



Original Research Article

Decline in blood loss with use of tranexamic acid in cases of hysterectomy: A retrospective observational study in a teaching hospital of central India

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ABSTRACT

Introduction: Hysterectomy the most commonly performed gynaecological surgery world over is mostly a planned surgery commonly done for benign uterine conditions, though relatively high rates of complications have been reported. Blood loss during surgery seems to be a major complication. Anaemia being prevalent in Indian women, adds to the risk of prolong recovery time and postoperative morbidity with excessive blood loss intra operatively. Tranexamic acid (TXA) being an anti fibrinolytic agent have been found to decrease blood loss and requirement of blood transfusion in various surgical procedures and aids in better recovery.

Objective: To find the effectiveness of tranexamic acid in decreasing blood loss in patients undergoing hysterectomy for benign indications and the need for blood transfusion.

Materials and Methods: Type of study- Retrospective observational study over a period of 1 year in 200 patients.

Study was conducted in Obstetrics and Gynaecology department of L.N. medical college, J.K hospital and research centre Bhopal.

Approval for conducting study from ethical committee of hospital was taken. A retrospective analysis of all patients record was done who underwent hysterectomy for benign indications over the study period of one year and patient were sorted out in two groups, one (group 1) who received tranexamic acid (TXA) during surgery and other one (group 2) who did not receive TXA during surgery.

Outcome of the study was assessed on following parameters - amount of blood lost (measurement of blood loss was done by the amount of blood collected in suction bottle and soiled mops), postoperative haemoglobin level after 24 hours of surgery, blood transfusion requirement, duration of hospital stay.

Results: Significantly less intraoperative loss of blood and need for blood transfusion was found in group 1 as compared to group 2. (P=0.0001).

Conclusion: In the present study we concluded that a single dose of tranexamic acid given during surgery significantly reduces the blood loss, operating time and need for blood transfusion in patients undergoing hysterectomy for benign indications. Tranexamic acid being an anti fibrinolytic agent can be safely recommended as prophylactic measure for reducing blood loss in hysterectomies specially in low resource setting.

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1. Introduction

Hysterectomy is one of the most frequently performed major gynaecological surgical procedures worldwide. Although, mostly it is performed for benign indications, a

substantially high rates of complications has been reported, out of them most common complication is bleeding during perioperative period. Considering the high incidence of anaemia in India, excessive blood loss during surgery adds to delay in postoperative recovery and increase in post operative complications like wound healing.

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A variety of antifibrinolytic drugs has been used prophylactically to reduce perioperative blood loss such as tranexamic acid, Epsilon amino caproic acid (EACA) and Aprotinin.

Tranexamic acid is an antifibrinolytic agent approved for treatment of various types of haemorrhage. It acts by inhibiting fibrin degradation, thereby enhancing stable blood clots formation. In several countries, the drug is used as prophylactic treatment prior to major surgery. A vast number of Cochrane systematic reviews carried out in different surgical settings had also recognised the effectiveness of preoperative administration of Tranexamic acid as prophylactic measure in reducing blood loss and blood transfusion requirement.¹⁻⁴

A number of studies have also been conducted to find the effectiveness of tranexamic acid for treatment of patient with menorrhagia.^{4,5} These studies have found menorrhagia is associated with enhanced levels of fibrinolytic activity. This may contribute to the explanation of the relatively high rates of bleeding complications related to hysterectomy, as menorrhagia is one of the most common indications for the hysterectomy.^{6,7} Consequently, women undergoing hysterectomy might benefit from prophylactic Tranexamic acid during surgery. The commonly reported side effects of tranexamic acid include gastric disturbances like nausea, vomiting, diarrhoea, dyspepsia and headache. No clinical trial has demonstrated any major side effects of it as well as no risk of thrombosis have been demonstrated up till now.⁸

World health organisation (WHO) has added tranexamic acid in the list of Essential Medicines and for the treatment of adult patients with trauma and ongoing haemorrhage. (Selection and Use of Essential Medicines guideline - March 2011). Under class 1A recommendation, the use of tranexamic acid in the case of traumatic and perioperative bleedings has been advocated by The European societies Task Force for Advanced Bleeding Care in Trauma and European Society of Anesthesiology.⁹

American society of Anesthesiologists (ASA) practice guidelines for perioperative blood management in surgical patients with excessive bleeding also recommend use of TXA.⁹

Therefore the present study was done to find out the effectiveness of tranexamic acid in reducing perioperative blood loss in patients undergoing hysterectomy as well as postoperative complications and hospital stay in study subject.

