

EFFICACY OF TRANEXAMIC ACID IN THE MANAGEMENT OF MENORRHAGIA

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ABSTRACT

Dysfunctional uterine bleeding (DUB) is most common cause for menorrhagia which can be treated medically in most of the times. Tranexamic acid is a best drug for treating menorrhagia. The aim of the present work was to study efficacy of tranexamic acid in the management of menorrhagia. This study was carried out with 100 cases from a total of 500 cases attended hospital with menorrhagia. The efficacy of tranexamic acid was studied by using pictogram PBAC score, and to know menstrual blood loss before and after treatment and thus analyzed whether drug is effective or not. The results of the present study concludes that Tranexamic acid is very much effective in reducing blood loss in DUB. Blood loss was reduced in 72% of patients and it reduced blood loss by 50% to 60%.

INTRODUCTION

Menorrhagia is excessive menstrual bleeding that interferes with a women's physical, emotional, social and material quality of life [1]. It is an important health care problem for women of reproductive age, their families, and society [2]. Dysfunctional uterine bleeding (DUB) is one of most common cause for menorrhagia and reason for referral to gynecologists. In 1990, 60% of women with heavy menstrual bleeding went for hysterectomy.¹ It is estimated that 30% of women of reproductive age suffer from menorrhagia, the prevalence increasing with age and peaking just prior to menopause [2]. It has been found that once referred to a Gynaecologist, 60% of women with menorrhagia will have a hysterectomy within 5 years, accounting for up to 75% of all hysterectomies performed worldwide [3]. About half of all women who proceed to

hysterectomy for their heavy bleeding have a normal uterus removed [4]. Most of women complaining of menorrhagia have no pelvic pathology and are diagnosed cases of dysfunctional uterine bleeding. In DUB, the increased fibrinolysis [5, 6, 7] or altered endometrial prostaglandin balance, are the theoretical causes. The notion of DUB is highly subjective [8] and systematically measuring menstrual blood loss is not feasible in clinical practice. DUB is frequent in women of reproductive age; infact its prevalence is high in perimenopausal age group. Medical therapy, with the avoidance of possibly unnecessary surgery is an attractive treatment option [6, 7]. It is indicated for patients who do not wish surgery or for whom surgery is unsuitable. The main objective of treatment is to achieve symptomatic relief and improve women's quality of life and to improve anemia [3].

The main treatment of DUB is medical and involves use of NSAID's, Antifibrinolytics, and Hormones. In DUB fibrinolytic activity of menstrual fluid is increased [4], tranexamic acid decreases fibrinolysis and thus menstrual blood loss [4, 5]. Tranexamic acid, a synthetic amino acid, was introduced in Sweden as

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cyclokapron in 1969 and has since been used in a number of countries for the treatment of menorrhagia. Tranexamic acid exerts antifibrinolytic effect by inhibiting activation of plasminogen to plasmin by binding to plasminogen and plasmin receptor sites and thus inhibiting the binding of plasminogen to fibrin filaments, thus preventing clot dissolution [6]. Plasmin responsible for degradation of fibrin. Fibrin is a protein that forms framework of blood clot. A more recent survey showed that 47 % of general practitioners would now consider tranexamic acid, following a report in the effective health care bulletin (1995) as very much effective medical treatment for menorrhagia [7].

Tranexamic acid given during menstruation is safe and highly effective treatment for excessive bleeding. Patients with DUB should be offered medical treatment with tranexamic acid before decision is made for surgery. Tranexamic acid causes 50% reduction in menstrual bloodloss [8] and improves quality of women's life [9]. The aim of the present work was to study the efficacy and effectiveness of Tranexamic acid in the management of menorrhagia,

MATERIALS AND METHODS

This study was carried out in the department of Obstetrics and Gynaecology, in Yashoda Super Speciality Hospital, Hyderabad from August 2009 to June 2012. For this 100 cases are selected for the study from total of 500 cases attended hospital with menorrhagia during study period by random sampling method which are fulfilling selection criteria and who complained of regular excessive menstrual bleeding during cycles between 24 to 35 days.

