IJBPAS, April, 2025, 14(4): 2221-2228

ISSN: 2277–4998

International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)

'A Bridge Between Laboratory and Reader'

www.ijbpas.com

TO COMPARE THE EFFICACY AND SAFETY OF TRANEXAMIC ACID IN COMBINATION WITH MEFENAMIC ACID VS TRANEXAMIC ACID ALONE IN PATIENTS FOR TREATING ABNORMAL UTERINE BLEEDING

VENKATESWARA RAO J[1], BALA SIVA DEEP G[2*], LIKHITA J[2], DIVYA SRI CH[2], SIVA BHARATH G[2], VENKATA RAMA RAO N[2], RAMA RAO N[2] AND VENKATESWARA RAO B[3]

1: Assistant Professor, Lovely Professional University, Phagwara, Punjab, India

2: Department of Pharmacy Practice, Chalapathi Institute of Pharmaceutical Sciences, Lam, Guntur, Andhra Pradesh, India

3: Professor- Department of Obstetrics and Gynaecology, Government General Hospital, Guntur, Andhra Pradesh, India

***Corresponding Author: Dr. Goli Bala Siva Deep: E Mail: dr.balasivadeep.goli@gmail.com**

Received 15th Dec. 2023; Revised 19th Jan. 2024; Accepted 1st July 2024; Available online 1st April 2025

https://doi.org/10.31032/IJBPAS/2025/14.4.8921

ABSTRACT

Introduction Abnormal Uterine bleeding (AUB) can seriously affect the quality of life of women since it interferes with the physical, emotional, social, and material quality of life and may identify serious health concerns as the adolescent transitions to adulthood. **Methods** A prospective cohort study was performed in 250 individuals diagnosed with AUB are screened for inclusion and exclusion criteria. The safety and efficacy were evaluated by using PBAC score, hemoglobin levels, and MMAS score. The improvement of lab parameters is assessed by performing data analysis by using paired t test and significance p-value. **Results:** The change in PBAC score was from 226.16±18.63 to 80.19±10.88 in group-1 and in group-2 it was from 223.80±18.56 to 83.34±10.21, the significant reduction in PBAC scores is seen more in the tranexamic acid+mefenamic acid group. The improvement in the quality of life, MMAS score was from 41.67±12.84± to 84.75±11.99 in group-1 and in group -2 it was from 41.13±13.73 to 81.08±14.15, improvement in the QoL is seen more in tranexamic acid+mefenamic acid group. The reduction of pain is seen in tranexamic acid+mefenamic acid treated group is 80% which is higher than the tranexamic acid alone treated group i.e. 38.09% after 3 months. **Conclusion:** Our study

concludes that tranexamic acid+mefenamic acid combination is superior and safer in reducing menstrual blood loss and is also safe in reducing the pain, menstrual cramps during uterine bleeding and improvement in the patients wellbeing, enhancing quality of life.

Keywords: Abnormal uterine bleeding (AUB), Tranexamic acid (TXA), Mefenamic acid, Pictorial Blood loss Assessment Chart (PBAC), Menorrhagia Multi-attribute Scale (MMAS), Quality of Life (QoL)

INTRODUCTION

Abnormal uterine bleeding (AUB) is a common gynecologic complaint, accounting for one-third of all outpatient visits to gynaecologists and more than 70% of all gynecologic consults during the perimenopausal and postmenopausal years **[1]**. Normal monthly menstrual blood loss is about 35 ml with a 90%value of 80 ml. Menstrual loss in excess of 80 ml is widely accepted as an objective definition of menorrhagia **[2]**.

It is defined as excessive menstrual blood loss that occurs alone or in conjunction with other symptoms and has a negative impact on a woman's physical, social, emotional, and/or material quality of life (QoL) **[3]**.

