Original Article

A Comparative Study of Tranexamic Acid and Ethamsylate in Dysfunctional Uterine Bleeding

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ABSTRACT

Background: Dysfunctional Uterine Bleeding is irregular uterine bleeding that occurs in the absence of recognizable pelvic pathology, general medical disease or pregnancy. Bleeding may be excessively heavy or light and may be prolonged, frequent or random. About 1-2% of women with improperly managed an ovulatory bleeding eventually may develop endometrium cancer. There is less evidence which states the effectiveness of both the drugs because of which this study has been performed. **Aim and Objectives:** The objective of the study was to compare the efficacy of tranexamic acid and ethamsylate and to study the reduction in heavy menstrual bleeding. **Materials and Methods:** This study is a prospective comparative study which was conducted at Employee State Insurance Hospital, Ayanavaram, and Chennai. Of 56 patients recruited for the study with randomisation, 28 patients were in group A (tranexamic acid) and 28 patients were in group B (ethamsylate). Four patients were lost for follow up and two patients discontinued the given drugs. Hence 50 patients were included in the study. Group A received Tranexamic acid 500mg, BD, from 1 to 5 days of the menstruation for three consecutive cycles. Similarly Group B received Ethamsylate 500mg, BD from 1 to 5 days of the menstruation for three consecutive cycles. **Results:** Female patients between the age group of 39-45 years are mostly affected with dysfunctional uterine bleeding (DUB). PBAC mean score showed a significant reduction in menstrual blood loss both with tranexamic acid (293.84 ± 137.50) and ethamsylate (326.24 ± 83.89), but tranexamic acid proved to be more efficacious. Hb level in tranexamic acid (12.96 ± 0.99) group was seen to be increased slightly when compared with ethamsylate group (12.024 ± 1.07). The Endometrium thickness of the patients receiving tranexamic acid (3.404 ± 0.99) was between the normal ranges. Use of tranexamic acid and ethamsylate improved health-related quality of life. **Conclusion:** This study suggests that both tranexamic acid and ethamsylate are effective in management of dysfunctional uterine bleeding. Tranexamic acid was superior to ethamsylate in terms of effectiveness, reduction in blood loss and improvement in quality of life.

Key words: Dysfunctional uterine bleeding, Endometrium thickness, Tranexamic acid, Ethamsylate, Menstruation.

INTRODUCTION

Frequent consultations to the gynaecology department is due to menstrual disorders such as dysfunctional uterine bleeding. 11% of women in their reproductive age undergoes heavy menstrual bleeding and this is known as menorrhagia.[1] Abnormal uterine bleeding can be irregular, non-cyclic bleeding, prolonged or heavy menstrual bleeding.[2]

Dysfunctional uterine bleeding is also known as abnormal uterine bleeding which has no relation with a physical lesion, inflammation or pregnancy. It is defined as excessively heavy, prolonged or frequent bleeding of uterine origin that is not due to pregnancy or any recognisable pelvic or systemic disease. 90% of dysfunctional uterine bleeding is an ovulatory. It effects reproductive teens and perimenopausal women. Teens experience dysfunctional uterine bleeding due to immature hypothalamic- pituitary – adrenal axis and it occurs in perimenopausal women due to decline in ovarian function.[3,4]

Women with heavy menstrual bleeding are unable to perform normal activities due to frequent changing of sanitary products and fear of staining of outer clothing.[5,6] The cause of heavy menstrual bleeding is unknown. 50% of women do not have any structural abnormalities or uterine pathologies.[7,8]

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DUB can be managed by knowing the amount of blood flow, the degree of associated anemia and the comfortableness of patient and their family members with different treatment modalities. The drugs that can be used to treat DUB are oral contraceptives, non-steroidal anti-inflammatory drugs (NSAIDs), progestogens, antifibrinolytics such as tranexamic acid, GnRH analogues, Danazol, hemostatic agent such as ethamsylate, Levonorgestrel releasing intra uterine system (LNG IUS).[9]

MATERIALS AND METHODS

This study is a prospective comparative study which was conducted at Employee State Insurance Hospital, Aynavaram, and Chennai from Sept 2019 – March 2020 (7 months). The study was approved by IEC (Institutional Ethics Committee with reference number VISTAS-SPS/IEC/V/2019/04).

