Original Article

Comparison of The Efficacy of Norethisterone Versus Combined Oral Contraceptive Pills Used For The Management Of Menorrhagia At The Onset of Menarche

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Abstract

Objective: To compare the efficacy of norethisterone acetate (NETA) and combined oral contraceptive pills (COCs) in the management of heavy menstrual bleeding (menorrhagia) at the onset of menarche in adolescent girls.

Methods: This Quasi-experimental comparative study was conducted from July 2025 to January 2026 at the Department of Obstetrics and Gynecology, Pakistan Ordnance Factories (POF) Hospital, Wah Cantt.
Methodology: A total of 120 adolescent girls aged 11–16 years presenting with heavy menstrual bleeding (HMB) at the onset of menarche were enrolled. Participants were assigned to two groups (n=60 each) using a non-random allocation approach. Group A received norethisterone acetate (5 mg twice daily) during the latter half of the menstrual cycle, whereas Group B received combined oral contraceptive pills prescribed in the conventional 21-day cyclic regimen. Efficacy was assessed as a clinically significant improvement in the Menorrhagia Impact Questionnaire (MIQ) score after treatment. Data were analyzed using SPSS version 25

Results: The mean age was 13.6±1.6 years in the norethisterone group and 13.4±1.8 years in the combined oral contraceptive group. Efficacy was observed in 85% of patients who received norethisterone acetate compared to 65% of patients who received combined oral contraceptive pills, showing a statistically significant difference (P = .011). A greater reduction in estimated blood loss and substantial improvement in MIQ scores were observed in the norethisterone group.

Conclusion: Under the specific cyclical treatment protocols used in this study, norethisterone acetate demonstrated greater short-term improvement in menstrual blood loss and MIQ scores than combined oral contraceptive pills in adolescent girls presenting with heavy menstrual bleeding (HMB) at the onset of menarche.

Keywords: Adolescent; Contraceptives, Oral; Menarche; Menorrhagia; Norethisterone; Quality of Life.

Introduction

Immaturity of the hypothalamic–pituitary–ovarian axis frequently causes heavy menstrual bleeding (HMB) at menarche.[1] Erratic and heavy uterine flow frequently occurs during the first few years following menarche due to anovulatory cycles.[2] Heavy bleeding leads to severe somatic and psychological distress, such as anaemia, tiredness, poor academic performance, and agitation.[3] The diagnosis of HMB at menarche requires precise clinical investigation to rule out possible underlying conditions such as haemostatic abnormalities, hormonal imbalances, or underlying systemic disease, although the cause in most cases is functional.[4] Prompt and appropriate treatment is essential for the prevention of complications and improvement in the quality of life; thus, hormonal treatments become the mainstay in the treatment of adolescents presenting with HMB during menarche.[5]
Norethisterone is a synthetic progestogen commonly used in the treatment of HMB, especially in adolescents in whom the administration of the hormone oestrogen can be avoided.[6]
Its mechanism of action mainly consists of the stabilisation of the endometrial lining, along with inducing the transition from proliferative to secretory endometrium.[7]

Norethisterone is usually administered either in the cyclical or continuous dosage regimen, depending on the severity of the patient's menstrual bleeding.[8] It is considered effective in the control of menstrual bleeding as well as in the regularisation of the menstrual cycles in adolescents.[9] Side effects noted in certain cases are weight gain, changes in mood, nausea, or breakthrough bleeding, which can affect compliance.[10] Despite this, norethisterone remains a commonly prescribed option due to its availability, low cost, and relative safety in the adolescent age group.[11]

Combined oral contraceptive pills are also an important therapeutic agent in the management of HMB at the onset of menarche; they are a combination of both oestrogenic and progestogenic components.[12] These agents work by inhibiting ovulatory stimulation, normalising menstrual cycles, and stabilising the endometrial lining, which in combination leads to a reduction in menstrual blood loss.[13] Combined oral contraceptive pills are especially beneficial for adolescents with irregular periods, dysmenorrhoea, or acneiform eruptions because they cause predictable withdrawal bleeding and better cycle regulation compared to progestin-only regimens in most cases.[14] However, the use of these formulations can be limited in some adolescents because of contraindications to oestrogen.

