



A COMPARATIVE STUDY OF EFFICACY OF NORETHISTERONE AND COMBINED ORAL CONTRACEPTIVE PILL IN THE TREATMENT OF PUBERTY MENORRHAGIA

Obstetrics & Gynaecology

Dr. Shrikant Warade

Associate Professor, Dept of Obstetrics and Gynecology, SVNGMC, Yavatmal, Maharashtra.

Dr. Anju P. K.*

Junior Resident, Dept of Obstetrics and Gynecology, SVNGMC, Yavatmal, Maharashtra.
*Corresponding Author

ABSTRACT

Background: Menstrual disorders are quite common constituting significant morbidity during this difficult period of puberty among adolescent girls. Girls suffering from menorrhagia commonly complain about heavy menstrual bleeding (HMB), irregular bleeding or spotting between periods. Medical treatment to lower menstrual blood loss consist of combined oral Contraceptive (COC) pills, gonadotrophin-releasing hormone (GnRH) analogues and oral progestones. This study has been planned to compare the efficacy of norethisterone and COC pills in the reduction of blood loss in puberty menorrhagia. **Methodology:** An observational study was conducted on 100 cases fulfilling the inclusion and exclusion criteria patients aged between 12 to 18 years presenting with heavy menstrual loss. In 50 patients, Norethisterone and in remaining 50 patients, low-dose COC pill was given, once daily from day 5 to day 25 of the cycle and outcome of both groups were compared. Data was analysed using appropriate statistical tests. Level of Significance was taken as $P \leq 0.05$. **Results:** Most common complaint was menstrual complaints among both groups. Majority were having symptoms for more than a year in both groups. Mean Hb levels on start of treatment in group I was 9.32 ± 1.9 gm/dL and in group II was 8.52 ± 1.3 gm/dL. Mean Hb levels at end of 3rd cycle in group I was higher (10.1 ± 1.9 gm/dL) as compared to group II (9.21 ± 2.3). After treatment PBAC in Group I was lower (189.3 ± 98.7) as compared to group II (276.1 ± 102.1). There was improvement in mean MIQ scores. Adverse event was more seen among group II. Treatment success rate was significantly higher among group I, (88%) females had good results and among group II 35 (70%). **Conclusion:** Norethisterone was found to be more effective and safer than low-dose COC pills in reduction of blood loss and better tolerated in DUB. Further studies are needed to compare norethisterone and COC pills in compliance to treatment for a prolonged period.

KEYWORDS

Menorrhagia, Norethisterone, Combined Oral Contraceptive Pill.

INTRODUCTION:

Puberty is a period of substantial physical and psychological transformation for adolescent girls. According to WHO, adolescence includes the age group of 10–19 years. Menstrual disorders are quite common constituting significant morbidity during this difficult period for adolescents and their families. The prevalence of menorrhagia requiring hospitalization ranges from 3 to 20 %. Adolescent girls with gynecological ailments need a degree of solitude and sensitive handling.

Puberty menorrhagia is defined as excessive bleeding in quantity (>80 ml) or in duration (>7 days) between menarche and 19 years of age. Its occurrence includes the entire period of time during which secondary sexual characteristics develop, menstruation begins in females and psychosexual approach of a human changes. Girls suffering from menorrhagia commonly complain about heavy menstrual bleeding (HMB), irregular bleeding, spotting between periods, or spotting after sex. 8,9

The most common cause of puberty menorrhagia is anovulatory cycles, which are related to immaturity of the hypothalamic-pituitary-ovarian axis. 11 Diagnosis of puberty menorrhagia depends on detailed history, clinical examination, estimation of blood loss in menstruation along with complete blood count (CBC), ultrasonography and wherever possible hysteroscopy, biopsy, and magnetic resonance imaging. 13

There are several treatment strategies for puberty menorrhagia according to the cause of the disorder. Medical treatment to lower menstrual blood loss consist of combined oral Contraceptive (COC) pills, gonadotrophin-releasing hormone (GnRH) analogues and oral progestones.