Selection of Cases: done on basis of inclusion and exclusion criteria.

Inclusion Criteria

- Age group between 20 – 45 years
- No Obvious pelvic pathology based on clinical examination, investigations and ultrasound.
- Patients having menstrual blood loss of more than 80ml, as per pictorial chart.
- No detection of other medical or hormonal diseases.
- Cases purely fitting into DUB with regular cycles between 24 to 35 days.

Exclusion Criteria: important as DUB is diagnosis of exclusion.

- Organic Pathology like fibroids, polyps, severe PID, Endometriosis, ectopic pregnancy, hydatidiform mole, abortion.
- Platelet disorders
- Coagulopathies, bleeding disorders.
- Endocrine disorders
- Diabetes, thyroid problems, tuberculosis.
- Personal History of thromboembolic disorders
- Family history of DIC, thrombosis

- Renal insufficiency, Hepatic disorders
- Malignancies
- Lactating women
- Known sensitivity to the drug
- Color vision defects
- 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 murmurs or additional sounds. Blood pressure was recorded.
- per abdomen examination
- A Gynaecological examination done including per speculum and bimanual examination to rule out any pelvic pathology.

Following investigations: done before recruiting into the study.

- CBP, CT. BT
- TSH
- RBS
- LFT
- RFT
- Ultrasound

Diagnostic Dilatation and Curettage:

- Using pippelle done in women beyond 35 years of age.
- Done in those who were anxious about endometrial pathology.
- Done in those who showed endometrial thickness more than 9 mm in ultrasound.

➤ Method

Before prescribing tranexamic acid, menstrual blood loss assessment was done for two menstrual cycles using pictogram serving as controls and compared with 3 post treatment cycles.

- Women encouraged to chart their menstrual bloodloss using pictogram given to them and bring with them while coming to hospital and seeing that PBAC scoring is given.
- Treatment started with oral tab tranexamic acid 500 mg tid starting from 1st day of periods and continued for 5 days during periods for 3 months.

METHOD OF ASSESSMENT OF MENSTRUAL BLOODLOSS USING PICTOGRAM AND GIVING PBAC SCORE:

Most of the patients were literate. In such patients, pictogram was shown and they were asked how their pad was soaked and PBAC score given and initially pad was observed personally to check whether they understood the pictogram or not and saying correctly about their soakage.



Then they were given copies of pictogram to document number of sanitary pads/towels/tampons used, in the column provided which had degree of soiling as shown in picture. They were taught how to write number of sanitary pads/towels/tampons used each day given in separate columns. Day 1 is first day of period. Each day according to visual appearance of each sanitary pads/towels/tampons used, PBAC score given. Extra Score is added if there is presence of any clots or episodes of flooding. Each day scoring is added to get final score for entire period and thus depending on score indirectly menstrual blood loss assessed. Women having PBAC score more than 100 considered to have menstrual blood loss more than 80 ml and menorrhagic. Then patients considered as having menorrhagia were prescribed tablet tranexamic acid 500 mg tid from 1st day of menstrual cycle to 5th day for three next cycles.

Follow up was done and patients treated for 3 months and all treating patients are called after periods these 3 months and they are again followed for 6 more cycles after periods. At each visit amount of bleeding, number of bleeding days, passage of clots, number of sanitary pads used and any episodes of flooding were asked and were assessed using pictogram and PBAC score given. Adverse effects if any were recorded. Effect on dysmenorrhoea, patient satisfaction and well being are asked. At the end of the study patient acceptability was assessed by asking "would you be prepared to continue with this treatment?" If the patient answered "no" the reasons were recorded. And thus efficacy of drug was analyzed before and after treatment with tranexamic acid. All women were advised to use same type of sanitary products which have similar absorbent capacities. Few women didn't come for regular follow up during treatment.