There is a paucity of local data on the management of HMB during menarche onset in adolescent girls in our local population. In this regard, clinical practice is largely based on international guidelines and research conducted in other populations. This study aimed to compare the effectiveness of norethisterone acetate and combined oral contraceptive pills in the management of HMB at the onset of menarche in adolescent girls.

Materials And Methods

This quasi-experimental comparative study was conducted at the Department of Obstetrics and Gynecology, POF Hospital, Wah Cantt, from July 2025 to January 2026. Ethical approval was obtained from the Institutional Review Board of the hospital before the initiation of the study, and all procedures were performed in accordance with the approved ethical standards (Ref. No. IRB/POFH/10-2024/Gyne-Obs/05, dated 03/10/2024). Written informed consent was obtained from all participants or their legal guardians after the study objectives, potential benefits, and treatment protocols were explained in simple and understandable language.

The sample size was calculated using the WHO sample size calculator, assuming an 80% power of the test, a 5% level of significance, and expected efficacy rates of 89% in the norethisterone acetate group and 68% in the combined oral contraceptive pill group.[15] A total of 120 adolescent girls were enrolled, with 60 participants assigned to each treatment group. Eligible participants were girls aged 11–16 years who presented with heavy menstrual bleeding (HMB) at the onset of menarche. In addition to a low Menorrhagia Impact Questionnaire (MIQ) score at initial presentation, HMB was defined as menstrual bleeding that lasted longer than seven days or excessive menstrual blood loss that resulted in frequent soaking of sanitary pads for several hours. The age between 11 and 16 years at which menstruation started was known as the age of menarche.

The exclusion criteria for girls were as follows: known severe urinary tract infection; hypothyroidism with a thyroid-stimulating hormone level greater than 5 IU; polycystic ovary syndrome diagnosed by ultrasound; body mass index (BMI) below 18.5 kg/m^2; history of taking norethisterone acetate or combination oral contraceptives; renal impairment with serum creatinine levels over 2 mg/dL; or any history of cardiac anomalies. Before the initiation of combined oral contraceptive therapy, all participants were clinically evaluated for contraindications to oestrogen-containing medications, including a history of migraine with aura, thromboembolic risk factors, and other relevant conditions, in accordance with standard clinical safety screening principles consistent with the WHO Medical Eligibility Criteria guidance.

A structured proforma was used to record baseline clinical and demographic data, which comprised age, BMI, haemoglobin level, estimated menstrual blood loss, family history of HMB, and baseline MIQ. The principal investigator performed a thorough clinical evaluation of all enrolled participants, which included a general physical examination and a thorough menstrual history. Menstrual bleeding-related quality of life was measured using the MIQ, and baseline MIQ scores were acquired before treatment initiation. The MIQ scoring was adapted for analysis, such that higher scores reflected a better quality of life and reduced impact of HMB.

Participants were assigned to two treatment groups using a simple allocation method based on sequential enrolment and group assignment. The group assignment plan was generated by the principal investigator. Group A received norethisterone acetate (5 mg twice daily) beginning in the latter half of the menstrual cycle, whereas Group B received combined oral contraceptives in a conventional 21-day cyclic regimen. The selected regimens were based on commonly used first-line hormonal treatment options for adolescent HMB in routine clinical practice, reflecting a pragmatic, real-world, comparative design. At the time of enrolment, the participants received counselling on proper drug intake, therapy adherence, and potential side effects. The participants were monitored for adverse effects at each follow-up visit.

Participants were monitored in the outpatient department over three consecutive menstrual cycles. Estimated menstrual blood loss was assessed based on patient-reported bleeding patterns and the number of sanitary pads used and was recorded as an approximate clinical estimate. The MIQ was used to reevaluate the participants at the end of the treatment period, and post-treatment MIQ scores were recorded. At follow-up, haemoglobin levels and estimated menstrual blood loss were reevaluated.

