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Prophylactic Tranexamic Acid on Blood Conservation in Women Undergoing Abdominal Hysterectomy: A Comparative Study

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Abstract: ***Background:*** Hysterectomy, the second most common surgery for women, addresses issues like severe pelvic pain, irregular bleeding, and cancer, often for those unresponsive to medication or not planning more children. It can be performed abdominally, vaginally, or laparoscopically, with abdominal procedures being the most common worldwide. Blood loss is a significant risk, especially for those with anemia or heart disease. Tranexamic acid (TA) and other antifibrinolytics help reduce bleeding, though side effects like nausea and, in severe cases, hypotension can occur. ***Aim of the study:*** This study aims to evaluate the effect of prophylactic tranexamic acid on blood conservation in women undergoing abdominal hysterectomy. ***Methods:*** In this prospective comparative study at the Department of Obstetrics and Gynaecology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh., over one year from June 2017 to July 2018, 124 women undergoing abdominal hysterectomy were randomized into two groups: Group A (n=62), receiving tranexamic acid (TXA), and Group B (n=62), receiving a normal saline placebo. The study aimed to evaluate TXA's effect on blood loss, which was measured using the gravimetric method and hemoglobin levels 24 hours post-surgery. All patients underwent preoperative evaluation and postoperative monitoring for adverse events, including daily Doppler ultrasound for deep vein thrombosis (DVT) detection. Blood transfusion requirements and surgery duration were also assessed across both groups. ***Result:*** Group A (TXA) had a mean age of 37.68 years and required perioperative blood transfusions in only 11.29%, while Group B (placebo) had a mean age of 41.52 years and required transfusions in 41.94% (P=0.0007). Estimated blood loss was significantly lower in Group A (361.65±106.3 mL) compared to Group B (538.21±123.6 mL). Group A also had a shorter surgery duration (125.84±16.38 minutes vs. 146.74±15.37 minutes). The most common indication was fibromyoma (33.87% Group A, 41.94% Group B), with no significant differences in adverse events across groups. ***Conclusion:*** This study shows that prophylactic TXA significantly decreases blood loss and transfusion needs in abdominal hysterectomy without added adverse effects. The TXA group had lower blood loss, shorter surgery time, and fewer transfusions than the placebo group, supporting TXA's efficacy and safety as a cost-effective blood conservation method.

Keywords: Prophylactic Tranexamic Acid, Blood Conservation and Abdominal Hysterectomy.

INTRODUCTION

A total hysterectomy involves the removal of both the uterus and cervix. The ovaries and fallopian tubes (adnexae) may or may not be removed as part of the procedure. In contrast, a supracervical or subtotal hysterectomy leaves the cervix intact [1]. Hysterectomy is the second most common major surgical procedure performed on women worldwide, surpassed only by cesarean section [2]. It is estimated that about 33% of women undergo a hysterectomy during their lifetime [3]. Hysterectomy is mostly required in women aged 40-49 years [4]. These procedures can be performed using one of three main approaches:

abdominal hysterectomy (AH), vaginal hysterectomy (VH) or laparoscopic hysterectomy (LH) [1]. The approach is determined by the surgeon's preference, the reason for the surgery, the nature of the condition, and the patient's characteristics [5]. Worldwide, most of the hysterectomies are performed abdominally [6]. Problems such as severe pelvic pain, heavy and irregular menstrual bleeding, or uterine cancer are some cases that sometimes leave no choice but to remove the uterus through surgery [4]. A hysterectomy is performed to treat certain gynecological conditions that have not responded adequately to medication. It may also be a preferred option for women who no longer plan to have children or wish to avoid ineffective and repeated treatments for issues such as uterine fibroids, uterine prolapse, cervical dysplasia, menstrual irregularities, cancer, endometriosis, and endometrial hyperplasia [7,8]. Hysterectomy is often associated with significant perioperative blood loss, and some women may require a blood transfusion before surgery. The procedure impacts the coagulation system, and due to the increased release of plasminogen activator inhibitor, the fibrinolytic system becomes suppressed, leading to coagulopathy and an increased risk of bleeding [9]. A healthy woman can generally tolerate blood loss of up to 1000 mL with minimal impact on her health. However, for a woman with severe anemia or cardiovascular disease, even a blood loss as small as 200 mL can be life-threatening and may necessitate immediate medical intervention [10]. Blood products are a limited resource and come with certain risks. To reduce the need for transfusions, several blood conservation strategies should be implemented. Antifibrinolytic agents, such as Tranexamic acid (TXA), Epsilon amino caproic acid (EACA), and Aprotinin, have been shown to effectively decrease blood loss and transfusion needs in various elective surgeries [11]. Tranexamic acid (TA) is an antifibrinolytic agent approved for the treatment of various types of hemorrhage. It inhibits fibrin degradation, thereby promoting the blood's ability to form stable blood clots. In several countries, the drug is used as a prophylactic treatment prior to major surgery. In a Cochrane review addressing TA's efficacy in all types of surgery, a significant reduction of bleeding was found, corresponding to a mean of 414 mL [12]. Similar results have been found within traumatology [13]. Nausea, diarrhea, headache, sinus and nasal symptoms, back pain, abdominal pain, muscle aches, anemia and fatigue are some of its complications. Side effects of this drug include visual disturbances, hypotension and anaphylaxis in case of rapid injection, nausea and vomiting and diarrhea [14]. The use of this drug in gynecological and obstetric surgeries has been widely debated, yet few studies have been conducted. This study aims to evaluate the effect of prophylactic tranexamic acid on blood conservation in women undergoing abdominal hysterectomy.