In the view of the above facts, this study has been planned to compare the efficacy of norethisterone and COC pills in the reduction of blood loss in puberty menorrhagia.

MATERIAL AND METHODS:

An observational study was conducted on 100 cases fulfilling the inclusion and exclusion criteria patients aged between 12 to 18 years presenting with heavy menstrual loss presented at Outpatient Department of Obstetrics and Gynecology, SVNGMC Medical College and Hospital, India. Out of 100 patients, 50 patients (Group-I) had been given Norethisterone 5mg twice daily from day 5 to day 25 of

the cycle and remaining 50 patients (Group-II) had been given low-dose COC pill (containing 30 mcg ethinylestradiol and 150 mcg levonorgestrel), once daily from day 5 to day 25 of the cycle and outcome of both groups were compared. A written informed consent from parent was obtained for each patient. Patients detailed medical and drug intake history was recorded. A detailed medical, surgical examination was done for the presence of any abnormality other than heavy menstrual blood loss.

The outcome variables were change in PBAC score, change in hemoglobin level score from baseline to the end of 3 cycles, change from baseline in health-related quality-of-life parameters, estimation of blood loss and effect on hemoglobin level at the end of the study, number of adverse events during the study period. Patients was trained to score the card during menstruation by a female expert. After one menstrual period, the patients appeared in the hospital with the PBAC score and was recorded in register with a number. Qualitative health-related quality-of-life assessments were based on responses to the Menorrhagia Impact Questionnaire (MIQ) that was completed by participants after study. There was a total of 2 study-associated visits per patient: 1 at baseline and 2 at the end of 3 cycles.

Data was analysed using SPSS V 15.0. Student's unpaired t tests was used to compare means between 2 groups for continuous normal data. Chi square tests was used to compare percentages of more than 2 groups. All tests will be 2 tailed. Level of Significance was taken as $P \leq 0.05$.

RESULTS:

In the present study, we took 50 patients in each group (Group I and II). Mean age in group I was 17.1 ± 1.2 years and in group II was 16.9 ± 1.6 years. Majority were in 15 to 18 years in both groups. On socioeconomic status majority belonged to lower middle class among both groups. On education majority females were educated till secondary school. No significant difference was seen in age, socioeconomic status and education status of the patients and the groups were comparable.

Table 1: History And Clinical Presentation

History and Clinical Presentation		Group I	Group II	P value
Menstrual pattern	Menorrhagia	29	25	0.2
	Menometrorrhagia	25	27	0.34
	Metrorrhagia	12	18	0.09
	Polymenorrhagia	7	5	0.26

Presenting complaints	Menstrual compliant	50	50	NA
	Vaginal discharge	24	25	0.42
	Lower abdominal pain	13	14	0.4
	Weight problem	12	11	0.4
	Urinary problem	7	5	0.26
Duration of symptoms	< 6 months	4	5	0.15
	6 to 1 year	16	14	
	More than 1 year	30	31	
	Total	50	50	
	Mean +SD	1.32±0.9	1.51±0.3	
Body mass Index (BMI) (Kg/m ²)	<18.5	4	5	0.002
	18.6 to 24.9	22	25	
	25-30	18	15	
	>30	6	5	
	Mean +SD	25.9±3.4	24.3±1.2	

Most common menstrual pattern was menorrhagia and menometrorrhagia. Most common presenting complaint was menstrual complaint seen in all patients. 24 (48%) had vaginal discharge in group I and 25 (50%) had vaginal discharge in group II. Menstrual complaint showed significance difference. Mean duration of symptoms in group I was 1.32±0.9 days and in group II was 1.51±0.3 days. Majority were having symptoms for more than a year in both groups. Difference between the groups was not significant (p=0.15). (Table 1)

Mean BMI in group I was 25.9±3.4 kg/m² and in group II was 24.3±1.2 kg/m². Majority were in normal range in both groups. Statistical significance was seen (p=0.002) (Table 1)

Table 2: Haemoglobin Levels And Duration Of Blood Loss:

