

Study to Evaluate the Efficiency of Tranexamic Acid & Mefenamic Acid in DUB**Sahil D. Patel¹, Harshdeep K. Jadeja², Bhavesh B. Airao³**¹3rd Year Resident, OBS-GYN department C.U. SHAH Medical College & Hospital, Surendranagar²Associate Professor, OBS-GYN department C.U. SHAH Medical College & Hospital, Surendranagar³Professor & HOD, OBS-GYN department C.U. SHAH Medical College & Hospital, Surendranagar

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Abstract:**Introduction:** Dysfunctional uterine bleeding is one of the most commonly expressed complaints of women at reproductive age leads to anaemia and its complications. This study compares the efficacy and acceptability of tranexamic acid with mefenamic acid in treating DUB in order to show the most effective drug.**Objectives:** To determine if tranexamic acid and mefenamic acid can effectively and safely reduce menstrual blood loss & pain.**Materials and Methods:** 100 cases selected for the study who complained of regular long/ heavy menstrual bleeding more than 7 days or blood loss more than 80ml, who are at the age of 20-45 years. Drug Tranexamic acid 500mg QID were given to the patients who had mean menstrual blood loss of more than 80 ml based on assessment in the previous two menstrual cycles and dosage of mefenamic acid is 500 mg OD then 250 mg QID for 3 days.**Results:** The total study shows the affect of drugs on the amount of bleeding is 41.6% (P-value <0.05), there is significant reduction is seen in number of sanitary pad usage from 5.44 to 3.96 (P- value <0.05) and there is significant reduction in duration of bleeding. There are minimal gastrointestinal side effects, and there is 32% discontinuation of treatment in our study as patients are not satisfied and effective reduction in pain.**Conclusion:** Treatment with tranexamic acid and mefenamic acid could potentially improve the quality of life of women.**Keywords:** DUB, Tranexamic Acid, Mefenamic Acid.

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Introduction

Menorrhagia happens when there is an increase in menstrual bleeding in multi regular subsequent cycles or the time the bleeding duration rises to more than 7 days.[1] Most of the patients who complain of menorrhagia have no known organic diseases and have normal physical examinations, laboratory tests and imaging (sonography) results. Menorrhagia, if repeated, causes a decrease in iron reserve and anaemia and subsequently, anaemia causes psychological and cardiac complications and dysfunction in other organs. So, paying attention to menorrhagia and its treatment can lead to lower morbidity in reproductive aged women. It is worth noticing that most of the iron-deficient anaemia morbidities are the result of more than 60 ml bleeding per cycle. The evaluation of the actual bleeding volume is not an easy task because women's evaluation of their own bleeding volume is not reliable. 25% of the women who consider their bleeding levels as high had menstrual bleeding less than 35 ml. The estimation of blood loss volume

was done based on the number of pads or tampons soaking per day or per cycle. The patient's estimations of the bleeding volumes are not accurate and reliable because they are not well aware of the normal range of bleeding and their evaluations are inexact. All of the techniques used for menorrhagia research purposes are difficult and clinically impractical. Examples are Alkaline Haematin Test and Radioisotope Techniques. So, we need an accurate method of estimating the blood loss which is clinically applicable. In this way treatment without indication is prevented. Worldwide use of hormonal therapy is based on the wrong assumption that menorrhagia happens because of imbalance in hormones and ovulatory cycles, but the fact is most of the women with abnormal bleeding show no evidence of hormonal imbalance and based on some studies 95% have regular ovulatory cycles. The mechanisms of controlling menstrual bleeding are poorly understood. In the past decades, studies had shown that the increase in endometrial fibri-

nolysis and an imbalance in prostaglandin caused functional uterine bleeding.

Dysfunctional Uterine Bleeding (DUB) Causes

The most common aetiology for DUB is chronic anovulation or abnormal ovulation leading to an imbalance in the hormonal milieu of the endometrium. A diagnosis of DUB can be made only after excluding other possible organic causes of bleeding like pregnancy and its complications, benign condition such as cervical or endometrial polyps, adenomyosis, or uterine leiomyomas, precancerous changes or malignancies of the cervix or endometrium. DUB can be classified as ovulatory DUB and anovulatory DUB.

A. Ovulatory DUB

20% of DUB occurs as a result of the loss of local endometrial hemostasis. In DUB the ratio of PGF₂α and PGE₂ is decreased and levels of PGI₂ is increased. There are other contributors to induction and control of menstrual bleeding. Nitric oxide is a potent vasodilator and inhibitor of platelet aggregation.

B. Anovulatory Bleeding

80% of DUB anovulatory bleeding reflecting the transient fall in oestrogen withdrawal bleeding, reflecting the transient fall in oestrogen levels resulting from regression of the most recent follicular cohort or oestrogen breakthrough bleeding due to overgrown structurally fragile endometrium under continuous oestrogen stimulation. Anovulatory DUB is common in extremes of age groups like perimenopausal and perimenarchal because of alterations in hypothalamic-pituitary axis. Anovulatory DUB can also be accompanied by PG imbalance where in relative absence of progesterone leads to almost deficient PGF₂α, so unopposed activity of vasodilator prostaglandins like PGI₂ leads to heavy painless flow.