The main aim of the study is to compare the effectiveness of tranexamic acid and ethamsylate in dysfunctional uterine bleeding. Primary objective and secondary objective includes the comparison of the efficacy of tranexamic acid and ethamsylate and to study the reduction in heavy menstrual bleeding respectively.

Patient who was diagnosed with dysfunctional uterine bleeding were randomly divided into two groups i.e. Group A and Group B. Enrolled patients were assessed based on their symptoms and data was collected using predesigned Performa. Of 56 patients recruited for the study with randomisation, 28 patients were in group A (tranexamic acid) and 28 patients were in group B (ethamsylate). Four patients were lost for follow up (three in group A and one in group B) and two patients discontinued the given drugs (two in group B). Hence 50 patients were included in the study with an intention to treat and analyse the outcome. Group A received Tranexamic acid 500mg, BD, from 1 to 5 days of the menstruation for three consecutive cycles. Similarly, Group B received Ethamsylate 500mg, BD from 1 to 5 days of the menstruation for three consecutive cycles. Before starting the treatment, inpatients were educated to fill the Pictorial Blood Assessment Chart (score 1 was given for lightly soiled pad, score 5 was given for moderately soiled pad and score 20 for heavily soils pad, score 1 for 25p coin and score 5 for 1re coin)[10] Menorrhagia impact questionnaire (MIQ was scored on a 1 to 5 point scale 1: Extremely; 5: Not at all)[11] and their Hb levels, endometrium thickness were measured. Patients were informed to continue the drugs for three consecutive menstrual cycles even after getting discharged from the hospital. After three months patients were reviewed in outpatient department of hospital by using Pictorial Blood Assessment Chart, Menorrhagia impact questionnaire and their Hb levels, endometrium thickness was measured. Pre-treatment results and after treatment results were analysed statistically.

Inclusion criteria: Female inpatient with age group of 18-45years who were diagnosed with abnormal uterine bleeding with or without complaints of dysmenorrhoea, menorrhagia, polymenorrhagia were included in the study.

Exclusion criteria: Women who have a suspected or verified pregnancy, lactating women, post-menopausal women, thromboembolic disorders, hyperlipidemia, existing renal and hepatic disease were excluded from the study.

Statistical Analysis

All statistical analysis was performed by using the statistical software SPSS 21.0. Significance level (p value of <0.0001) was determined by using independent t-test (unpaired). Comparison of tranexamic acid and ethamsylate for its effectiveness in dysfunctional uterine bleeding was performed by analysis of Variance (Two Way Anova).

RESULTS

Among 50 patients, 25 patients received tranexamic, and another group of patients received ethamsylate. The study's findings were obtained by the scores of different parameters at baseline and after the completion of treatment. 10 patients (20%) were in the age group of 16-24 years, 8 patients (10%) were in the age group of 25-31 years, 15 patients (30%) were in the age group of 32-38 years, 17 patients (34%) were in the age group of 39-45 years (Figure 1). So it indicates that more number of people in the age group of 39-45 years were affected with DUB. Gradual decrease was seen in PBAC mean score (Figure 2) in tranexamic acid group (293.84± 137.50) when compared with PBAC mean score of ethamsylate group (326.24±83.89). Mean score of Hb level (Figure 3) in tranexamic acid group (12.96± 0.99) was seen to be increased slightly when compared with ethamsylate group (12.024± 1.07). Mean score of endometrium thickness (Figure 4) in tranexamic acid group (3.404± 0.99) were seen to be decreased when compared with ethamsylate group (7.64± 2.53). The normal range of endometrium thickness lies between 2mm-4mm. So it indicates that tranexamic acid was more effective than ethamsylate.

Gradual increase was seen in MIQ mean score (Figure 5) in tranexamic acid group (10.48± 3.40) when compared with ethamsylate group (8.95± 3.10) (Table 1). Among

the parameters measured by the MIQ were impairment in social activities, blood loss, work inside and outside, physical activities.[11] There was mean improvement in MIQ score for social activities related question in both treatment groups compared to baseline (Figure 6). For blood loss related question, there was mean improvement in tranexamic acid group compared to baseline (Figure 7). But there was no change in MIQ score for ethamsylate group compared to baseline in work inside and outside related question (Figure 8). Mean improvement was observed in MIQ scores for physical activities related questions in both the treatment groups (Figure 9). However, the total mean score was higher in tranexamic acid group (23.2) compared to ethamsylate group (21.5). Hence, tranexamic acid was better than ethamsylate in terms of effectiveness.

