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Original Article

Tranexamic Acid in Reducing the Need for Blood Transfusion: A Prospective Randomized Controlled Trial.

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ABSTRACT

Background: Open abdominal myomectomy is associated with a significant risk of haemorrhage and blood transfusion. Tranexamic acid is a synthetic lysine derivative with antifibrinolytic activity used in Gynaecological and other surgical disciplines to reduce blood loss during surgery. However, its efficacy in reducing blood transfusion requirements when used as an adjunct to pericervical tourniquet has not been well elucidated. **Materials and Methods:** In a placebo-controlled trial, we assessed the effect of intravenous tranexamic acid when used as an adjunct haemostat with pericervical tourniquet on blood loss and transfusion requirements following open abdominal myomectomy in 132 women, aged 18–65 years. The patients were randomly allocated to receive either intravenous Tranexamic acid 1gm or placebo pre-operatively. The volume of intraoperative blood loss, blood transfusion rate and the total number of units transfused and the complications associated with the use of tranexamic acid were evaluated during the first 72 hours following surgery. **Results:** One hundred and thirty-one (131) patients completed the study. Patients who received tranexamic acid recorded a significantly reduced blood loss of 415.4 ± 173.2ml compared to the placebo group 807.5 ± 366.6ml ($p < 0.001$). Blood transfusion was significantly higher in the placebo group 47(72.3%) than in tranexamic acid group 6 (9.1%) ($p < 0.001$) with a statistically significant decrease in the mean postoperative haemoglobin in the placebo group 8.7 ± 1.9g/dl (median = 8.4, range = 4 – 12) compared to the tranexamic acid group 9.3 ± 1.1g/dl (median = 9.8, range = 7 – 11.5). There was no difference in the occurrence of complications between the groups. **Conclusion.** In patients who underwent open abdominal myomectomy tranexamic acid as an adjunct haemostat to pericervical tourniquet reduced blood loss and blood transfusion requirements with comparable side effects when compared to placebo.

Keywords: Uterine fibroid, Myomectomy, Blood transfusion, Blood loss, Tranexamic acid, Peri-cervical Tourniquet

INTRODUCTION

Haemorrhage during open abdominal myomectomy could be a great challenge as this increases the need for perioperative blood transfusion. [1,2] Allogenic blood transfusion is associated with an increased risk of immune reactions, disease transmission, postoperative infection and increased costs of care.[3,4] Tranexamic acid (TXA) is an antifibrinolytic agent that has been used to reduce intraoperative blood loss and transfusion requirements.[5] For women undergoing open abdominal surgeries reports are conflicting about the reduction in blood loss and transfusion requirement.[6-10] However in general, TXA appears to decrease perioperative blood loss and transfusion requirements. The use of pericervical tourniquet is considered standard practice and is commonly used by most gynaecologists during open abdominal myomectomy in Nigeria and my institution reduce blood loss[11,12,13] In a Cochrane-based study, several interventions to reduce blood loss have been explored and these include among other interventions, the use of antifibrinolytic agents, and peri-cervical tourniquet.[5] These studies concluded single agents versus placebo and none have utilized adjunct techniques against methods considered standard protocol in developing countries such as Nigeria that use a peri-cervical tourniquet to reduce blood loss. Compared to other forms of pharmacological interventions such as Vasopressin and GoRH analogues, Tranexamic acid is cheap and readily available [1, 11].This study sought to establish its effectiveness in reducing the need for allogeneic blood transfusion when used as an adjunct hemostat with peri-cervical tourniquet during open abdominal

MATERIAL AND METHOD

This was a prospective double-blind randomized placebo-controlled trial that assessed the effectiveness of Tranexamic acid in reducing the need for perioperative blood transfusion when used as an adjunct haemostat to pericervical tourniquet. The study was carried out in the gynaecological wards and main operating theatre suites at the University of Abuja Teaching Hospital following ethical approval by the hospital's Health Research Ethics Committee. Using a structured consent form written informed consent was obtained from all participants in the study. The data collected were treated as confidential.

The study population was drawn from patients aged 18-50years with American Society of Anesthesiologists (ASA) physical status classification 1 and 2 scheduled for elective open abdominal myomectomy with uterine size between 16 and 36 weeks. The study was double-blinded such that neither the patients nor the researcher was not aware of the medication the patient was receiving.

Randomization was undertaken by an investigator who is not the researcher and was not involved in patient evaluation. Other individuals involved in patients' care were also unaware of which treatment group the patient belonged to. Patients were randomly assigned to one of two study groups with the aid of computer-generated numbers. This was done and saved on the laptop of the research assistant. These numbers were written on small pieces of paper, folded and kept in an opaque sealed envelope. On entering the theatre patients made a pick of the folded paper containing the randomized number in the envelope to place them in a treatment group.