Diagnosis of Menorrhagia [1]

The American College of Obstetricians and Gynecologists (ACOG) recommends testing for von Willebrand "disease in adolescents with severe menorrhagia, in adult women with menorrhagia, and in women undergoing hysterectomy for the sole indication of menorrhagia.

Assessment of Menstrual Blood Loss

The only way to get an accurate measurement of menstrual blood loss is to assess haemoglobin content using the alkaline hematin method. Since it is not feasible to use in clinical practice, the pictorial blood assessment chart (PBAC) has been used as a semiobjective method of choice. The PBAC consists of a series of diagrams representing lightly, moderately, and heavily soiled towels and tampons. The numbers at the top of the chart represent the

days of the menstrual cycle. Women are instructed to mark the appropriate box each time a towel and/or tampon is discarded, after comparing its degree of saturation with those depicted on the chart. Passage of clots and episodes of flooding are also recorded. Lightly stained towels or tampons obtain a score of 1, moderately stained towels or tampons a score of 5, completely soaked tampons a score of 10, and completely soaked towels a score of 20. A total score of greater than 100 per cycle has been shown to be a reasonably good predictor of menstrual blood loss of more than 80 mL. A drawback of the chart is that it must be completed prospectively, and results are not available at the time of an initial evaluation. Nonetheless, the PBAC is a simple and inexpensive tool and has been used successfully to monitor response to treatment.

Medical Management of Menorrhagia [2-4]

There are no exact guidelines in the management of menorrhagia. However, among the available pharmacological management of menorrhagia, oral contraceptive pills (OCP) are the most widely accepted to reduce menorrhagia blood loss. Of the available OCPs, combined OCP including estrogens and progestogens and progestogen only pills are the effective drugs advised to menorrhagia. Oral progestogens are the effective drugs that are to be administered in the luteal phase of the menstrual cycle. The levonorgestrel IUDs have been recently replacing the medical management of menorrhagia. The advantages include the cost effective, minimal systemic involvement, decreased gastrointestinal side effects, increased compliance, effective and continuous availability of progesterone, and reversible contraception.

Tranexamic Acid (TA)

Tranexamic acid is a synthetic derivative of amino acid, lysine. The mechanism of action of TA includes an antifibrinolytic effect by reversibly blocking lysine binding sites on plasminogen and thus preventing fibrin degradation. Tranexamic Acid (TA) is a non-hormonal drug that enhances blood clotting by reversibly blocking lysine binding sites on plasminogen and thus fibrin degradation and can be promoted as treatment for DUB. It was first approved by the FDA and has been used to prevent bleeding in patients with haemophilia after tooth extraction.

Mefenamic Acid

Mefenamic acid is a member of the anthranilic acid derivatives class of nonsteroidal anti-inflammatory drugs and is used to treat mild to moderate pain. Its name derives from its systematic name, dimethylphenylaminobenzoic acid.

Materials and Methods

This study was carried out in the institute of the Department of OB GYN of C.U. Shah Medical College and Hospital from May 2022 to May 2023.

For this purpose, 109 cases selected for the study who complained of regular long or heavy menstrual bleeding lasting >7 days or involving blood loss >80ml and effectiveness in reducing pain and 9 were drop out.

Inclusion Criteria

Patients in the age group of 18 to 49 years with complaints of menorrhagia were evaluated. Menstrual blood loss was assessed by a pictorial blood loss assessment chart (PBAC). Menstrual blood loss was assessed by a pictorial blood loss assessment chart (PBAC). Patients with a PBAC score of more than 100, normal pelvic examination, and normal cervical cytology were selected for the study.

Exclusion Criteria

- Excluded patients are with history of,
 - Hypertension
 - Renal or hepatic impairment
 - Previous thromboembolic disease
 - Inflammatory bowel disease
 - Peptic or intestinal ulceration
 - Coagulation or fibrinolytic disease.
 - Malignancies

Investigations

- CBC
- Coagulation profile
- Blood grouping and Rh typing
- USG

Method

Before prescribing tranexamic acid and mefenamic acid, menstrual blood loss assessment was done for two menstrual cycles using pictorial blood assessment chart (PBAC) & dysmenorrhoea by VAS should be done.

Follow up

At each follow up visit amount of bleeding, number of bleeding days, number of sanitary pads were assessed using a pictorial blood assessment chart. Adverse effects if any were recorded. Effect on dysmenorrhoea, patient satisfaction and well-being were asked. At the end of the study patient satisfaction was assessed by asking “would you like to continue with this treatment?”. If the patient answered “no” the reason was recorded. Efficacy of drug was analysed before and after treatment with tranexamic Acid and mefenamic acid was done.

Result

Tab Tranexamic acid 500mg tid to qid was given to this patient who has objectively measured blood loss of more than 80 ml per cycle and mefenamic acid is 500 mg OD then 250 mg QID for 3 days in a total 100 cases.