Acute AUB is described as "an episode of bleeding in a woman of reproductive age who is not pregnant that is of sufficient quantity to necessitate quick intervention to prevent further blood loss. "Chronic AUB is defined as "uterine corpus bleeding that is abnormal in duration, volume, and/or frequency and has been present for the majority of the last 6 months."**[4]**

It is the most common reason for reproductive-age women to seek medical attention. This issue has a significant impact on quality of life, promoting school absenteeism and social limitations **[5]**.

The global prevalence of abnormal uterine bleeding among reproductive-aged women is estimated to be between 3% and 30%, with a higher incidence occurring around menarche and perimenopause **[6]**. HMB is an important cause of ill health in women: prevalence estimates range from 4% to 51% **[7]**.

Heavy menstrual bleeding (HMB) is estimated to affect 6.5 percent of women aged 12–51 years, with 5 percent of women aged 30–49 years seeking medical attention each year **[8]**. Sixty percent of women referred with menorrhagia have a hysterectomy within five years **[9]**.

Sign and symptoms include spotting or bleeding between menstrual periods, menstrual periods that last more than seven days, soaking a tampon or pad in one hour or less during your menstrual period. Other symptoms include bloating, pain or pressure in the pelvic region, weakness, heavy bleeding lasting one to two hours **[10]**.

Diagnosis can be done by performing endometrial sampling, PBAC score, complete blood count to rule out anaemia

and severity of bleeding, and pelvic imaging for suspicion of an underlying bleeding disorder **[1]**.

Anemia, infertility, and endometrial cancer are all possible complications of chronic abnormal uterine bleeding. If prompt treatment and supportive care are not initiated in the case of acute abnormal uterine bleeding, severe anaemia, hypotension, shock, and even death may occur **[6]**.

The standard procedure for determining MBL combines a woman's self-perception of her menstrual flow (light, normal, or heavy) with haemoglobin level and/or menstrual markers such as length of period, number of the sanitary pads used, number of days of 'heavy' bleeding, number of flooding episodes, and size of clots passed **[5]**. Although menorrhagia is usually not life-threatening, it can cause significant social embarrassment, discomfort, and disruption in many women's lives **[11]**.

Tranexamic acid improves the quality of life of women being treated for abnormal uterine bleeding considerably (AUB). The suggested dosage varies between studies, however it is often administered every 1-5 days beginning on the first day of the menstrual cycle. The side effects are minimal and mostly moderate. The occurrence of thrombotic events linked with its use is quite low. A thromboembolic disorder that is active is a contraindication **[12]**.

Mefenamic acid, an anthranilic acid derivative and an NSAID, is also known to relieve mild to moderate pain from a variety of ailments. It is also used to decrease menstrual pain and blood loss. Some studies have predicted a 20% reduction in menstrual blood loss by mefenamic acid alone **[13]**.

Previous studies shows that menstruation discomfort (46.2 %), headache (43.9 %), and back pain (23.1 %) were the most commonly reported treatment-emergent side events for tranexamic acid. Ocular adverse events were reported by a minor percentage of subjects (3.8 %) **[14]**.

Anemia, infertility, and endometrial cancer are all possible complications of chronic abnormal uterine bleeding. If prompt treatment and supportive care are not initiated in the case of acute abnormal uterine bleeding, severe anaemia, hypotension, shock, and even death may occur **[6]**.

MATERIALS AND METHODS

Study Design/Settings

This is a Prospective Cohort study conducted in the Department of Obstetrics and Gynecology, Government General Hospital, Guntur, for a period of 6 months i.e. from October 2021 to March 2022. The subjects diagnosed with Abnormal Uterine Bleeding and receiving tranexamic acid+mefenamic acid combination and

tranexamic acid alone in two separate groups are included.

Inclusion Criteria:

- Female Patients who are diagnosed with abnormal uterine bleeding.
- Female Patients who are taking oral tranexamic acid+mefenamic acid & tranexamic acid alone for abnormal uterine bleeding.
- Female patients within the age group 18-70yrs.
- Female patients who are non-pregnant women are selected.
- Female Patients who are willing to participate & follow-up during the study are included.