RESULTS

Tab Tranexamic acid 500 mg tid for 5 days starting from 1st day of menstruation was given to the patients who had objectively measured blood loss of more than 80 ml per cycle and PBAC score more than 100 per cycle, in a total of 100 cases of essential menorrhagia. Essential menorrhagia cases are more in age group of 36 to

45 yrs age indicating its prevalence more in perimenopausal age group. Present study results on parity distribution showed that, Unmarried were 5, Nullipara 8, Para 1 -12, Para 2 were 20, and Multipara were 55 respectively. Majority of essential menorrhagia cases are multipara.

Clinically, normal uterus was found in 78% of cases. 22 % of cases showed bulky uterus (6-8 wks) in which other causes for uterine enlargement like leiomyoma, adenomyosis and pregnancy causes were excluded. Bulky uterus may be due to multiparity. No adnexal pathology was detected in 96 % of cases and only 4 % had cystic ovaries.

A total of 97% of the cases had normal endometrial thickness. Only 3 % of the cases had thickness more than 9mm. In these cases, endometrial hyperplasia and carcinoma were ruled out by DD and C. 50 cases selected for DD&C only 45 cases accepted for procedure and 40 cases had secretory type of Endometrial, 4 had proliferative endometrium, 1 had irregular ripening and no cases of irregular shedding and hyperplasia. From this it is clear that most of the cases are ovulatory. In the present study, improvement in hemoglobin was observed in the patients this may be due to decreased menstrual blood loss after treatment with tranexamic acid.

Menstrual blood loss decreased in 72 % of cases, remained same in 20% of cases and increased in 8% due to poor compliance. Out of 72 patients overall who had decreased amount of blood loss, most of them had decrease in 50- 60 % of blood loss showing that drug is very effective in reducing menstrual blood loss.

Minor side effects mostly of gastrointestinal origin were seen only in 6 out of 100 patients. Out of this only 2 patients dropped out of study because of nausea, vomiting indicating that intolerable side effects are very minimal with the drug. 72 % of the patients are satisfied with the drug. 28% patients are unsatisfied because of no decrease in blood loss and due to side effects. Drop outs are only 6%, 2 patients after 1st treatment cycle because of side effects, 4 more patients after 2nd cycle because of no effects of drug.

Figure 1. Pictogram

| Date: Week | | 5/11 | 5/18 | Days of bleeding | | | | | | | | Number of used sanitary towel | |
|--|------|------|------|------------------|------|-----|-----|----|---|---|---|-------------------------------|-------|
| | | | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | | |
| Sanitary towel | | | | | | | | | | | | | |
| Intensity of bleeding per sanitary towel | x 1 | | | // | / | / | / | // | / | | | | |
| | x 5 | | | | ### | /// | // | | | | | | |
| Factor: | x 20 | | | | // | // | | | | | | | |
| and/or Tampons | | | | | | | | | | | | | |
| Intensity of bleeding per tampon | x 1 | | | | / | | | / | | | | | |
| | x 5 | | | | // | /// | // | | | | | | |
| Factor: | x 10 | | | | ###/ | /// | | | | | | | |
| Daily points: | | | | | 2 | 137 | 101 | 21 | 3 | 1 | | | = 265 |









| PBAC Scoring System | | |
|---------------------|--|---|
| Pads | | |
| 1 point | For each lightly stained pad |  |
| 5 points | For each moderately stained pad |  |
| 20 points | For each completely saturated pad |  |
| Tampons | | |
| 1 point | For each lightly stained tampon |  |
| 5 points | For each moderately stained tampon |  |
| 10 points | For each completely saturated tampon |  |
| Clots/Flooding | | |
| 1 point | For each small clot (size of a nickel or indian 50paise coin) | |
| 5 points | For each large clot (size larger than nickel or Indian 2Re coin) | |
| 5 points | For each episode of flooding | |