Data are shown as mean ± standard deviation of PBAC: Pictorial Blood Assessment Chart, Hb: Haemoglobin (g/dL) Endometrium Thickness (mm) and Menorrhagia Impact Questionnaire (MIQ). Unpaired t test were used to determine significance.

DISCUSSION

The present study compares the effectiveness of two non-hormonal drugs used in dysfunctional uterine bleeding in terms of reduction in menstrual blood loss, improvement in Hb level, endometrium thickness and improvement in health related quality of life in patients as reflected by the acceptance of treatment. When comparing the scores before and after the treatment, both medications

Table 1: Different Parameters of Patients.

Parameter	Group I(*n*=25)	Group II (*n*=25)	*P* value (intergroup)
PBAC			
Baseline	367.12± 177.27	352.84±108.22	0.3740
3 months	293.84±137.50	326.24±83.89	0.0465
P value	<0.0001	<0.0001	
Hb			
Baseline	11.044±1.32	10.896±1.16	0.6762
3 months	12.96±0.99	12.024±1.07	0.0024
P value	<0.0001	<0.0001	
Endometrial thickness			
Baseline	9.0428±4.40	7.9852±5.39	0.4515
3 months	3.404±0.99	7.64±2.53	<0.0001
P value (within group)	<0.0001	<0.0001	
MIQ			
Baseline	3.96±1.14	3.72±1.12	0.8425
3 months	10.48±3.40	8.95±3.10	0.0456
P value (within group)	<0.0001	<0.0001	

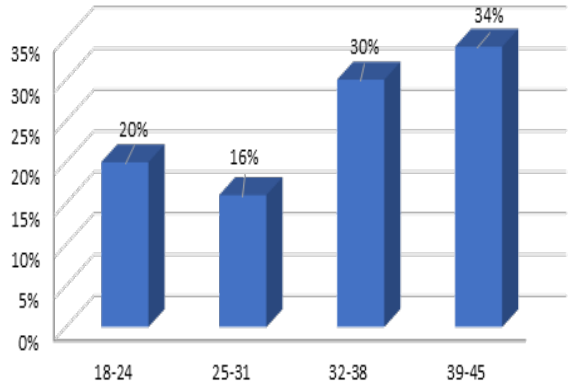

Figure 1: Distribution pattern based on Age.

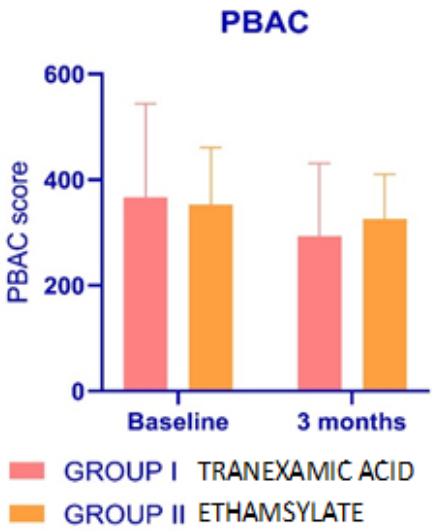

Figure 2: Distribution pattern based on Pictorial Blood Assessment Chart.

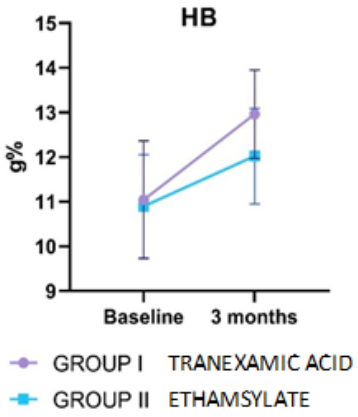

Figure 3: Distribution pattern based on Hemoglobin level.