METHODOLOGY & MATERIALS

A prospective comparative study was conducted with 124 patients scheduled for abdominal hysterectomy. The study took place in the Department of Obstetrics and Gynaecology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh., over one year from June 2017 to July 2018. Patients were randomly divided into two groups using a sealed-envelope method:

- **Group A (N = 62):** Tranexamic acid (TXA) group
- **Group B (N = 62):** Placebo group (normal saline)

Inclusion Criteria

- Women aged 18 years and above
- ASA physical status ≤3
- Indications for abdominal hysterectomy included benign conditions such as dysfunctional uterine bleeding, uterine fibroids, adenomyosis, pelvic inflammatory disease, adnexal masses, or endometriosis
- Hysterectomy procedures combined with unilateral/bilateral salpingectomy or oophorectomy, ovarian cystectomy, appendectomy, or cystoscopy

Exclusion Criteria

- Known allergy to TXA
- History of bleeding or clotting disorders, thromboembolism (such as deep vein thrombosis or pulmonary embolism), or recent anticoagulant use
- Existing cardiovascular or respiratory conditions, cancer, acquired color vision deficiency, preoperative liver or kidney issues, and any psychiatric or mental health disorder

Postoperative Assessment

Informed consent was obtained, and the institution's ethics committee grantedgrinstitution's clearance. Patients were transfused with packed red blood cells (PRBC) 48 hours before surgery to reach a hemoglobin level of ≥10 g/dL if required. Hemoglobin levels were also rechecked a day before the procedure. Preoperative evaluations included anesthesiology consultation and adherence to ASA fasting guidelines. Standard preoperative medications were administered, and upon arrival, ECG, pulse oximetry, and blood pressure monitoring were implemented.

The TXA group (Group A) received a 15 mg/kg dose of TXA in a 100 mL saline solution intravenously 15 minutes before surgery. In contrast, the placebo group (Group B) received a similar saline solution without TXA.

Measurement of Blood Loss

Blood loss was quantified using the gravimetric method, where surgical drapes, sponges, and pads were weighed pre-and post-surgery. The blood loss calculation was as follows:

Total blood loss = [(post-surgery weight of materials) - (pre-surgery weight)] + blood collected in the suction container

Hemoglobin was measured again 24 hours after surgery, and patients were monitored for adverse effects, including daily Doppler ultrasound for three days to check for deep vein thrombosis (DVT). Additional postoperative metrics included blood transfusion needs and surgery duration.

Statistical Analysis

Data were organized into tables for clarity, and descriptions accompanied each table for easy interpretation. Analysis was conducted using SPSS (version 26), with quantitative variables analyzed through Student's, and qualitative variables compared using the Chi-square and Fisher's tests. A p-value of <0.05 was considered statistically significant.