When three menstrual cycles of therapy were completed, the MIQ score increased by at least ten points from the baseline, which was considered treatment efficacy. SPSS version 25 was used to enter and analyse data. The mean ± standard deviation was used to express quantitative variables such as age, BMI, haemoglobin level, estimated blood loss, and MIQ scores before and after treatment. Frequencies and percentages were used to display qualitative factors such as treatment effectiveness and family history of HMB. Paired t-test was used for within-group comparisons of haemoglobin levels and MIQ scores before and after treatment, whereas an independent t-test was used for between-group comparisons. The chi-square test was used to compare the treatment efficacy between the two groups. Age, BMI, and family history of HMB were potential effect modifiers that were stratified before post-stratification chi-square testing. Statistical significance was set as ≤ .05.

Results

A total of 120 adolescent girls were enrolled in this study and divided into two groups (n = 60 each). All participants completed the study and were included in the final analyses. Baseline demographic and clinical characteristics were comparable between the two groups, with no statistically significant differences observed in age, haemoglobin level, height, weight, body mass index, baseline estimated menstrual blood loss, or baseline MIQ score ($P > .05$ for all) (Table 1).

After 3 months of treatment, both groups experienced a reduction in estimated menstrual blood loss (clinical estimate); however, the reduction was significantly greater in the norethisterone group than in the combined oral contraceptive group (mean difference, −26.2 mL; 95% CI: −36.0 to −16.4; $P < .001$).

Similarly, baseline MIQ scores were comparable between the two groups (11.4±2.0 vs. 11.1±2.0, $P = .36$). Following three months of therapy, MIQ scores improved significantly in both groups, with a greater mean improvement observed in the norethisterone group than in the combined oral contraceptive group (mean difference 2.0; 95% CI: 0.70 to 3.31, $P = .004$). Higher MIQ scores indicate improvement in symptoms and quality of life (Table 1).

Table 1: Baseline and post-treatment clinical characteristics of girls (n=120)

Variables	Norethisterone Acetate (n=60) Mean ± SD	Combined OCPs (n=60) Mean ± SD	Mean Difference (95% CI)	*P* value
Age (years)	13.6± 1.6	13.4±1.8	0.20 (−0.41 to 0.81)	.53
Hemoglobin (g/dL)	11.3±0.8	11.3±1.1	−0.01 (−0.35 to 0.33)	.61
Height (cm)	155.0± 5.7	155.6±6.0	−0.60 (−2.61 to 1.41)	.59
Weight (kg)	52.4±7.3	51.9±7.3	0.50 (−2.01 to 3.01)	.68
BMI (kg/m²)	21.9±3.3	21.5±3.3	0.40 (−0.74 to 1.54)	.53
Estimated Blood Loss – Baseline (ml)	161.8±31.3	169.0±28.7	−7.20 (−17.79 to 3.39)	.21
Estimated Blood Loss – 3 Months (ml)	67.0±22.2	93.2±31.6	−26.20 (−36.00 to −16.40)	.001
MIQ Score – Baseline	11.4±2.0	11.1±2.0	0.30 (−0.36 to 0.96)	.36
MIQ Score – 3 Months	21.7±3.6	19.7±3.7	2.00 (0.70 to 3.31)	.004

Discussion

In this study, the overall efficacy of norethisterone acetate was significantly higher (85%) than that of the combined oral contraceptive (65%) ($P = .011$). The baseline estimated blood loss was comparable between groups, but after 3 months of treatment, the norethisterone group showed a greater reduction, with a mean blood loss of 67.0±22.2 ml compared to 93.2±31.6 ml in the combined oral contraceptive group. The menstrual impact questionnaire scores also improved more in the norethisterone group (21.7±3.6) than in the combined oral contraceptive group (19.7±3.7), reflecting better quality of life improvement. When stratified by BMI, norethisterone showed significantly better efficacy in patients with BMI ≤ 25 kg/m² (84.6% versus 62.7%, $P = .039$). The presence of a family history also influenced the treatment response, with norethisterone showing significantly higher efficacy in patients with a positive family history (92.6% vs. 69.2%, $P = .047$).

