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Efficacy of Mefenamic Acid and Tranexamic Acid in the Management of Dysfunctional Uterine Bleeding

Damadari Bai M[1], Purna ChandrakalaM[2]

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ABSTRACT

Introduction: *Dysfunctional uterine bleeding is one of the most commonly expressed complaints of women at reproductive age leads to anemia 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.* ***Materials and methods****: During 2010-2011, 60 patients aged 15-49, with DUB who referred to Government maternity hospital, Hanmakonda, Warangal, were randomly divided into 2 thirty-patient groups. The first group received mefenamic acid and the other received tranexamic acid during the first three days of their period for 2 subsequent cycles; following that, their bleeding changes were evaluated.* ***Results:****Repeated measures anova analysis pointed out that while the decreasing pattern of bleeding for each drug was statistically significant (p value =0 /001), the difference between the decreasing pattern of bleeding resulted from the use of the two drugs was not significant (p=0/059). Both groups depicted the same level of satisfaction (p=0/079) and no serious complications were reported.* ***Conclusion:****The efficacy of mefenamic acid and teranexamic acid in treating menorrhagia was the same for both groups.*

Keywords*: DUB, Mefenamic Acid, Tranexamic Acid*

INTRODUCTION

DUB is one of the most commonly expressed complaints for which approximately 5% of 30–49 year old women consult the doctors per year[1] Menorrhagia is defined as complaint of heavy menstrual bleeding over several consecutive cycles. The upper limit of monthly bleeding is 80 ml per cycle, which is 2 standard deviation from the mean (mean menstrual bleeding per cycle is 36 – 52ml).[2] 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.[3] Most of the patients who complain of menorrhagia have no known organic diseases and have normal physical examinations, laboratory tests and imaging (sonography) results.[4] Menorrhagia, if repeated, causes a decrease in iron reserve and anemia and subsequently, anemia 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 anemia morbidities are the result of more than 60 ml bleeding per cycle.[5] 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 level as high had menstrual bleeding less than 35 ml.[6] 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.[7] Although Janssen and colleagues (1995) take low Hb% as a good sign of menorrhagia, there might be normal Hb% patients with menorrhagia. So it is not an ideal screening test.[8] All of the techniques used for menorrhagia research purposes are difficult and clinically impractical. Examples are Alkalin Haematin Test and Radio Isotop Techniques. So, we need an accurate method of estimating the blood loss which is clinically applicable. In this way treatment without indication is prevented. In this study a

Address for Correspondence:
[1]Assistant Professor **(Corresponding Author)**
Department Of Pharmacology
Kakatiya Medical College, Warangal, Telangana, India
Email: damodari1964@gmail.com
Mobile: +919963282705
[6]Associate Professor of Pharmacology, Kakatiya Medical College, Warangal, India

pictorial chart for the evaluation of menorrhagia was designed. This chart showed high clinical accuracy and its application was feasible. Worldwide use of hormonal therapy is based on the wrong assumption that menorrhagia happens because of imbalance in hormones and an 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.[9]

The mechanisms of controlling menstrual bleeding are poorly understood. In the past decades, studies had shown that the increase in endometrial fibrinolysis and an imbalance in prostaglandin caused functional uterine bleeding.[10] Tranexamic acid (250 mg oral capsule) which ISA synthetic amino acid was introduced in sweden as cyclokapron® in 1969 and has since been used in order to decrease menstrual blood loss. It's anti fibrinolytic effects are achieved by preventing the plasminogen from binding to fibrin filaments and so, it prevents clot dissolution. Mefenamic acid is an nsaid and exerts its anti-prostaglandin effects by inhibiting prostaglandin synthesis, so it balances prostaglandins and decreases menstrual bleeding. Anti fibrinoletic drugs such as tranexamic acid and anti-prostaglandin drugs such as mefenamic acid are preferred to hormonal drugs the time the contraception is not a goal, as they are used only during menstrual period. Although several studies have evaluated and compared the effects of mefenamic acid and tranexamic acid and compared their effects with each other and on other drugs, so far no specific study has compared the effects of these two drugs on the treatment of menorrhagia in iranian women to show which one must be preferred as the first choice.

