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Original Research Article

Efficacy of ormeloxifene versus norethisterone in the management of abnormal uterine bleeding

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ABSTRACT

Background: Abnormal uterine bleeding (AUB) is a common gynecological issue that significantly affects the quality of life of women, particularly those in the reproductive and perimenopausal age groups. Ormeloxifene, a selective estrogen receptor modulator, and norethisterone, a synthetic progestogen, are commonly used in its medical management. Objective of this study was to evaluate and compare the efficacy and safety of ormeloxifene and norethisterone in the management of AUB.
Methods: A prospective comparative study was conducted on 100 women aged 35 years and above diagnosed with AUB at D. Y. Patil Hospital, Navi Mumbai between July 2023 to December 2024. Participants were randomly assigned to two treatment groups. Group A received ormeloxifene (60 mg twice a week for 12 weeks, then once weekly for four weeks), while Group B received norethisterone (5 mg twice daily from day 5 to 25 of the menstrual cycle for 4 cycles). The primary outcome was the change in PBAC score. Secondary outcomes included hemoglobin levels, endometrial thickness, and incidence of side effects, evaluated at baseline, 2 months, and 4 months.
Results: Group A showed a 76.15% reduction in PBAC score, a 2.91 g/dl increase in hemoglobin, and a 4.09 mm decrease in endometrial thickness. In contrast, Group B demonstrated a 45.97% reduction in PBAC score, a 1.31 g/dl increase in hemoglobin, and a 3.50 mm decrease in endometrial thickness. Acne and gastrointestinal side effects were more common in the norethisterone group.
Conclusions: Ormeloxifene was more effective and better tolerated than norethisterone for the treatment of AUB. Its weekly dosing schedule, superior hematological improvement, and lower side-effect profile make it a preferable first-line therapy.

Keywords: Abnormal uterine bleeding, Ormeloxifene, Norethisterone

INTRODUCTION

Abnormal Uterine Bleeding (AUB) refers to bleeding from the uterine corpus that is irregular in volume, duration, or frequency, and not associated with pregnancy. It may present as heavy, prolonged, frequent, or irregular bleeding, and is classified into acute and chronic categories.[1] The PALM-COEIN system, developed by the International Federation of Gynecology and Obstetrics (FIGO), standardizes the etiology into structural (polyp, adenomyosis, leiomyoma, malignancy/hyperplasia) and non-structural causes (coagulopathy, ovulatory dysfunction, endometrial, iatrogenic, and not otherwise classified).[1,4]

Management options for AUB range from pharmacological to surgical interventions. Norethisterone is a widely used synthetic progestogen that has been

effective in reducing menstrual blood loss.[14,15,17] However, its use is limited by progestogenic side effects like mood swings, weight gain, bloating, headaches, and deranged lipid profile and poor compliance due to its frequent dosing regimen.[2,10,23] Ormeloxifene, a third-generation selective estrogen receptor modulator (SERM), offers a non-steroidal alternative with anti-estrogenic action on the uterus and a favorable once- or twice-weekly dosing schedule.[7-9,11,12,16] This study compares the efficacy and safety of these two agents in the treatment of AUB.

METHODS

Study design

A prospective, comparative clinical study was conducted at the Department of Obstetrics and Gynecology, Dr. D. Y. Patil Medical College, Navi Mumbai, over a period of 18 months from July 2023 to December 2024.

Inclusion criteria

Women aged 35 years and above, diagnosed with AUB with no structural abnormalities on ultrasound who were willing to participate in the study and provide informed consent were included.

Exclusion criteria

Women with any known liver or renal pathology, structural uterine anomalies or endometrial hyperplasia, malignancy, or systemic illness were excluded from the study. Sample Size and Grouping: A total of 100 participants were recruited and randomly divided into two equal groups:

Group A (Ormeloxifene): 60 mg twice weekly for 12 weeks, then once weekly for 4 weeks.

Group B (Norethisterone): 5 mg twice daily from day 5 to 25 of the cycle for 4 cycles.

Evaluation parameters

Initial screening

Thyroid-stimulating hormone (TSH) levels were tested to exclude hypo or hyperthyroidism.

Pelvic ultrasonography and Pap smear was conducted to exclude other diseases.

Only patients with no detected abnormalities other than AUB were included in the study.

Pictorial blood loss assessment chart (PBAC) – used to quantify menstrual blood loss.[18]

Hemoglobin levels (Hb) – assessed to monitor improvement in anemia

Endometrial thickness (ET) – measured by transvaginal ultrasonography

Side effects and compliance – documented throughout the study

Statistical analysis

Data were analyzed using SPSS version 23. Paired and unpaired t-tests were used to compare intra- and inter-group differences. A p-value<0.05 was considered statistically significantly.

RESULTS

PBAC score reduction

Group A showed a significant reduction in PBAC scores from a baseline mean of 283.54 to 67.62 at 4 months, reflecting a 76.15% decrease. Group B showed a reduction from 268.10 to 99.94 (45.97%). The difference was statistically significant (p<0.001).