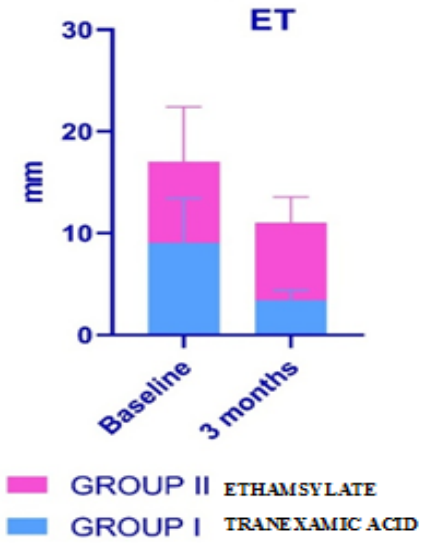

Figure 4: Distribution pattern based on Endometrium Thickness.

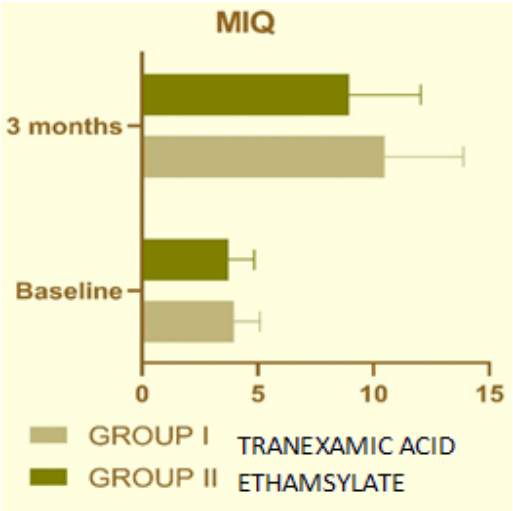

Figure 5: Distribution pattern based on Menorrhagia Impact Questionnaire.

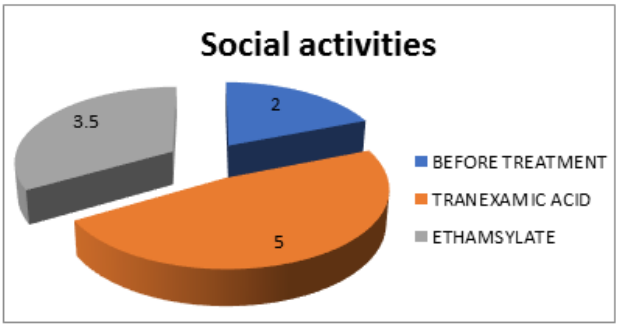

Figure 6: Effects of tranexamic acid and ethamsylate on mean score- social activities.

showed statistically significant findings, suggesting that both agents are beneficial in the treatment of DUB. While on comparison on the basis of efficacy tranexamic acid

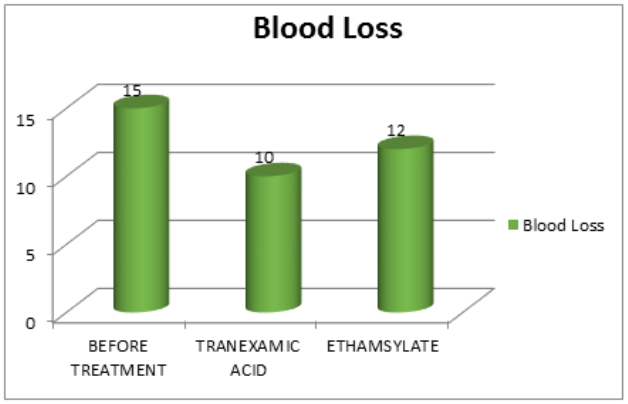

Figure 7: Effects of tranexamic acid and ethamsylate on mean score- Blood Loss.

Figure 8: Effects of tranexamic acid and ethamsylate on mean score- work inside and outside.

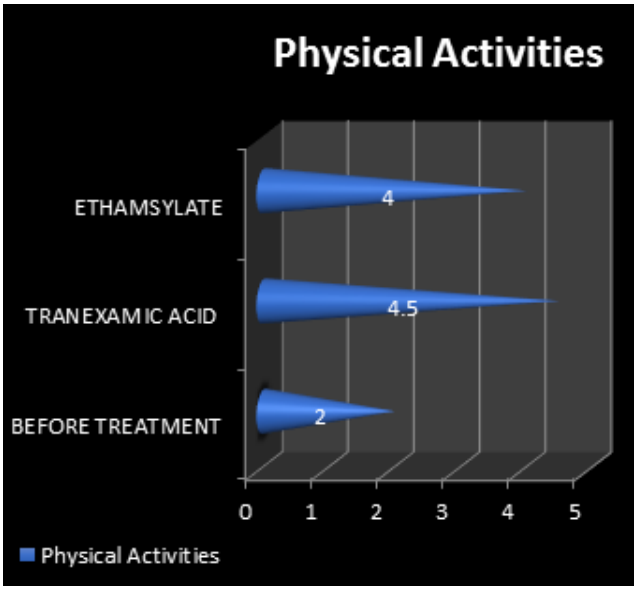

Figure 9: Effects of tranexamic acid and ethamsylate on mean score- physical activities.

was better than ethamsylate.

