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Original Research Article

To study the role of tranexamic acid in the management of menorrhagia

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ABSTRACT

Background: Heavy menstrual bleeding is a significant case of morbidity during the reproductive years. Approximately 30% of women complain of menorrhagia and it is the main presenting problem of women consulting a gynaecologist. In addition, excessive menstrual bleeding accounts for about two-thirds of all hysterectomies. This amount of blood loss can cause disturbance of the woman's social, occupational or sexual life, as well as medical risks such as chronic iron deficiency anemia. Objective of the study was to determine if tranexamic acid can effectively and safely reduce menstrual blood loss in menorrhagia.

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. This study includes measurement of menstrual blood loss, duration of bleeding, number of sanitary pad usage for two menstrual cycles who complained of regular excessive menstrual bleeding using pictogram and taken history of IUCD insertion. Abdominal, gynaecological examination and ultra sound has been done to rule out any pelvic pathology. Drug Tranexamic acid 500mg QID were given to the patients who had mean menstrual blood loss of more than 80ml based on assessment in the previous two menstrual cycles.

Results: The total study shows the effect 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 patient is not satisfied.

Conclusions: Treatment with tranexamic acid could potentially improve quality of life of women. It is also effective treatment for menorrhagia caused by IUCD. Current clinical evidence concludes that size and type of fibroid has significant influence on effect of treatment. Tranexamic acid has been documented and found to have no effect on uterus with adenomyosis and endometrial polyp.

Keywords: Haemoglobin, Tranexamic acid, Menorrhagia, Hypertension

INTRODUCTION

Heavy menstrual bleeding (HMB) has a significant impact on quality life of a women.¹ Menorrhagia can be defined subjectively as "Abnormally long or heavy menses, lasting >7 days or involving blood loss >80 ml."² Objectively it is a total menstrual blood loss greater than or equal to 80ml per period.³ Excessive menstrual

bleeding is a significant cause of morbidity during the reproductive years. Approximately 30% of women complain of menorrhagia and it is the main presenting problem of women consulting a gynaecologist.⁴ In addition, excessive menstrual bleeding accounts for about two-thirds of all hysterectomies and a large proportion of endoscopic endometrial destructive surgery, therefore using substantial health-care resources.⁵ This amount of

blood loss can cause disturbance of the woman's social, occupational or sexual life, and give rise to concern about possible underlying serious disease (in particular cancer), as well as medical risks such as chronic iron deficiency anemia.

Heavy periods can be debilitating, can lead to social embarrassment and medical problems, symptoms such as fatigue, exhaustion, shortness of breath, and anemia. Depending on the type of treatment or cause, women with menorrhagia office visits can range from 2-6 times a year. What is known/unknown about the condition is that the most common causes include anovulation and abnormal growths in the uterus (polyps or fibroids), having condition that increases bleeding. Some symptoms and effects of menorrhagia is the constant need to change pads >3hrs or use >21 pads during a period.⁶ Menorrhagia also leads to Iron Deficiency Anemia (IDA). Treatment depends on cause of bleeding, preferences of the woman, and the desire for children. The usual methods that are used to treat the condition are Pharmacological management including Hormonal birth control, hormonal IUD, Implant, Depo-Provera, Antifibrinolytics, NSAIDS, Progestin, GnRH agonists. If pharmacological management do not control symptoms, surgery is an option. Surgeries include endometrial ablation and hysterectomies. A significantly elevated Fibrinolytic activity in the endometrium caused by a premenstrual rise in tissue Plasminogen activators is believed to be an underlying mechanism for Menorrhagia.⁷ Plasminogen activator Inhibitors (anti fibrinolytic agents) have therefore been promoted as a treatment for menorrhagia.⁸ Tranexamic Acid (TA) is one such non-hormonal antifibrinolytic agent that enhances blood clotting. Hence the present study was aimed to evaluate the efficacy and safer use of Tranexamic acid in decreasing the symptoms of menorrhagia and observe its untoward side effects among patients attending Navodaya medical college, Raichur.

The objective of the study was to determine if tranexamic acid can effectively and safely reduce menstrual blood loss in menorrhagia.

METHODS

This study was carried out in the institute of Navodaya Medical College Hospital and Research Center from January 2014 to December 2015.

For this purpose 100 cases selected for the study who complained of regular long or heavy menstrual bleeding lasting >7 days or involving blood loss >80ml.

Selection of cases

Inclusion criteria

- Patient of 20-45 years complaining of regular heavy menstrual bleeding.

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

Detailed history was taken from the patients regarding presenting complaints, history of IUCD insertion, onset of excessive bleeding and past menstrual history.

A thorough general examination was done for the presence of pallor, thyroid enlargement, breast pathology and spine. Heart and lungs are auscultated for any additional sounds. Blood pressure was recorded.

A per abdominal examination and gynaecological examination was done including per speculum and bimanual examination to rule out any pelvic pathology.

Investigations

- Hb
- PCV
- Peripheral smear
- Coagulation profile
- Platelet count
- Blood grouping and Rh typing
- Pap smear
- Endometrial sampling beyond 35 years of age patients
- USG

Before prescribing tranexamic acid, menstrual blood loss assessment was done for two menstrual cycles using pictorial blood assessment chart (PBAC).