Haemoglobin levels	Group I	Group II	P value
<7	8	10	0.01
7 to 9	32	28	
>9	10	12	
Mean ±SD	9.32±1.9	8.52±1.3	
Haemoglobin levels at end of 3 rd cycle			
<7	6	8	0.03
7 to 9	22	25	
>9	22	17	
Mean ±SD	10.1±1.9	9.21±2.3	
Duration of days of Blood Loss			
<5	12	8	0.17
5 to 7	32	29	
>7	6	13	
Total	50	50	

Mean Hb levels on start of treatment in group I was 9.32±1.9 gm/dL and in group II was 8.52±1.3 gm/dL. Majority had Hb in range of 7 to 9 gm/dL in both groups. Statistical significance was seen (p=0.01). Mean Hb levels at end of 3rd cycle in group I was significantly higher (10.1±1.9 gm/dL) as compared to group II (9.21±2.3 gm/dL) (p=0.03). Majority duration of days of blood loss was between 5 to 7 days among both groups. Statistical significance was not seen (p=0.17). Mean PBAC score on admission was 318.1±108.9. And after treatment in group I, it was significantly lower (189.3±98.7) as compared to group II (276.1±102.1) (p<0.0001). (Table 2)

MIQ Scoring showed that there was mean improvement in MIQ scores for tiredness, productiveness, hygienic condition and depressiveness related questions in both treatment groups compared to baseline. (Table 3)

Table 3: MIQ Score:

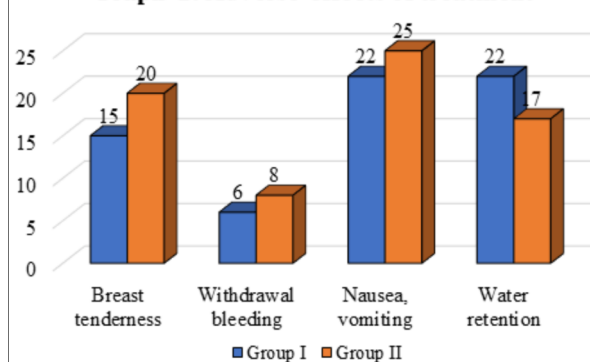
MIQ score	Before treatment	After treatment Group I	After treatment Group II
Social activity	2	4	3
Work performance	1	2	2
Tired/exhausted	2	4	3
Feeling productive	2	4	3
Unclean/ unhygienic	1	2	2
Depressed	2	4	3
Total	10	20	16
P value		0.1	0.9

Adverse Events:

Adverse event was more seen among group II. Among group I, 20

females showed breast tenderness, 8 had withdrawal bleeding, 25 had nausea, vomiting and 17 had water retention and in group II 15 females showed breast tenderness, 6 had withdrawal bleeding, 22 had nausea, vomiting and 22 had water retention. (Graph 1)

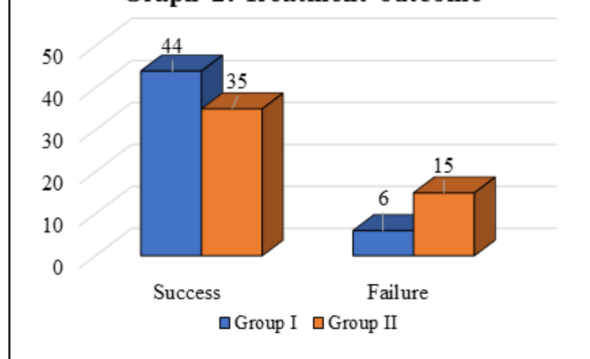
Graph 1: Adverse effects of treatment



Treatment Outcome:

Treatment success rate was significantly high among group I, 44 (88%) females had good results as compared to group II, 35 (70%) females had good results (p=0.01). (Graph 2)

Graph 2: Treatment outcome



DISCUSSION:

In the present study, mean age in group I was 17.1±1.2 years and in group II was 16.9±1.6 years. No statistical significance was seen (p=0.4). Study by Sen S et al (7) showed that mean age 28.62 ± 9.84 years comprised the Group and a total of 50 patients with a mean age 28.42 ± 10.08 years comprised the Group II. Ashraf et al.(56) reported that mean age and mean duration of the disease for group A was 34.16±6.327 years and 6.18±2.415 years, respectively, compared to 34.21±3.595 years and 6.21±2.418 years, respectively, in group B. This study is similar to the study of Sanjay Rao et. al.(58)