Exclusion Criteria:

- Female patients who are pregnant.
- Female Patients who are <18yrs & >70yrs of age.
- Female Patients with risk of thromboembolic disease.
- Female Patients with history of PCOD.
- Female Patients appeared with convulsions, malignancies like fibroids, cancer, etc.
- Female patients who are not willing to participate & follow-up during the study are excluded

Data Collection

After obtaining approval from Institutional Ethics Committee, A 260 individuals, diagnosed with AUB are screened for inclusion and exclusion criteria and after taking Informed consent the subjects are divided into 2 categories. In group-1, 126 subjects of tranexamic acid+mefenamic acid combination receiving individuals of doses 500mg and 250mg respectively thrice daily from day 1-5 and in group-2, 124 subjects of tranexamic acid alone receiving individuals of dose 500mg thrice daily from day 1-5 during menstrual cycle and remaining 10 subjects are excluded as they failed to follow up the study. The safety and efficacy of both the treatment groups was evaluated by using pictorial blood assessment chart (PBAC) scoring to assess menstrual blood loss, hemoglobin levels to rule out anemia, menorrhagia multi-attribute assessment scale (MMAS score). The improvement of lab parameters in both the treatment groups after 3 months is assessed by performing data analysis by paired t test and significance p-value.

Outcome Parameter

Pictorial Blood loss Assessment Chart [PBAC]

Haemoglobin level

Menorrhagia Multi Attribute Scale [MMAS]

Statistical Analysis and Interpretation

The data obtained was entered in advanced Microsoft excel spread sheet and evaluated. For statistical analysis paired t-test is utilised to calculate the p-value.

Ethical considerations

After obtaining approval from Institutional Ethics Committee the study was conducted.

RESULTS & DISCUSSION

A total of 250 subjects were included in the study after a thorough screening based on inclusion and exclusion criteria, patients diagnosed with abnormal uterine bleeding have been involved in the study. In this study, we conducted a comparison between combination of tranexamic acid+mefenamic acid using individuals Vs tranexamic acid alone using individuals. Among those 250 subjects, in group-1 a total of 126 subjects using tranexamic acid+mefenamic acid were included, in group-2 a total of 124 subjects using tranexamic acid were included **(Table 1)**.

Table 1: Socio-Demographic Comparison of Treatment Groups (At Baseline)

Characteristics	Tranexamic Acid + Mefenamic Acid (n=126)	Tranexamic acid (n=124)	P-value
Age (in yrs)	35.18±10.89	34.96±10.66	0.8788
Weight (in kg)	56.88±6.61	56.81±6.69	0.9381
BMI (in kg/m^2)	23.85±4.16	23.95±3.74	0.8428
Hb (in gm/dl)	8.31±0.39	8.21 ±0.47	0.0643
MMAS	41.67±12.84	41.13±13.73	0.7462
PBAC	226.16±18.63	223.80±18.56	0.3149

Mean age of tranexamic acid+mefenamic acid group individuals is 35.18±10.89, whereas the mean age of the tranexamic acid group is 34.96±10.66. The p-value is 0.8788 with no mean significant difference in age in both treatments.

The mean weight of the tranexamic acid+mefenamic acid group is 56.88±6.61 and mean weight of the tranexamic acid group individuals is 56.81±6.69. The p-value is 0.9381 with no mean significant difference in weights in both treatment groups.

Mean BMI of tranexamic acid+mefenamic acid group individuals is 23.85±4.16, whereas the mean age of the tranexamic acid group is 23.95±3.74. The p-value is 0.8428 with no mean significant difference in BMI in both treatments.

Mean hemoglobin concentration was 8.31±0.39 in the tranexamic acid+mefenamic acid group and 8.21 ±0.47 in the tranexamic acid group. The p-value is 0.0643 with no mean significant difference in hemoglobin in both treatment groups.