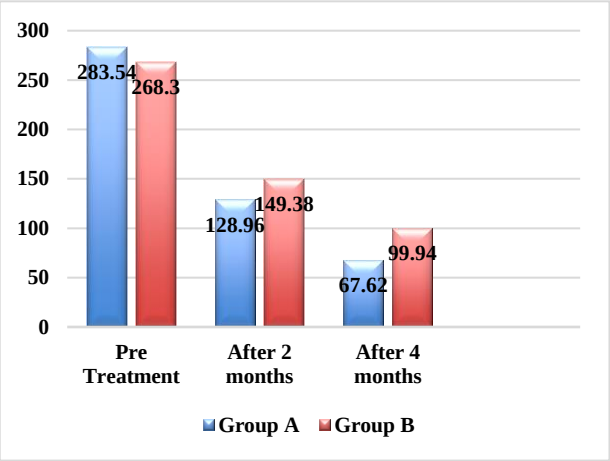

Figure 1: Intergroup comparison of PBAC.

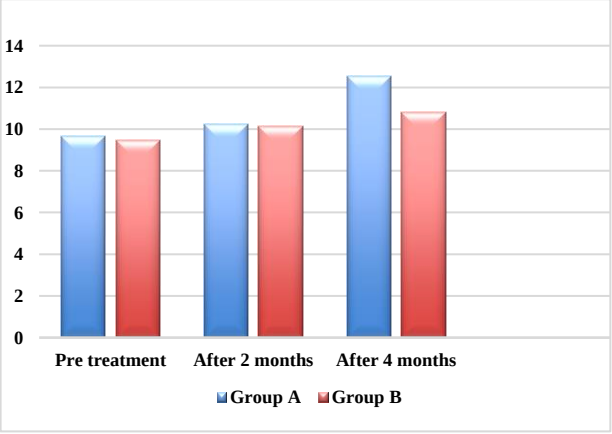

Figure 2: Intergroup comparison of Hb level.

Hemoglobin level improvement

Group A's mean Hb rose from 9.12 g/dl at baseline to 12.03 g/dl at 4 months (increase of 2.91 g/dl), while Group B's Hb increased from 9.17 g/dl to 10.48 g/dl (increase of 1.31 g/dl). The difference was statistically significant ($p<0.001$).

Endometrial thickness reduction

Group A exhibited a decrease in ET from 8.89 mm to 4.80 mm, while Group B saw a reduction to 5.66 mm. Although both were statistically significant within groups, Group A showed a greater decline ($p<0.001$).

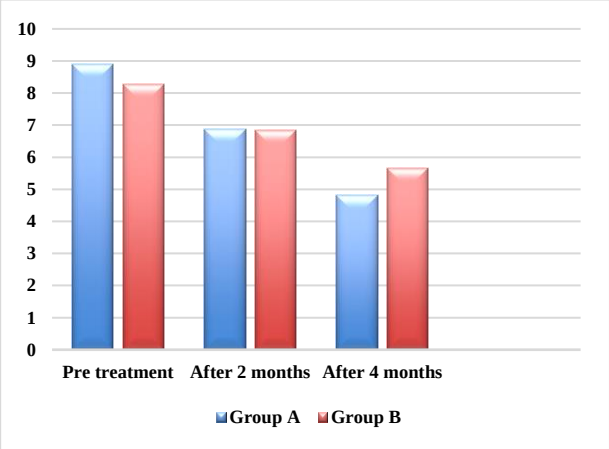

Figure 3: Intergroup comparison of endometrial thickness.

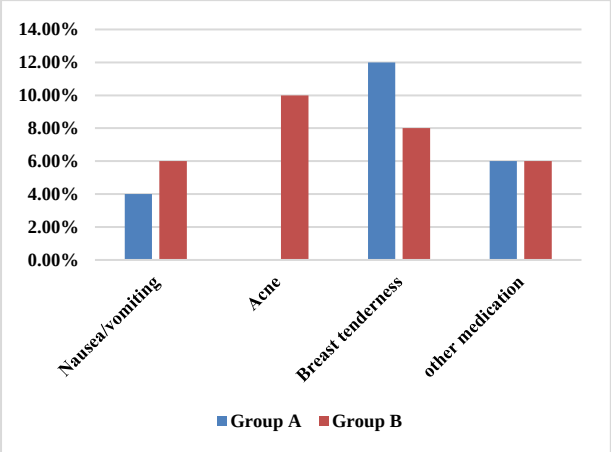

Figure 4: Intergroup comparison of side effects of treatment.

Side effects

Adverse effects were more frequent in Group B. Acne (10%) and gastrointestinal symptoms (6%) were notably higher compared to Group A. Breast tenderness was observed in both groups (12% in Group A, 8% in Group B), but without statistical significance.