2. Materials and Methods

1. Type of study - Retrospective observational study
2. Duration of study- 1 year from July 2019 to July 2020
3. Study centre- study is conducted in department of obstetrics and gynaecology of LN medical college J.K hospital and research centre Bhopal.
4. Sample size - 200 patients - 100 patients in each group.

2.1. Sample size calculation

$$\text{Sample size} = \frac{N=Z^2 p(1-p)}{D^2}$$

N=Sample size. Z= Standard error from the mean corresponding to 95% confidence level=1.96

P=6% taken to be estimated prevalence of hysterectomy (18).

D = 0.05

Here incidence is less than 6%, hence D will be 1/4 of incidence =0.015.

After considering the non response rate of 10%, the sample size calculated was 47 in each group.

So 47 was the minimum required sample size in each group, to increase the authenticity of results we have taken sample size of 100 patients in each group.

2.2. Inclusion criteria

1. Abdominal hysterectomy for any benign indication
Like abnormal uterine bleeding, leiomyomas <10 cm in size, adenomyosis, chronic pelvic inflammatory disease not responding to medical treatment, uterovaginal prolapse.
2. Hysterectomy alone or with salpingectomy or oophorectomy.

2.3. Exclusion criteria

1. Diagnosed or suspected case of pelvic malignancy
2. Patients with coagulopathy
3. History of venous/arterial thromboembolism
4. Known case of hypersensitivity to tranexamic acid
5. Patients on anticoagulant therapy
6. Known case of Hepatic or renal dysfunction

Before conducting the study approval was obtained from ethical committee of the hospital. In this study case records of all the patients who underwent hysterectomy for benign indications over the study period of 1 year were reviewed regarding intraoperative blood loss, medications received during surgery, preoperative and postoperative blood loss, need for blood transfusion after surgery, postoperative complications, duration of hospital stay. Out of total hysterectomies performed in the institute patients were selected using consecutive sampling method till sample size of 200 patients was attained based on decided criteria and sorted out in two groups, group 1 in which patients have received 1 gm tranexamic acid intravenously during surgery for bleeding and other one (group 2) who did not receive tranexamic acid during surgery. Case record and data of both groups were analysed retrospectively in terms of preoperative and postoperative haemoglobin level, blood loss, need for blood transfusion and post operative complications. Patients with comparable demographic factors in terms of age, weight, height, medical comorbidities were included in the study. Primary outcomes

measured in terms of postoperative fall in haemoglobin level and need for blood transfusion.

In all the participants hysterectomy was performed by the equally competent surgical team. The haemostatic technique during surgery other than tranexamic acid was done by diathermy coagulation and conventional sutures ligation, using vicryl sutures. Routine method of blood loss estimation was used in both groups.

2.4. Blood loss estimation

In our institute The following method of blood loss estimation is routinely followed in all cases and intraoperatively blood loss is mentioned in patients case record.

1. Intraoperative blood loss was measured by combined blood drained in suction bottle and by weighing soiled mops.
2. Preoperatively, Under all aseptic precautions all surgical Drapes and sponges were weighed.
3. After surgery, all blood soaked drapes, sponges and gauze were weighed again in an electronic weighing machine. In cases of vaginal hysterectomy the tray in which blood is collected during surgery is weighed before and after the surgery. Difference in weight was noted.
4. 1mg weight was taken equivalent to 1ml of blood. Blood loss during surgery was measured as follows.
5. Amount of blood loss (ml) = (weight of sponges, pads and drapes after surgery – weight of sponges, pads and drapes prior to surgery) + amount of blood collected in suction container.

2.5. Statistical analysis

Quantitative parameters were performed using unpaired t-test whereas qualitative parameters are compared using Chi square test.