RESULT

Regarding age distribution, there were no significant preoperative differences between Group A and Group B in age, height, weight, or BMI. Group A had a mean age of 37.68 years, height of 157.31 cm, weight of 56.6 kg, and BMI of 28.77, while Group B had corresponding values of 41.52 years, 153.36 cm, 59.67 kg, and 27.3 (Table 1). ASA classifications were similar, with 27.42% of Group A and 30.65% of Group B in ASA I, 58.06% and 53.23% in ASA II, and 14.52% and 16.13% in ASA III, respectively. Preoperative blood transfusions occurred in 27.42% of Group A and 33.87% of Group B. Both groups had comparable baseline systolic and diastolic blood pressure, preoperative hemoglobin, platelet count, prothrombin time, and activated partial thromboplastin time, all with P-values indicating no statistical significance (NS) (Table 2). The most common indication was fibromyoma, present in 33.87% of Group A and 41.94% of Group B. Dysfunctional uterine bleeding was seen in 32.26% of Group A and 22.58% of Group B. Other indications included adenomyosis (8.06% vs. 9.68%), pelvic inflammatory disease (14.52% vs. 19.35%), adnexal mass (9.68% vs. 6.45%), and endometriosis (1.61% vs. 0%), with all differences being statistically non-significant (Table 3). Table 4 shows that Group A exhibited significantly better outcomes in blood conservation compared to Group B. Perioperative blood transfusion was required in only 11.29% of Group A versus 41.94% in Group B (P=0.0007). Group A also had lower estimated blood loss (361.65±106.3 mL vs. 538.21±123.6 mL) and shorter surgery duration (125.84±16.38 minutes vs. 146.74±15.37 minutes) (Table 4). This study found no significant differences in adverse events between the two groups. Nausea was reported in 11.29% of Group A and 6.45% of Group B, while both groups had an equal incidence of vomiting (1.61%), diarrhea (1.61%), and no cases of serious complications (Table 5).

Table 1: Demographic characteristics of the study population

Variables	Group A (N=62)	Group B (N=62)	P-value
	Mean±SD		
Age (years)	37.68±7.27	41.52±4.216	NS
Height (cms)	157.31±3.43	153.36±7.63	NS
Weight (Kg)	56.6±12.8	59.67±9.8	NS
BMI (kg/m^2)	28.77±2.63	27.3±4.27	NS

S: Significancy, NS: Non-significancy

Table 2: Preoperative clinical features of the study population

Variables	Group A (N=62)		Group B (N=62)		P-value
	N	%	N	%	
	Mean±SD		Mean±SD		
ASA I	17	27.42	19	30.65	NS
ASA II	36	58.06	33	53.23	NS
ASA III	9	14.52	10	16.13	NS
Preoperative blood transfusion	17	27.42	21	33.87	NS
Baseline Systolic blood pressure (mmHg)	126.74±13.32		124.04±11.55		NS
Baseline Diastolic blood pressure (mmHg)	80.33±9.53		80.654±6.05		NS
Preop Hemoglobin (g/dL)	10.5±1.43		10.08±1.45		NS
Platelet count (x10^3/µL)	246.4±39.41		239.78±37.75		NS
Prothrombin time (sec)	11.3±1.54		11.38±1.64		NS
Activated partial Thromboplastin time (sec)	35.88±0.06		32.54±3.08		NS

Table 3: Indications for abdominal hysterectomy

Variables	Group A (N=62)		Group B (N=62)		P-value
	N	%	N	%	
Fibromyoma	21	33.87	26	41.94	NS
Adenomyosis	5	8.06	6	9.68	NS
Dysfunctional uterine bleeding	20	32.26	14	22.58	NS
Endometriosis	1	1.61	0	0.00	NS
Pelvic inflammatory disease	9	14.52	12	19.35	NS
Adnexal mass	6	9.68	4	6.45	NS

Table 4: Outcomes of the study population

Variables	Group A (N=62)	Group B (N=62)	P-value
	Mean±SD	Mean±SD	
Perioperative Blood transfusion n (%)	7(11.29%)	26(41.94%)	0.0007 S
Estimated blood loss (mL)	361.65±106.3	538.21±123.6	<0.00001 S
Postoperative hemoglobin (g/dL)	8.21±1.48	8.24±1.42	<0.00001 S
Duration of surgery (minutes)	125.84±16.38	146.74±15.37	<0.00001 S

Table 5: Incidence of adverse events among patients

Variables	Group A (N=62)		Group B (N=62)		P-value
	N	%	N	%	
Nausea	7	11.29	4	6.45	NS
Vomiting	1	1.61	1	1.61	NS
Diarrhoea	1	1.61	1	1.61	NS
Thromboembolic phenomena	0	0	0	0	NS
Seizures	0	0	0	0	NS
Visual disturbances	0	0	0	0	NS