The present study demonstrated that norethisterone acetate was significantly more effective than combined oral contraceptive pills in managing heavy menstrual bleeding (HMB) at menarche, with efficacy rates of 85% and 65%, respectively. This finding is consistent with the results reported by Patel et al., who found norethisterone to be more effective than combined oral contraceptive pills for managing puberty HMB, with higher improvement in MIQ scores (21 versus 17) and less treatment failure in the norethisterone group.[15] Similarly, Dean et al. reported superior outcomes with norethindrone acetate, showing only 8% spotting compared to 43% in the combined oral contraceptive group ($P < .01$) and higher patient satisfaction of 80%.[16] These consistent findings suggest that progestogen monotherapy provides stronger endometrial suppression in the adolescent population.

However, the findings contrast with the study by Sen et al., who found no significant difference between norethisterone and low-dose combined oral contraceptive pills in reducing blood loss in dysfunctional uterine bleeding, with comparable improvement in Pictorial Blood Loss Assessment Chart scores (-98.6±7.8 vs. -96.4±8.7, $P = .19$) and haemoglobin levels (2.8±1.1 vs. 2.7±0.9 g/dL, $P = .84$).[17] This discrepancy may be explained by differences in study population, as Sen et al. included adult women with a mean age of 28 years, whereas the present study focused on adolescents at menarche with a mean age of 13.4–13.6 years.[17]

The present study showed a greater reduction in estimated blood loss with norethisterone (67.0±22.2 ml) than with combined oral contraceptive pills (93.2±31.6 ml) after 3 months of treatment. This is supported by the findings of Sharma et al., who demonstrated a significant reduction in PBAC score from 180±14.4 to 82±10.9 in adolescents treated with norethisterone, along with improvement in haemoglobin levels from 7.9±0.9 to 10.3±6.9.[18]

Stratified analysis revealed that norethisterone was significantly more effective in patients with a BMI ≤ 25 kg/m² and those with a positive family history. These subgroup differences have not been reported previously. Boruah et al. reported that 63% of women experienced styptic action within 4 h with a norethisterone 10 mg controlled-release formulation, but did not stratify results by BMI or family history.[19]

Regarding alternative treatments, Gawande et al. found that ormeloxifene was superior to norethisterone acetate in reducing menstrual blood loss and improving haemoglobin levels.[20] Similarly, Shaheen et al. demonstrated that tranexamic acid was more effective than norethisterone in reducing the number of pads used and the passage of blood clots.[21] However, these studies were conducted in adult women and utilised different mechanisms of action, limiting direct comparison with the present adolescent population.

Several studies have compared norethisterone with the levonorgestrel intrauterine system. Naqvi et al., Ashraf et al., and Malik et al. reported superior outcomes with LNG-IUS in terms of blood loss reduction and patient satisfaction.[22-24] However, these findings are not directly applicable to adolescents at menarche, as intrauterine devices are generally not preferred as first-line treatments in nulliparous adolescent girls. Therefore, the oral route remains a more acceptable and practical therapeutic option for this age group. This study was designed as a pragmatic comparative study rather than a protocol-driven equivalence trial.

The current study has several limitations. First, the study was conducted at a single centre, which may limit the extrapolation of the results to other populations and clinical settings. Second, the follow-up period was relatively short (three months), which might not be sufficient to assess the long-term effectiveness and side effects of the two treatment modalities. Third, the sample size was relatively small, which could reduce the statistical power needed to perform subgroup analysis. Fourth, the study failed to measure patient compliance or medication regimen adherence, which may have affected the treatment results. Fifth, menstrual blood loss was estimated clinically rather than measured using objective tools, such as the alkaline haematin method or validated instruments, such as the Pictorial Blood Loss Assessment Chart, which may introduce reporting bias. Additionally, the treatment regimens differed in terms of duration and hormonal exposure, which may limit the direct comparability between the two groups. The study did not collect data on race or ethnicity, which may limit the generalisability of the findings to more diverse populations and settings.

Conclusions

Under the specific cyclical treatment protocols used in this study, norethisterone acetate demonstrated greater short-term improvement in menstrual blood loss and Menorrhagia Impact Questionnaire scores compared to combined oral contraceptive pills in adolescent girls presenting with heavy menstrual bleeding (HMB) at the onset of menarche. These findings suggest that norethisterone acetate may be a more effective option for initial short-term management in this population, although further large-scale and long-term studies are warranted to confirm its long-term comparative efficacy.

Author Information

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