Data are shown as mean \pm standard deviation and in absolute numbers or percentages. $p < 0.05$ was considered statistically significant.

3. Results

In this study both groups i.e TXA group and Non TXA group were found to be comparable with respect to various demographic features like age, height and weight (Table 1).

The preoperative parameters like haemoglobin, platelet count, coagulation profile and history of prior abdominal surgery were also similar in both the groups. In each group indications for hysterectomy were also similar with almost comparable number of patients (Table 2). Thus, the preoperative patient characteristics in both the groups were similar and comparable.

Table 1: Demographic and preoperative characteristics of patients

Characteristics	Group 1- received TXA	Group 2 Not received TXA
Age (yrs)	49.05 \pm 4.48	49.70 \pm 6.2
Height (cms)	143.14 \pm 6.2	144.34 \pm 6.9
Weight (kg)	50.42 \pm 5.7	51.52 \pm 8.5
Preoperative Hb (gm%)	11.52 \pm 1.83	11.74 \pm 0.52
History of prior abdominal surgery (%)	11	10

Chi square test was applied for statistical analysis of these factors and p value was < 0.05 . Hence both the groups were comparable with respect to preoperative features.

Table 2: Indications of hysterectomy in both groups.

Indication of hysterectomy	Group 1 (%)	Group 2 (%)
Uterine fibroid	22	25
Adenomyosis	12	10
AUB	16	20
PROLAPSE	36	34
CHRONIC PID	12	11

Chi square statistics is 0.8983, the p value is 0.92481 so the result is not significant at p value < 0.05 .

The blood loss estimated in group 1 and group 2 were 412.18 \pm 103.1 ml and 585.22 \pm 138.9 ml respectively. Thus, there was a significant reduction in mean blood loss in group 1 when compared to group 2 and the difference was statistically significant with p value < 0.05 (0.000) at 95% confidence interval and 5% alpha error. Statistical analysis was done using unpaired t test. There was significant fall in postoperative haemoglobin level in patients who had not received tranexamic acid injection during surgery.

In Group one, 2% patients required single unit of PRBC transfusion compared to 6% patients in Group 2 and it was statistically significant ($p < 0.05$).

The postoperative haemoglobin measured at 24 hours postoperatively was significantly lower in group 2 (9.44 \pm 0.22 g/dL) when compared to group 1 (10.78 \pm 0.54 g/dL). Fall in haemoglobin was statistically significant in group 2 compared to group 1 with p value 0.000 using unpaired t test method of statistical analysis.

The operating time was also significantly shorter in group 1 compared to group 2 (102.86 versus 138.64 minutes) and this was statistically significant with p value < 0.05 . Also patients in group 1 had lesser hospital stay as compared to patients in group 2 (6.32 days vs 8.59 days) which came out to be statistically significant. Postoperative complications were significantly less in group 1 compared to group 2 (Table 3), which was also statistically significant with p value < 0.05 .

Table 3:

Outcome	Group 1	Group 2	P value
Blood loss	412.18±103.1ml	585.22 138.9ml	<0.05
Postoperative Hb (gm/dL)	10.78±0.54	9.44±0.22g	<0.05
Mean Operating time	102.86 min	138.64 min	<0.05
Mean Duration of hospital stay	6.32 days	8.59 days	<0.05
Need for blood transfusion	2 patients	6 patients	<0.05

Minor adverse effects like gastric disturbances, nausea, vomiting were noted in both the groups thus not contributing to the minor side effect of TXA. No major adverse effects were observed in both groups post operatively.

4. Discussion

Over a period of years it has been noted that, the anaemia has shown a significant rise from 51.3% to 56.1% among Indian women. This corresponded to a 1.11-fold increase in anaemia prevalence after adjustment for age and parity.¹⁰ With burden of anaemia so high in our country, it can be assumed that major portion of women undergoing hysterectomy are already suffering from anaemia and they have borderline haemoglobin status, heavy menstrual bleeding further adds to increase risk of anaemia in them. Such women are at greater risk of postoperative morbidity because they cannot tolerate even small volume blood loss as occurring during surgery. Due to these reasons there is a need to adopt some prophylactic measures to reduce blood loss during hysterectomy.