Table 1. Improvement in Hemoglobin concentration after treatment with tranexamic acid

| Hb increase in gm % | No. of cases | Percentage |
|---------------------|--------------|------------|
| 0.5-1 | 28 | 28 |
| 1-2 | 10 | 10 |
| 2-3 | 22 | 22 |
| >3 | 40 | 40 |

Table 2. Effect of Drug on Amount of Bleeding (Mean \pm SD)

| | |
|---------------------------|--------------|
| Before Treatment (n=100) | 118 \pm 30 |
| After Treatment | 76 \pm 17 |

DISCUSSION

The present study was aimed to study the efficacy and effectiveness of Tranexamic acid in the management of menorrhagia in the individuals attending department of Obstetrics and Gynaecology, in Yashoda Super Speciality Hospital, Hyderabad. Out of 100 cases that showed decreased blood loss, the mean decrease in sanitary pad usage was from 15 \pm 5 to 8 \pm 2. Treatment with tranexamic acid decreased the incidence of hysterectomy avoiding major surgery and its associated complications like anesthetic complications, intraoperative blood loss, blood transfusion reactions, prolonged hospital stay, high expenditure, morbidity and mortality and hormonal problems. Treatment with tranexamic acid increases quality of life of women by reducing impairment of social activities and impairment at work and there is substantial improvement in overall well being.

Average percentage of blood loss after treatment with Tranexamic acid is 51 % in the study group, the present study observations are in accordance with earlier authors where Bonnar and Sheppard study showed 54% of blood loss after treatment with Tranexamic acid [10], whereas, Joseph group observed 47.5% [11].

Present study also showed that treatment with Tranexamic acid decreased bloodloss in 72% of women, which are in agreement with other earlier studies [10, 11]. In study group mean menstrual bloodloss is 118 ml and 76

ml before and after treatment respectively, similar observation was seen in the study done by Joseph group showed 143-178ml and 72-75ml before and after treatment respectively [11].

In the study group and Ireland group, there is no significant difference in the duration of bleeding but significant decrease in number of sanitary pad usage. Bonnar and Sheppard study showed [10] significant decrease in PBAC score after treatment and increase in haemoglobin after treatment.

Side effects are present in 6% of the cases in study group and improvement in dysmenorrhoea is seen in 15.27% of cases in the present study group whereas, 9% and 30% of side effects was observed in earlier studies [10, 11]. Acceptability rate is high in Ireland and Canada group about 77% and 72% respectively. But in study group acceptability is relatively less about 65% due to relatively high cost of drug and prolonged treatment.

Study done by Lethaby and co-workers [12] showed that antifibrinolytic therapy compared to placebo showed a significant reduction in mean blood loss. The other different clinical trials were conducted 3 of which were randomized, double blind cross over studies with tranexamic acid, showed dose dependent reduction of 35 – 51 % of menstrual blood loss in essential menorrhagia. Antifibrinolytics appear to be more effective than placebo,



[13-15], NSAIDs, and ethamsylate [16]. Tranexamic acid and NSAIDs reduce menstrual blood loss by about one half and one third, respectively [11]. Antifibrinolytics have been a popular choice for treatment of menorrhagia since last few years. In the study group, patients were reviewed after six months. Out of 100, 18 patients opted for other group of drugs as there was no effect with the tranexamic acid. In remaining, 61 only came for follow up after six months. In them 40 patients had normal menstrual blood flow, 4 patients continued using tranexamic acid and 17 cases had excessive menstrual blood flow, not willing to continue tranexamic acid, underwent hysterectomy as they had completed their family life.

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CONCLUSION

To conclude, Tranexamic acid given during menstruation is a safe, well tolerated and highly effective treatment for excessive bleeding. Patients with dysfunctional uterine bleeding should be offered medical treatment with tranexamic acid before a decision is made for surgery. It may be utilized as first line therapy in DUB.

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CONFLICT OF INTEREST:

The authors declare that they have no conflict of interest.