Methodology

This study was a single blind clinical trial that was approved by ethics committee of Kakatiya Medical College, Warangal. During 2011-2012, 60 patients, aged 15-49 suffering from menorrhagia that referred to gynecology clinic of Government Maternity Hospital, Hanmakonda, Warangal were enrolled. Organic causes of menorrhagia were excluded by gynecological examination, sonography, endometrial biopsy and a cervical smear test and patients with a history of renal or hepatic impairment; previous thromboembolic disease, peptic ulcer and coagulation disorders were not enrolled. The entire patient signed the informed consent form. Sixty patients with more than 80 ml menstrual bleeding or those who had experienced menstrual duration for more than 7 days were selected and divided into two groups (a & b) randomly.

Group **A** took 2 tranexamic acid capsules and **Group B** received 2 mefenamic acid capsules three times a day during the first three days of menstruation. Patients were asked to mark the charts during menses for 2 treatment cycles and one cycle after discontinuation.

RESULTS

Before this study, the mean of menstrual bleeding volume in **Group A**patients (who received tranexamic acid) was 166.35 ml and in mefenamic acid group (**Group B**) it was 146.52 ml. After the first and second cycles of treatment, it reduced to 122.12 and85.77 ml in group a patients and 111.09 and 85 ml in Group B patients. So, the reduction of bleeding volume after the two cycles of treatment was 102.88 ml forGroup A and72.39 ml for Group B. Although the difference between the two groups was 30 ml, T-test evaluation showed that it was not statistically meaningful. The bleeding volume in the first cycle following the treatment was 63.46 for Group A and 74.13 for Group B.

Repeated measures anova shows that the decline of bleeding volume for each drug was statistically meaningful (p-value= 0/001). Paired T-test pointed out that the decreasing pattern of bleeding volume was statistically meaningful for both drugs (**Figure 1**).

Then SPSS software (11th edition) was used for data analysis. Ultimately, repeated measure Anova and Paired t test was used for comprehensive analysis.

Bleeding duration for tranexamic acid group before and after the treatment was 9.68 and 7.28 days and for mefenamic acid was 7.87 and 6.65 days respectively. This decline is statistically meaningful (p-value<0/001). The difference between decreased days of bleeding for the two groups was 1/18 days. T-test evaluation pointed out that the difference was not statistically meaningful.

70% of the patients in Group A and 43.3% inGroup B were completely satisfied with the treatment. Although 70% of the patients in group a declared that they would choose the drug if the problem recurs, only 50% of Group B patients made such a remark. The difference in the level of satisfaction between the two groups was not significant (p=0.079). Twenty patients belonging to Group A and 24 patient from Group B reported no complications. In Group A, vertigo was the most common complication which 5 patients suffered and in Group B 3 patients had dyspepsia and 2 patients complained about epigastric pain.

Table 1 Bleeding volume during and after the administration of Mefenamic acid and Tranexamic acid

Treatment		Mean	Std. Deviation
Mefenamic Acid	Bleeding before	146.52	51.133
	First visit bleeding	111.09	56.002
	Second visit bleeding	85.00	32.369
	Bleeding after	74.13	30.993
Tranexamic Acid	Bleeding before	166.35	52.375
	First visit bleeding	122.12	50.974
	Second visit bleeding	85.77	48.347
	Bleeding after	63.46	36.763

Table 2 Comparison of mean difference of bleeding & its duration before & after usage of both drugs

			Mean	Std. Deviation	Pvalue
Mefenamic Acid	Pair 1	Bleeding before – Bleeding after	72.391	53.553	< 0.001
	Pair 2	Duration before – During after	1.217	1.953	0.007
Tranexamic Acid	Pair 1	Bleeding before – Bleeding after	102.885	56.146	< 0.001
	Pair 2	Duration before – During after	2.400	3.096	0.001