DISCUSSION

Abdominal hysterectomy is a common surgical procedure for various gynecological conditions, but it can lead to significant perioperative blood loss, resulting in complications such as anemia and prolonged hospitalization. To address this issue, blood conservation strategies, including the use of antifibrinolytic agents like TXA, have gained attention for their ability to reduce bleeding. While TXA has shown efficacy in various surgical contexts, its specific application in gynecological surgeries remains under-researched. This observational study aims to assess the impact of prophylactic TXA on blood conservation in women undergoing abdominal hysterectomy, ultimately enhancing surgical outcomes and patient safety. We know that hysterectomy is frequent in women 40-49 years old, and sometimes there is no way to treat them other than surgical removal of the uterus [4]. In this study, the mean age of patients was 37.68 years for Group A and 41.52 years for Group B. Our study is comparable with the observation of Menaka et al. [15]. No significant differences between the groups, with Group A having a mean height of 157.31 cm and a mean weight of 56.6 kg, compared to Group B, which had a mean height of 153.36 cm and a mean weight of 59.67 kg. These findings are similar to the results of Nivedhana et al. [16]. The BMI, which serves as an indicator of body composition, was also comparable between the two groups, with Group A having a mean BMI of 28.77 kg/m² and Group B having a mean BMI of 27.3 kg/m². Almassinokiani et al. found a mean BMI of 27.973 kg/m² and 28.025 kg/m² for the intervention group and control group, respectively [14]. ASA classification showed similar distributions of ASA I, II, and III between the groups. Other studies also investigated the ASA rate [14,16,17]. Preoperative blood transfusion was required in 27.42% of patients in Group A and 33.87% in Group B. Baseline systolic and diastolic blood pressure, hemoglobin levels, platelet counts, and coagulation markers (prothrombin and activated partial thromboplastin time) were also comparable between the two groups which are similar to other studies [14,16,17]. Fibromyoma, dysfunctional uterine bleeding, adenomyosis, pelvic inflammatory disease, and adnexal masses were common reasons for surgery in both groups. Endometriosis was noted only in Group A. Overall, the surgical indications showed no significant differences between the two groups. Menaka et al. found that AUB + Fibroid uterus was the most common indication of abdominal hysterectomy [15]. Other common causes in both groups were AUB and multiple fibroids. Another study also reported that fibromyoma, followed by Dysfunctional uterine bleeding, was the most common indication for abdominal hysterectomy [16]. Despite the finding that the placebo group received significantly more PRBC transfusions, the postoperative hemoglobin levels were significantly higher in the treated group when compared to the placebo. Shaaban et al. also reported significantly lower postoperative hemoglobin levels in the placebo group [19]. Though minor adverse events like nausea, vomiting, diarrhea, dyspepsia and headache were

common and transient, there are still some concerns regarding the safety of TXA use in view of risks like seizures, thromboembolic phenomena and visual disturbances [20]. In this study, the incidence of minor adverse effects like nausea, vomiting, and diarrhea was low and comparable between both groups. There was no incidence of major adverse events like seizures, thromboembolic phenomena and visual disturbances in both the groups. Topsoee et al. and Shady NW et al. also did not report any major adverse events in the TXA-treated patients [3,21]. Goswami et al., in their study on the effect of TXA on postpartum blood loss, had made an observation that in spite in spite of a 5-6 times higher incidence of thrombosis during pregnancy and puerperium, no increased risk of thrombosis was found [22]. Similarly, despite the fact that malignancy is a hypercoagulable state, Gupta et al. and Lundin ES et al., in their study on the efficacy of TXA in cancer surgery, revealed no significant incidence of major adverse events [23,24]. From the study's limitation, the observational design of the study restricts causal inferences regarding the effectiveness and safety of TXA in reducing blood loss for abdominal hysterectomy.

CONCLUSION

This study demonstrates that prophylactic administration of TXA significantly reduces blood loss and the need for blood transfusions in women undergoing abdominal hysterectomy. The TXA group experienced lower estimated blood loss, shorter surgery duration, and reduced transfusion rates compared to the placebo group, without increased adverse effects. These findings support TXA as a safe and effective blood conservation strategy in abdominal hysterectomy, improving surgical outcomes and potentially lowering healthcare costs by minimizing transfusion-related resources.

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