DISCUSSION

Abnormal uterine bleeding (AUB) is one of the most common complaints encountered in gynecological practice, accounting for a significant proportion of outpatient visits and hysterectomies globally.[5,6] It has a profound impact on a woman's physical health, emotional well-being, and socio-economic productivity.[6] The medical management of AUB seeks to alleviate symptoms, prevent anemia, improve quality of life, and avoid or delay surgical interventions.[14,15,17] Among the pharmacological options, progestogens like norethisterone have been widely used, although newer agents such as selective estrogen receptor modulators (SERMs), including ormeloxifene, offer promising alternatives.[16]

In the present study, both ormeloxifene and norethisterone significantly reduced menstrual blood loss, as assessed by PBAC scores. However, the reduction was substantially greater in the ormeloxifene group (76.15%) than in the norethisterone group (45.97%). This aligns with findings by Surabhi et al, who reported a PBAC reduction of over 78% with ormeloxifene, and by Das et al, who noted a more pronounced decrease in bleeding with ormeloxifene compared to norethisterone.[19,22] The higher efficacy of ormeloxifene may be attributed to its selective antagonism of estrogen receptors in the endometrium, leading to a reduction in proliferative activity and stabilization of the endometrial lining.[7-9,11,12]

Hemoglobin levels showed a statistically significant increase in both groups, indicating effective control of blood loss and reversal of anemia. However, Group A (ormeloxifene) demonstrated a more marked improvement (2.91 g/dl) compared to Group B (1.31 g/dl). This hematologic benefit is critical, especially in resource-limited settings where anemia is prevalent among reproductive-age women. Similar hemoglobin improvement has been documented by Agarwal et al and Srinivasan, who reported an average rise of 2.88 g/dl after three months of ormeloxifene therapy.[21,23]

Endometrial thickness (ET) serves as both a diagnostic and monitoring parameter in AUB management. The present study showed a greater reduction in ET in the ormeloxifene group (mean decrease of 4.09 mm) compared to the norethisterone group (3.50 mm), consistent with findings by Amruta et al, who highlighted the superior efficacy of ormeloxifene in reversing endometrial hyperplasia and reducing thickness.[20] The estrogen-antagonistic effect of ormeloxifene on uterine tissue likely mediates this response, supporting its mechanism of reducing endometrial proliferation and normalizing menstrual patterns.[7-9,11,12]

An important aspect of any medical therapy is its tolerability and patient compliance. In this study, Group A had a better compliance profile, likely due to the weekly dosing regimen of ormeloxifene compared to the daily administration required with norethisterone. This finding

corroborates the work of Chitrangada et al who emphasized the role of simplified dosing in improving long-term adherence.[10] Additionally, side effects were fewer in the ormeloxifene group. Acne, a known progestogenic side effect, was significantly more common in the norethisterone group (10% vs. 0%), and gastrointestinal disturbances were also slightly higher. Breast tenderness was similar across both groups but not statistically significant.

Another factor favoring ormeloxifene is its dual role in contraception and menstrual regulation, making it particularly suitable for reproductive-age women with no immediate fertility desires.[3,13] Unlike norethisterone, which primarily works by suppressing ovulation and inducing a decidual response, ormeloxifene's action is tissue-selective and does not suppress ovulation, thus preserving natural hormonal cycles while exerting anti-estrogenic effects on the uterus.[13] Moreover, its lack of major hepatic or metabolic side effects, affordability, and availability through national health programs (as in India's "Chhaya" scheme) further increase its utility in public health contexts.

However, while ormeloxifene has shown superior short-term outcomes in this study and others, long-term safety and rare side effects, such as delayed ovulation or menstrual irregularities post-therapy, warrant further investigation. More large-scale, multicentric trials are needed to validate these findings and establish standardized guidelines for dosage and duration in different age and symptom groups. From a clinical perspective, ormeloxifene offers an ideal blend of efficacy, safety, and convenience. It is especially useful in perimenopausal women, where inducing amenorrhea or reducing bleeding burden significantly enhances quality of life without the need for surgery.[5] For younger women, its contraceptive benefits are an added advantage.[3] To summarize, the present study adds to a growing body of evidence suggesting that ormeloxifene surpasses norethisterone in clinical efficacy, hematological improvement, reduction of endometrial thickness, side-effect profile, and patient compliance. These findings advocate for its inclusion as a first-line therapy in evidence-based AUB management, especially where surgical options are contraindicated or undesired.

Limitations

Ormeloxifene's weekly regimen resulted in better patient adherence compared to the daily dosing required with norethisterone.

CONCLUSION

Ormeloxifene is more effective than norethisterone in reducing menstrual blood loss, improving hemoglobin levels, and reducing endometrial thickness. It is also better tolerated, with fewer side effects and improved compliance due to its convenient dosing schedule. Based on this study, ormeloxifene should be considered a preferred first-line medical therapy for the treatment of abnormal uterine bleeding in eligible women.

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Conflict of interest: None declared
Ethical approval: This study was approved by the Institutional Ethics Committee of Dr. D.Y. Patil Medical College, Navi Mumbai. All participants provided informed written consent

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