The mean PBAC score of the tranexamic acid+mefenamic acid group is 226.16±18.63 and the mean PBAC score of tranexamic acid group individuals is 223.80±18.56. The p-value is 0.3149 with no mean significant difference in PBAC score in both treatment groups.

Mean MMAS score of tranexamic acid+mefenamic acid group individuals is 41.67±12.84, whereas the mean MMAS score of the tranexamic acid group is 41.13±13.73. The p-value is 0.7462 with no

mean significant difference in MMAS scores in both treatments.

The subjects after the follow-up have been assessed with changes in Wt, BMI, Hemoglobin concentration, PBAC score, and MMAS score due to the change in treatment therapy and patient counseling. The values are then compared with the baseline results and their mean differences are calculated and tabulated. The resultant mean differences are taken into consideration and drawn graphs between the tranexamic acid+mefenamic acid group vs tranexamic acid group.

Table 2: Characteristic Mean difference of the variables at Baseline and After 3 months in both the treatments groups

Characteristics	Tranexamic acid+Mefenamic acid			Tranexamic acid		
	Baseline	After 3 months	Mean difference	Baseline	After 3 months	Mean difference
Hb	8.31±0.39	8.7±0.44	-0.39	8.21±0.47	8.42±0.44	-0.21
PBAC	226.16±18.63	80.19±10.88	145.97	223.80±18.56	83.34±10.21	140.46
MMAS	41.67±12.84	84.75±11.99	-43.08	41.13±13.73	81.08±14.15	-39.95

Table 3: Comparison of variables in both the treatments group-1 and group-2 with the p-value with baseline and after 3 months

Characteristics	Mean differences of tranexamic acid+ mefenamic acid	Mean differences of tranexamic acid	P-value	t-value
Hb (in gm/dl)	-0.39	-0.21	<0.001	5.066
MMAS	-43.08	-39.95	0.0140	2.475
PBAC	146.0	140.5	0.0021	3.114

Note: The mean differences were taken individually from each patient across the treatment groups and calculated the p-value between the tranexamic acid+mefenamic acid group and the tranexamic acid group.

The hemoglobin levels of all the individuals in both the treatments are compared with their mean hemoglobin differences and the p-value is <0.001. The p-value shows a significant improvement in the hemoglobin level in the tranexamic acid+mefenamic acid group i.e. 4.69%.

Likely PBAC scores, the individual mean PBAC score differences of both treatment groups are compared and done the p-value (0.0021). The p-value shows a significant difference in the treatment groups i.e.64.54% in arm-1 and 62.76% in arm-2, the mean reduction in the PBAC scores are seen in the tranexamic acid+mefenamic acid group than in the tranexamic acid group.

The MMAS scores of all the individuals in both the treatments are compared with their individual mean MMAS score differences and the p-value is 0.0140. The p-value shows a significant improvement in the MMAS scores in the tranexamic acid+mefenamic acid i.e. 103.38%.

CONCLUSION

According to the study findings, the tranexamic acid+mefenamic acid combination reduces PBAC score by 64.54 %, which is higher than the 62.76 % of tranexamic acid (p-value 0.0021). MMAS score improves the quality of life by 103.38 percent in tranexamic acid+mefenamic acid treated individuals, which is higher than in tranexamic acid treated individuals (p-value

0.0140). Our study concludes that tranexamic acid+mefenamic acid combination is superior and safer in reducing menstrual blood loss and is also safe in reducing the pain, menstrual cramps during uterine bleeding and improvement in the patients well being, enhancing quality of life.

Acknowledgements

The authors are grateful to all women who came to our center, for their excellent cooperation.

We are also very grateful to Obstetrics and Gynecology department for providing the grant for this study.

REFERENCES

[1] Khafaga, A., & Goldstein, S. R. (2019). Abnormal Uterine Bleeding. In *Obstetrics and Gynecology Clinics of North America* (Vol. 46, Issue 4, pp. 595–605). W.B. Saunders. https://doi.org/10.1016/j.ogc.2019.07.001

[2] Chamberlain, G., Freeman, R., Price, F., Kennedy, A., Green, D., & Eve, L. (1991). A comparative study of ethamsylate and mefenamic acid in dysfunctional uterine bleeding. In *British Journal of Obstetrics and Gynaecology* (Vol. 98).

