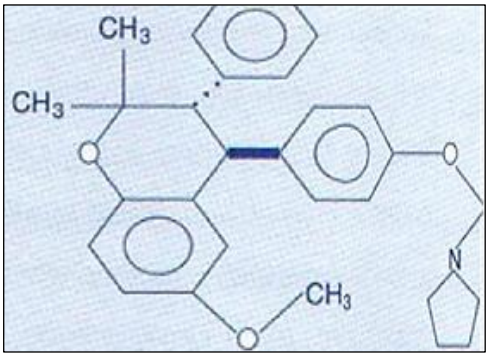
Mechanism of action of Ormeloxifene



The individual elements of the modulator structure give a tissue selectivity-different DNA transcription in different tissues:
Basic Amine Side chain causes Uterine Anti estrogenic action Pyrolidine side chain causes antagonistic action. Benzopyron group causes agonistic action.
It has very strong affinity for Estrogen receptors, Slow nuclear binding & prolonged release of ER Hence long half-life & prolonged action. Ormeloxifene as a contraceptive it prevents proliferation & decidualisation of the endometrium, Enhances blastocyst formation & embryo transport through oviducts. Normalizes bleeding from uterine cavity by regularizing expression of estrogen receptorson the endometrium. It is well absorbed from the GI tract. Peak levels are attained in 4 hours; terminal half-life is approximately 170 hours. It is widely distributed in tissues. It has little affinity to plasma proteins.

Indications of Use
It is currently indicated for DUB in all ages, but not suitable for women desiring pregnancy. It has got special benefit for peri menopausal women by causing relief of PMS symptoms. It is already approved for National Family Welfare programme.

Contraindications
1. Recent Liver disease or Jaundice.
2. PCOD.
3. Cervical dysplasia or Chronic cervicitis.
4. Hypersensitivity to drug.
5. Chronic illness.
6. Nursing mothers.
7. Allergic conditions.

Materials and Methods
This is a prospective observational study done from Jan 2021 to Jan 2022 in DR. B. R. Ambedkar Medical College and Hospital. 100 patients between the age group 25-45 years, clinically diagnosed with DUB were taken into the study. The mean age of the study group was 25-45 years and informed consent was obtained from the patient for the study. Although patients were multiparous women all other causes for abnormal bleeding was ruled out by taking proper history, clinical examination, blood investigation and ultrasonogram of abdomen and pelvis and dilatation and curettage. After ruling out the possible causes of Abnormal Uterine Bledding (AUB), a diagnosis of DUB was made and treatment was started. Group A with Oremloxifene and Group B with Norethisterone was started. Ormeloxifene 60 mg was administered orally twice a week for first 12 weeks and then once in a week for next 12 weeks. Norethisterone 5 mg twice a day from day 15-25 of cycle was administered. MBL was measured using pictorial blood loss assessment chart (PBAC), blood hemoglobin. All patients were followed till 6 months.
The relief of symptoms and patient acceptability were compared in both groups.
Group A: Ormeloxifene Group.
Group B: Norethisterone Group.

Results

Table 1: Age Distribution

Age in Years	Group-A	Group-B
25-30	6	8
30-35	14	16
35-40	24	22
40-45	6	4

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The mean age of the patients in both group was between 35-40 years.

Table 2: Showing Symptomatic Relief (reduction of PBAC scores) in Two Groups

Parity	Ormeloxifene Group (n=50)	Norethisterone Group (n=50)
Symptomatic relief present (reduction of PBAC)	41 (82%)	15 (30%)
Symptomatic relief not present	09 (9%)	35 (3%)
Total	50	50

Two groups are comparable, symptomatic relief was present with the ormeloxifene group which was statistically significant with P value= <0.001.

Table 3: Showing Number of Women Who Underwent Hysterectomy in Two Groups

	Ormeloxifene Group	Norethisterone Group
Finally underwent hysterectomy	06 (13%)	13 (26%)
Restored to other treatment and were satisfied	None	11 (24.5%)
Lost to follow up	02 (4%)	05 (10%)

Two groups are comparable and the ormeloxifene group had the least number of hysterectomies.

Table 4: Change in Hemoglobin

	Ormeloxifene Group	Norethisterone Group
Pre-treatment Hb	8.89 (6.40-11)	8.5 (6.2-10.5)
Post treatment Hb	10.7 (7.2-12.6)	9.5 (7-10.2)

Two groups are comparable and the Hb improved with the ormeloxifene group which was statistically significant with P value = < 0.001.

Discussion

Menorrhagia is socially embarrassing and physically incapacitating condition and has both emotional and financial drain. In this study PABC score was found to be significantly decreased in patients of post treatment using ormeloxifene. Our results are comparible with the study done in Indian population by BISWAS *et al*., [10] And KRIPLANI *et al*., [11].

In the present study our result suggested that there is significant increase in the Hb percentage our result were comparible with the study done by KRIPLANI *et al*., [11]. Our study observed significant decrease in the presence of clots in patients of post treatment using ormeloxifene. Presence of clots is an obvious evidence of anormal excessive menstrual blood flow [12]. A study also showed the improvement of clots in 85.71% of patients [10].

Conclusion

Ormeloxifene has better compliance and acceptability with marked relief in symptoms and helps in improving the hemoglobin percentage. Women who underwent hysterectomy after treatment were less in ormeloxifene group. Though the study size is small it highlights the role of ormeloxifene in reducing menorrhagia and avoiding surgery. Therefore, Ormeloxifene should be the drug of choice in patients with DUB.

Conflict of interest: The authors declare that there is no conflict of interest.

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