Most common menstrual pattern seen was menorrhagia and menometrorrhagia. Young et al (59) showed that 34.5% of 348 women reported irregular menstruation and among them 89.4% reported oligomenorrhea and 9.6% reported amenorrhea. Most common present complaint was menstrual complaints among both groups, 24 had vaginal discharge in group I and 25 had vaginal discharge in group II. Menstrual complaint showed statistical significance. Mean duration of symptoms in group I was 1.32±0.9 days and in group II was 1.51±0.3 years. Majority were having symptoms for more than a year in both groups. Statistical significance was not seen (p=0.15). study by Sen et al (7) also showed that in addition to the efficacy of norethisterone, this study also supports the use of low-dose COC pills in the improvement of blood loss associated with DUB.

Mean Hb levels on start of treatment in group I was 9.32±1.9 gm/dL and in group II was 8.52±1.3 gm/dL. Majority had Hb in range of 7 to 9 gm/dL in both groups. Statistical significance was seen (p=0.01). Mean Hb levels at end of 3rd cycle in group I was 10.1±1.9 gm/dL and in group II was 9.21±2.3.

Statistical significance was seen (p=0.03). Study by Sen S et al (7) showed that mean Hb in norethisterone group pretreatment was 7.64±0.58 and post treatment was 10.44±0.78, and among COC pills groups it was 7.72±0.5 pretreatment and 10.38±0.64 post treatment. Similar findings were seen in present study.

Mean PBAC score on admission was 318.1 ± 108.9 . And after treatment in group I it was 189.3 ± 98.7 and group II was 276.1 ± 102.1 . Statistical significance was seen ($p < 0.0001$).

Study by Sen S et al (7) showed that mean PABC after treatment in group I it was 176.16 ± 5.75 and group II was 175.58 ± 6.07 . Ashraf et al.(56) reported that Group A exhibited median PBAC score of 155 ± 3.256 and 59.45 ± 2.92 after 3 and 6 months of the treatment, respectively. Group B showed median PBAC score of 184 ± 2.29 and 80.87 ± 2.21 after 3 and 6 months of the treatment, respectively. study by Abu H et al (57) showed that no statistically significant differences were found regarding the mean PBAC score (90.2 ± 24.4 vs. 92.3 ± 26.7) and its percent reduction (68.6% vs. 69.5%), duration of menses (5.3 ± 1.2 vs. 5.5 ± 1.1 days).

There was mean improvement in MIQ scores for tiredness, productiveness, hygienic condition and depressiveness related questions in both treatment groups compared to baseline. Study by Patel NK et al (20) showed that for work performance related question, there was mean improvement in both the groups compared to baseline. Adverse event were more seen among group II. Study by Sen S et al (7) showed that nausea/vomiting was more experienced with low-dose COC (24% vs. 6%). In contrast, irregular menstrual bleeding (22% vs. 4%), weight gain (20% vs. 6%), and acne and hirsutism (12% vs. 0%) were higher with norethisterone treatment. Study by Patel NK et al (20) showed that side effects were more with OC pills as compared to norethisterone.

In the present study, treatment success rate was significantly high among group I. Ashraf et al.(56) reported that levonorgestrel-containing intrauterine device (IUD) is better than the oral norethisterone. However, IUD acceptance still faces challenges. Study by Patel NK et al (20) showed that 11% had treatment failure in group I and 32% in group II even added that study demonstrates that norethisterone or COC pills-mediated improvements in menorrhagia extend to adolescents.

CONCLUSION:

Norethisterone was found to be more effective and safer than low-dose COC pills in reduction of blood loss in DUB. Further studies are needed to compare norethisterone and COC pills in compliance to treatment for a prolonged period.

This study supports the use of norethisterone for the management of puberty menorrhagia than COC pills because it was more effective and better tolerated as compared to COC pills for the management of puberty menorrhagia.