[3] Xu, L., Lee, B. S., Asif, S., Kraemer, P., &Inki, P. (2014). Satisfaction and health-related quality of life in women with heavy menstrual bleeding; results from a non-interventional trial of the levonorgestrel-releasing intrauterine system or conventional medical therapy. *International Journal of Women's Health*, *6*(1), 547–553. https://doi.org/10.2147/IJWH.S57470

[4] Fraser, I. S., Critchley, H. O. D., Broder, M., & Munro, M. G. (2011). The FIGO recommendations on terminologies and definitions for normal and abnormal uterine bleeding. *Seminars in Reproductive Medicine*, *29*(5), 383–390. https://doi.org/10.1055/s-0031-1287662

[5] Ramalho, I., Leite, H., &Águas, F. (2021). Abnormal uterine bleeding in adolescents: A multidisciplinary approach. In *ActaMedica Portuguesa* (Vol. 34, Issue 4, pp. 291–297). CELOM. https://doi.org/10.20344/amp.12829

[6] Davis E, Sparzak PB. Abnormal Uterine Bleeding. [Updated 2022 Feb 10]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK532913/

[7] Bryant-Smith, A. C., Lethaby, A., Farquhar, C., & Hickey, M. (2018). Antifibrinolytics for heavy menstrual bleeding. In *Cochrane Database of Systematic Reviews* (Vol. 2018, Issue 4). John Wiley and Sons Ltd. https://doi.org/10.1002/14651858.CD000249.pub2

[8] Pattison, H., Daniels, J. P., Kai, J., & Gupta, J. K. (2011). The measurement properties of the menorrhagia multi-attribute quality-of-life scale: A psychometric analysis. *BJOG: An International Journal of Obstetrics and Gynaecology*, *118*(12), 1528–1531. https://doi.org/10.1111/j.1471-0528.2011.03057.x

[9] Irvine Lecturer, G. A., Campbell-Brown Senior Research Fellow, M. B., Lumsden Senior Lecturer, M. A., Heikkila Medical Adviser, A., Walker Professor, J. J., & Cameron Professor, I. T. (1998). Randomised comparative trial of the levonorgestrel intrauterine system and norethisterone for treatment of idiopathic menorrhagia. In *British Journal of Obstetrics and Gynaecology* (Vol. 105).

[10] https://www.dignityhealth.org/conditions-and-treatments/womens-services/gynecology/abnormal-uterine-bleeding/

[11] Shaw, R. W., Evans, L., Assistant, R., & Edwards, M. J. (1998). Perceptions of women on the impact of menorrhagia on their health using multi-attribute utility assessment. In *British Journal of Obstetrics and Gynaecology* (Vol. 105).

[12] Hurskainen, R., & Leminen. (2012). Tranexamic acid for the treatment of heavy menstrual bleeding: efficacy and safety. *International Journal of Women's Health*, 413. https://doi.org/10.2147/ijwh.s13840

[13] Rani, R., Bs, M., Singh, S., Patel, A., &Lata, R. (2016). Comparison of Tranexamic acid with a combination of Traneximic acid and Mefenamic acid in reducing menstrual blood loss in ovulatory Dysfunctional uterine bleeding (DUB). In *International Journal of Interdisciplinary and Multidisciplinary Studies (IJIMS)* (Vol. 3, Issue 2). http://www.ijims.com

[14] Lukes, A. S., Freeman, E. W., Van Drie, D., Baker, J., & Adomako, T. L. (2011). Safety of tranexamic acid in women with heavy menstrual bleeding: an open-label extension study. *Women's health (London, England)*, *7*(5), 591–598. https://doi.org/10.2217/whe.11.55