DISCUSSION

It is worth mentioning that tranexamic acid is a synthetically derivative of lysin amino acid which does its anti fibrinolytic effect through reversible block of lysin-attach sites on plasminogen molecules. So the drug inhibits plasminogen to plasmin change and prevents fibrinolysis and lysis of blood clotting.[11] Tranexamic acid, only in the form of 250 mg capsule, is available in the market. It is well tolerated and has few side effects such as mild gastrointestinal complications, as reported by this study. Earlier theoretical concerns about thromboembolism due to anti fibrin lytic action of tranexamic acid have been refuted by longitudinal studies. For example Rybo (1991) reported that during 1969 to 1987 the rate of thromboembolism in women suffering from menorrhagia was the same as normal individuals. Prostaglandin imbalance plays an important role in menorrhagia; so mefenamic acid in the form of 250 mg capsule which inhibits prostaglandin synthesis, is used to control menorrhagia. In this study, we observed a good therapeutic effect with tranexamic acid and mefenamic acid. It is in favor of meta-analysis of 7 studies[12] that showed more than 45% reduction in menstrual bleeding volume with tranexamic acid treatment. Sukanyasirnil and colleagues published an article in 2005. They treated 40 menorrhagia women with tranexamic acid capsule 1gm every 8 hours in the first five days of period. This led to 49% decrease in bleeding volume with no change in menstrual duration.[13] In another study, Tranexamic acid decreased blood loss by 44%compared to mefenamic acid, its effect was more but it was equal to progesterone, especially progesterone IUDs.[14] A similar study was conducted at Shahidsodughi University of Yazd in 2001-2005. Seventy women were treated in the first five days of their mens in 3 subsequent cycles. Thirty patients received Mefenamic acid 500 mg every 8 hours and 39 patients took Tranexamic acid 500 mg every 6 hours. Mefenamic acid decreased bleeding by 20% and Tranexamic acid by 50% and it was concluded that patients with abnormal bleeding should take Tranexamic acid therapy before surgery.[15] Tranexamic acid at a dose higher than the dose routinely used for preventing plasmin formation, inhibits plasmin activity directly.[16] It seems that the higher dose, used in some studies, justifies the better effect of tranexamic acid. This is the effect which was not observed in our study, as both drugs were effective to the same extent. In research studies, the gold standard of measuring menstrual blood loss is the alkaline haematin test[5] but it is expensive and time consuming. Methodological limitation of this study is the small sample size. Randomized double blind control trials with large numbers of patients are needed to compare the two drugs with each other and with other drugs.

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Conflicts of interest: None.

Contribution of authors: We declare that the authors named in this article did this work and all liabilities pertaining to claims relating to the content of this article will be borne by the authors.

Ethical clearance: Taken.

REFERENCES

1. Royal College of GeneralPractitioners, office of Population Censuses and Surveys, Department of Health and Social Security. Morbidity From General Practice. London. Hmso, 1986.
2. LosiufaiL. Modern management of menorrhagia. Hong Kong Practitioner Feb 1996;18(2):12-15.
3. AbbottJa, Hawe J, Garry R. Quality of life should be considered the primary outcome for measuring success of endometrial ablation. J Assoc Gynecol Laparasc 2003;10;491-5.
4. BonnarJ,ShepparolBl, Treatment of menorrhagia during menstruation. Randomized controlled trial of Ethamsylate, Mefenamic Acid and Tranexamic Acid. Bmj 1996;313:579-82.
5. Hall BergL, Hogdahl A, Nilssonl. Menstrual blood loss. A population study. Variation at different ages and attempts to define normality. Acta Obstet Gynevol Scand 1996;45:320-510.
6. Warner Pe, Critchley Ho, Lwmsden Ma, Campbell Brown M, Douglas A, Murray Gd. Menorrhagia. Is the 80ml blood loss criterion useful in management of complaint of menorrhagia? Am J Obstet gynecology 2004;190:1224-9.
7. Berek, J.S. Berek And Novak Gynecology (15ed). 2012.
8. Janssen Ca, Scholtenpc, HeintrzAp. A simple visual assessment technique to discriminate between menorrhaghia and normal blood loss- Obset Gynecol 1995; 85; 977-82.
9. HagnesPj, Hedgson H, Anderson. Measurement of menstrual blood loss in patient complaining of menorrhagioa. Br J Obstet gynaecol 1977;84:763-8.
10. Bonnar J, Sheppard Bl. The haemostatic system and dysfunctional uterine bleeding. Research and Clinical 1983;5:27-36.
11. Wikipedia, The free encyclopedia, Tranexamic acid 2011 Http://En.Wikipedia.Org/Wiki/Tranexamic Acid.
12. Coulter A, Kelland J, Peto V, Rees Mc. Treating menorrhagia in primary care. An overview of drug trials and a survey of prescribing practice int J Tech assess health care 1995;11:456-71.
13. SukanyaSirilMd, Unnopjaisamram Md. Treatment of idiopatic menorrhagia with tranexamic acid, J Med Assocthai 2005;Vol 88.
14. Hall P, Maclachlin N, Thorn N. Control of menorrhagia by the cyclo-oxygenase. 1987;94:554-8.
15. Sekhavat L, Zare F, Karimzade M. Comparison of Mefenamic acid and Tranexamic acid in treatment of hypermenorrhea. ShahidSedugh University, Department of Obstet and Gynec oilyazd 2001-2005.
16. Shahraz S, Ghazianit. Tranexamic acid- Mefenamic acid. A Comprehensive Text book of Drug Information.