Follow up

At each follow up visit amount of bleeding, number of bleeding days, numbers of sanitary pads were assessed using 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 were recorded.

Efficacy of drug was analyzed before and after treatment with tranexamic acid.

RESULTS

Tab Tranexamic acid 500mg TID to QID was given to this patient who has objectively measured blood loss of more than 80ml per cycle in a total 100 cases.

Table 1: Based on the age the IUCD menorrhagia and other causes of menorrhagia age group.

Age in years	No of cases		Total cases	Percentage
	IUCD Menorrhagia	Menorrhagia		
20 to 25	19		19	19%
26 to 35	5	32	37	37%
36 to 45	-	44	44	44%

Above table shows that majority of IUCD induced menorrhagia cases are within 25 years age group as in this group, IUCD users are more and other causes of menorrhagia cases are in age group of 35 to 45 years age indicating its prevalence more in perimenopausal age group.

Table 2: Based on parity.

Parity	No of cases		Total cases	Percentage
	IUCD Menorrhagia	Menorrhagia		
Nulli para	-	2	2	2%
Para 1	22	-	22	22%
Para 2	2	16	18	18%
Multi para	-	58	58	58%

This table shows that majority of IUCD induced menorrhagia cases are primi para and majority of multipara are due to other causes of menorrhagia and two are nullipara.

Table 3: Ultra sound findings.

Organs	Findings	No of cases
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

Most of the cases are with in normal range of BMI. (Body mass index is equal to weight in kgs/ height 2 in meters. 4 cases are obese (>30 BMI). The menstrual disturbances in the obese women may be due to hormonal disturbances.

Clinically, normal uterus found in 57% of cases. 23% of cases showed bulky uterus (6-8 weeks) 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.

Only in age group of 35 to 45 years D and C was done to know the type of endometrium and to rule out hyperplasia and carcinoma. Out of 54 cases 48 cases have secretory type of endometrium, 5 had proliferative endometrium, 1 had hyperplasia. From this it is clear that most of the regular cycles are ovulatory.

Table 4: Haemoglobin.

Hemoglobin in gm%	No of cases	Percentage
<6	3	3%
6-7.5	8	8%
7.5-9	39	39%
9-10.5	34	34%
>10.5	16	16%

Most of patients had haemoglobin concentration between 7.5 to 10.5gm%. 3 patients had haemoglobin less than 6gm% that were given blood transfusion. The factors contributing to anemia are excessive menstrual blood loss and nutritional deficiencies.

Table 5: Mean haemoglobin concentration before and after management.

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

Table 6: 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 68% of cases, remained same in 32% after taking the drug. The cases that had changed finally ended up in hysterectomy. P- value is <0.05 shows significant.

In 100 patients, pre-treatment pictorial blood assessment chart score is 319.1 and post treatment 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 7: 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 (500mg QID)	319.1	133.01	<0.05 significant	41.6%	-

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

Table 8: Effect of drug on duration of bleeding.

Effect of drug	Duration of bleeding (mean in days)	P-value
Before treatment	9	<0.05
After treatment	4	Significant

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

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.

From the above table dropouts are only 9%, 3 patients after first cycle, 6 patients after second cycle because of no effect of drug.

DISCUSSION

Study group

Department of obstetrics and gynaecology, Navodaya medical college hospital and research center, Raichur.

Other group

Department of obstetrics and gynaecology, New York university school of Medicine, New York, USA.

In this all trial (Freeman, Kouides and Lukes) is included involving the efficacy of tranexamic acid for the treatment of heavy uterine bleeding.

In our present trial of efficacy of tranexamic 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.

Table 10: Comparison of various studies with decrease menstrual blood loss.

	Decrease menstrual blood loss	Sanitary pad usage	Discontinue
Our study	41%	Significantly reduced	32%
Freeman	39%	Significantly reduced	36%
Kouides	38%	Significantly reduced	43%
Lukes	40%	Significantly reduced	24%

The other various randomized double cross clinical trails with tranexamic acid showed dose dependent reduction of 35- 51% of menstrual blood loss.

In all four clinical trials (our present study; Freeman; Kouides and Lukes) there is significant reduction in number of sanitary pad usage.

In Kouides and Lukes clinical trial there is no significant difference in duration of bleeding, but in Freeman trail there was significant reduction in number of days and bleeding in successive menstrual cycle.

In Kouides study group there is 43% discontinuation, 36% Freeman, 24% in Lukes and 32% in our study.

Tranexamic acid is a non-hormonal option that has proven to be an effective treatment for heavy menstrual bleeding. It reduced menstrual blood loss by 38-41% and it is significantly more effective than placebo, NSAIDS, oral cyclic luteal phase progestins or oral ethamsylate. Tranexamic acid significantly improves the quality of life of women trated for heavy menstrual bleeding. Adverse effects are few and they are mild.

CONCLUSION

Tranexamic acid is a non-hormonal and cost effective treatment in menstrual bleeding.

Treatment with tranexamic 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 well-being. It is also effective treatment for menorrhagia caused by IUCD.

This study and current clinical evidence concludes that size and type of fibroid has significant influence on effect of treatment. Tranexamic acid has been documented and found to have no effect on uterus with adenomyosis and endometrial polyp.

Treatment with tranexamic acid decreased 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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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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