Dr. M. Damadari Bai,[1] compared tranexamic acid and mefenamic acid with and without ethamsylate in management of DUB, in which the maximum prevalence of DUB is between the age group of 31-40 years i.e., 44% followed by 32% in the age group of 41-45 years.

There is a significant reduction in menstrual blood loss both with tranexamic acid and ethamsylate, but tranexamic acid proved to be more efficacious. This was in accordance with previous studies. Madhu J *et al.*[10] compared mefenamic acid and tranexamic acid in management of menorrhagia which states that reduction in menstural blood loss was observed more effectively in tranexamic acid group with PBAC mean score of (82.20± 11.88) when compared with mefenamic acid (104.04± 17.72).

Kriplani A *et al.*[12] compared tranexamic acid and medroxyprogesterone acetate for the management of DUB, which stated that tranexamic acid (60%) showed better effectiveness when compared with medroxyprogesterone (58%).

Dr. M. Damadari Bai,[1] compared tranexamic acid and mefenamic acid with and without ethamsylate in management of DUB, in which increase in Hb level was observed in patients receiving tranexamic acid, mefenamic acid and ethamsylate (13.5± 1.7) when compared with patients receiving tranexamic acid and ethamsylate (12.8± 1.97).

Nita K. Patel *et al.*[11] compared tranexamic acid and ethamsylate in management of menorrhagia which stated that both the drugs provided qualitative relief for women with menorrhagia. But women receiving tranexamic acid reported more improvement in health related quality of life.

Andrea S. Lukes *et al.*[13] reported that use of tranexamic acid significantly reduced menstrual blood loss from baseline and improved health-related quality of life while maintaining safety and tolerability.

CONCLUSION

This study suggests that both tranexamic acid and ethamsylate were effective in management of dysfunctional uterine bleeding. Tranexamic acid was superior to ethamsylate in terms of effectiveness, reduction in blood loss and improvement in quality of life.

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CONFLICT OF INTEREST

The authors have no conflicts of interest.

ABBREVIATIONS

DUB: Dysfunctional Uterine Bleeding; **HMB:** Heavy Menstrual Bleeding; **IEC:** Institutional Ethics Committee; **PBAC:** Pictorial Blood Assessment Chart; **MIQ:** Menorrhagia impact questionnaire; **ET:** Endometrium Thickness.

SUMMARY

Dysfunctional Uterine Bleeding is a clinically significant medical condition common to women. The impact of DUB on physical, social, emotional, and/or material quality of life adversely effects many aspects of a woman's daily activities and is often the reason for women to consult a physician, in many cases a general practitioner.

Both Tranexamic acid and Ethamsylate were effective in management of DUB. Both have the advantage of only being taken during menstruation. Tranexamic acid 500mg twice a day for 5 days is an effective treatment for DUB. Similarly Ethamsylate is an effective drug at a dose of 500mg twice daily for 5 days.

In the present study, female patients between the age group of 39-45 years are mostly effected with DUB. There is a significant reduction in menstrual blood loss both with tranexamic acid and ethamsylate, but tranexamic acid proved to be more efficacious. Hb level in tranexamic acid group was seen to be increased slightly when compared with ethamsylate group. The Endometrium thickness of the patients receiving tranexamic acid was between the normal range. Use of tranexamic acid and ethamsylate improved health-related quality of life. Tranexamic acid showed better improvement in health related quality of life compared to ethamsylate.

Tranexamic acid offers a first-line, non-hormonal, non-surgical treatment option for women with dysfunctional uterine bleeding that may become an important alternative to surgical procedures and medical treatments. Treatment of DUB with tranexamic acid seems to be cost-effective when compared with no treatment or NSAIDs. It is easy to use when needed and has better pharmacological effect.

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