Use of prophylactic antifibrinolytic drug like tranexamic acid as intravenous injection just before surgery can be adopted as one of the conservative approach to reduce blood loss during hysterectomy.

The naturally occurring serine protease inhibitor Aprotinin, the synthetic protease inhibitor Nafamostat and the synthetic lysine analogues EACA and tranexamic acid are some of the antifibrinolytic agents.⁹ Tranexamic acid being an antifibrinolytic agent acts by blocking the lysine binding sites reversibly on plasminogen molecule and hence preventing degradation of clot. It competitively inhibits plasminogen activation. Efficacy of tranexamic acid as antifibrinolytic agent is more in peripheral tissues with a longer half life of 3.1 hours compared to other synthetic analogues of lysine.⁶ It can be administered by oral, topical or parenteral route. Its onset of action after intravenous administration is 5-15 minutes and oral bioavailability ranges from 30-50%. Excretion of tranexamic acid is principally by the kidneys. Its absolute contraindications are hypersensitivity to the drug, history of or pre-existing active thromboembolic disorder, disseminated intravascular

coagulation, renal dysfunction, history of coronary or vascular stent placed within one year, acquired defective colour vision and acute subarachnoid haemorrhage. Relative contraindications include uncontrolled seizure disorder, renal dysfunction, high risk of venous or arterial thrombosis, or pre-existing coagulopathy or anticoagulant treatment.¹¹ Over a period of time various studies had been carried out to know the effect of tranexamic acid as a prophylactic measure in reducing blood loss during surgery and hence reduced need for blood transfusion. Ker et al in a systematic review of randomized clinical trials on the effectiveness of tranexamic acid on reducing surgical blood loss had revealed that it decreases need of blood transfusion by 38%.¹²

In this study we also observed a significant reduction in perioperative blood loss by giving dose of 1gm Intravenous injection of tranexamic acid during surgery (412ml vs 585ml). Similar results were observed by Topsoe et al in their study on effects of prophylactic tranexamic acid treatment in patients undergoing benign hysterectomy.² Shaaban et al in their study on the efficacy of TXA in reducing blood loss in patients undergoing open myomectomy has also obtained similar results. Need for blood transfusion was also less in TXA treated group (2% vs 6%)¹³ Celebi et al. had observed 30% reduction in the amount of preoperative bleeding with use of TXA for decreasing the need for blood transfusion in gynaecological cancer surgery, avoiding the negative effects of blood transfusions.¹⁴ Although the blood loss in vaginal hysterectomy is less compared to abdominal hysterectomy but in this study both groups have almost equal number of patients undergoing vaginal hysterectomy, so it will not affect our final results.

The reduction in blood loss have contributed in lowering operating time in tranexamic acid group by providing clear operating field and better haemostasis thus reducing the operating time (102.86 minutes vs 138.64 minutes). As far as cost-effectiveness is concerned, use of TXA is definitely more cost effective compared to blood transfusion. The incidence of postoperative complications like delayed wound healing and recovery were minimal in TXA treated group also reduces the cost of surgery.

Minor side effects like nausea, vomiting, diarrhoea, dyspepsia and headache were noted in few patients of TXA treated group but no incidences of thromboembolic events occurred in any of the patient. Similar results were obtained by Topsoe et al. and Shady NW et al. in their studies. Similarly, despite the fact that malignancy is a hyper coagulable state, Gupta et al. and Lundin ES et al. in their study on efficacy of TXA in cancer surgery had revealed no significant incidence of major adverse events.^{15,16}

5. Conclusion

Our findings conclude that TXA should be considered as prophylactic treatment prior to elective benign hysterectomy in order to reduce the risk of substantial bleeding and need for blood transfusion, early recovery and less hospital stay. It is especially helpful in developing countries like India where there is already a huge burden of anaemia and limited resources. With proper consideration of contraindications of TXA, it can be used safely in elective gynaecological surgeries. Further large scale trial for prophylactic use of TXA is needed for effective utilisation of it.

6. Source of Funding

None.

7. Conflict of Interest

The authors declare that there is no conflict of interest.

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