Table 1: Based On BMI

BMI	No of Cases	Percentage
<20	5	5%
20-25	61	61%
26-30	28	28%
>30	6	6%

Most of the cases are with in normal range of BMI. (body mass index is equql to weight in kgs/ height²in meters. 6 cases are obese (>30 BMI). The menstrual disturbances in the obese women may be due to hormonal disturbances.

Table 2: Ultrasound Findings

Uterus	Normal Size	57
	Bulky Uterus	23
	Fibroid	18
	Endometrial Polyp	2
Adnexa	Normal	94
	Cystic	6
Endometrial Thickness	1-5mm	47
	6-9mm	49
	>9mm	4

Clinically, normal uterus found in 57% of cases. 23% of cases showed bulky uterus (6-8weeks) in which other causes for uterine enlargement like adenomyosis were included. Fibroid found in 18%. No adnexal pathology was detected in 94% of cases

and only 6% had cystic ovaries. 47% had 1-5mm endometrial thickness, 49% had 6-9mm endometrial thickness, 4% had >9mm endometrial thickness. In these cases, endometrial hyperplasia and carcinoma were ruled out by D and C.

Table 3: Mean Hemoglobin Concentration Before and After Management

Hemoglobin%	Mean	SD	p-value
Before Treatment	8.5	0.8	<0.05 Significant
After Treatment	9.6	1.3	

The improvement in hemoglobin is due to decreased menstrual blood loss after treatment with tranexamic acid, mefenamic acid and with oral iron therapy.

Table 4: Effect of Drug on Menstrual Blood Loss

Effect on Menstrual Blood Loss	No Of Cases	Percentage	P-Value
Decreased	72	72%	<0.05
No Change	28	28%	Significant

It is clear that menstrual blood loss decreased in 72% of cases, remained same in 28% after taking the drug. The cases who had change finally ended up in hysterectomy. P- value is <0.05 shows significant.

Table 5: Effect of Drug on Amount of Bleeding

Treatment	Pre-Treatment Mean Pbac Score	Post Treatment Mean Pbac Score	P-Value	Mean Reduction In Menstrual Blood Loss In Present Study (%)	Mean Reduction In Mbl In Other Studies (%)
Tranexamic Acid & Mefenamic Acid	319.1	133.01	<0.05 Significant	41.6%	

In 100 patients, Pretreatment pictorial blood assessment chart score is 319.1 and posttreatment pictorial blood assessment chart score is 133.01, Mean reduction in menstrual blood loss is 41.6% after treated with tranexamic acid. P- value is <0.05 shows significant.

Table 6: Effect of Drug on Sanitary Pad Usage

Sanitary Pad Usage	Mean	P-Value
Before Treatment	5.44	<0.05 Significant
After Treatment	3.96	

From the above table it is implied that significant reduction in number of sanitary pad usage was found in patients treated with tranexamic acid and mefenamic acid. P- values <0.05 shows significant.

Table 7: Effect of Drug on Duration of Bleeding

Effect of Drug	Duration of Bleeding (Mean In Days)	P-Value
Before Treatment	9	<0.05 Significant
After Treatment	4	

From above table there is little difference in the duration of bleeding between the pretreatment and post treatment cycle. P- value is <0.05 shows significant.

Table 8: Side Effects Due to Drug Administration

Side Effects	No of Patients
Nausea	3
Dyspepsia	1
Diarrhea	2
Leg Cramps	1
Headache	0
Thrombosis	0

Minor side effects mostly of gastrointestinal origin were seen only in 7 out of 100 patients.

Table 9: Effect of Drug on Patient Satisfaction

	No of Cases	Percentage
Satisfied	68	68%
Unsatisfied	32	32%

From the above table, 68% of the patients are satisfied with the drug. 32% patients are unsatisfied because of no decrease in blood loss.

Discussion

In our present trial of efficacy of tranexamic acid and mefenamic acid for the treatment of heavy uterine bleeding the average percentage of blood loss after treatment with tranexamic acid is 41%, p-value is <0.05(significant) in our group. In trails conducted by Freeman, Kouides and Lukes the mean decrease. In menstrual blood loss is about 39%, 38% and 40% respectively, signifying that our study is on par with other studies conducted. There is significant reduction is seen in number of sanitary pad usage from 5.44 to 3.96 (P- value <0.05) and there is significant reduction in duration of bleeding.

Conclusion

Tranexamic acid & mefenamic acid is a non-hormonal and cost-effective treatments in abnormal uterine bleeding. Treatment with tranexamic acid & mefenamic acid could potentially improve quality of life of women by reducing impairment of social activities and impairment at work and there is substantial improvement in overall wellbeing. Treatment with tranexamic acid & mefenamic acid de-

creased the incidence of hysterectomy avoiding major surgery and its associated complications like anaesthetic complications, intra operative blood loss, blood transfusion reactions, prolonged hospital stay, morbidity and mortality.

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