Tranexamic acid was prepared in the pharmacy by the pharmacist on demand as a clear colourless solution diluted to 20ml containing 1g of tranexamic acid in a normal saline solution thus making it indistinguishable from the 20ml normal saline placebo. This ensured blinding of the anaesthetist and data collector (the researcher). On picking a number of the patient from the brown envelope, the number was sent to the research assistant who generated the numbers to know the group patient belonged. This information was passed to the pharmacist for the appropriate drug constitution

Patients were recruited during the preoperative evaluation in the ward. Following the patient's eligibility, detailed information about the study was explained to the patient and written informed consent was signed by the patient. One hundred and thirty-two (132) ASA 1–2 consenting patients aged 18–50 years scheduled to undergo open abdominal myomectomy were enrolled on the study.

1. Treatment group; patients in this group received intravenous tranexamic acid 1g after securing the intravenous access in the theatre and 45 minutes before the commencement of the procedure(knife on the skin) to allow for the institution of the epidural block, cleaning and

draping of the patient and other preparation.

2. Placebo group; patients in this group received a placebo (20mL of normal saline) at the same time.

The exclusion criteria included: Patient refusal to have Regional Anaesthesia; Prior treatment using gonadotropin-releasing hormone analogue; Family history of bleeding disorder; Current use of anticoagulant; History of deep vein thrombosis; Previous uterine fibroid embolization; Repeat myomectomy; Hypersensitivity to local anaesthetic agents and study drug (TXA); Haemoglobin level of < 10g/dl; Platelet count of < 150,000 platelets per microliter of blood; Fixed cardiac output states; contra-indications to Regional anaesthesia; Mental impairment and psychiatric diseases; History of congestive heart failure; Valvular heart disease; Renal or hepatic disease and patients with a body mass index (BMI) > 35 kg/m^2 as obesity with excess fatty tissue at the back makes the institution of the epidural block technically more difficult. In addition obesity with excessive abdominal fat is a significant risk factor for more surgical bleeding and longer surgery time.

Pre-operatively all patients were seen by the same anaesthetist to determine fitness for elective surgery, rule out exclusion criteria, provide information to the patient on the perioperative course, and technique of anaesthesia and allay anxiety. Following the patient's eligibility, during the pre-anaesthetic review, the patient was given detailed information about the study and written informed consent was obtained. Any patients who subsequently withdrew their permission for the study for whatever reason were given the standard care for the procedure

Demographic data were obtained from the patients as well as the patient's case files and these included: age, weight, height, presenting symptoms and uterine size. Weight estimation was done in the ward during preoperative review using the weighing scale available in the ward. All data collected was recorded on a preformed data collection form. A review of the relevant laboratory investigations was done and these included full blood count and urinalysis. The preoperative haemogram and platelet count were also recorded. The patients were classified according to the ASA physical status classification and were counselled on the ASA preoperative fasting guidelines. Patients were placed on nil per os from 12minight or 6 hours before the scheduled surgery while sips of water were allowed until 2 hours before surgery. Acid aspiration prophylaxis was given to patients with uterine size >20 weeks using an anaesthesia standard dosing regimen of oral metoclopramide 10mg and ranitidine 150mg the night before and also 2 hours before the procedure. Patients with uterine size > 20 weeks are considered to have full stomachs despite observing the fasting guideline from increased intraabdominal pressure from the enlarged uterus. This predisposes them to acid aspiration pneumonitis. Thus acid aspiration prophylaxis is a standard precaution. For this group of patients who had Metoclopramide, it also served as prophylaxis for postoperative nausea and vomiting. Before the arrival of the patient in the theatre, a "cockpit" drill was done and preparation was made for both general and regional anaesthesia. Resuscitation drugs were also made available.

On arrival in the theatre, patients were connected to a multiparameter monitor (Texan 007) for heart rate, non-invasive arterial blood pressure (NIBP), respiratory rate, arterial oxygen saturation (SpO2) and electrocardiography (ECG) monitoring and baseline values recorded. Intravenous access with a 16-gauge cannula was secured and (15mL/kg) Normal saline solution was given to all patients before the procedure. Tranexamic acid was prepared in the pharmacy by the pharmacist on demand on the day of surgery as a clear colourless solution diluted to 20ml containing 1g of tranexamic acid in a normal saline solution thus making it indistinguishable from the 20ml normal saline placebo. Depending on the group the patient belonged to, tranexamic acid or placebo was administered 45minutes before the commencement of the procedure (knife on the skin). This time lag allowed for the institution of the epidural block, cleaning and draping of the patient other preparation and for standardization of the time of administering the drugs. The researcher anaesthetized all the patients. The anaesthetic procedure was standardized and all patients had combined spinal epidural block instituted at the level of L2/L3 or L3/L4. Three millilitres of 0.5% hyperbaric bupivacaine was injected for the subarachnoid block while an extradural catheter was left in place for the epidural drug injection.

A test dose of 3mL of 1.5% Lidocaine with adrenaline diluted with sterile water to 1:200000 solution (0.005mg/ml) was injected through the epidural catheter to ascertain both intravascular and subarachnoid placement of the

catheter. Epidural Anaesthesia was activated for 90minutes following the subarachnoid block with the administration of 16–20 mL in 5 mL aliquots of plain bupivacaine (5.6 mg/mL)). Additional boluses of 5 mL bupivacaine (5.6 mg/ml) were administered if there were signs of inadequate analgesia. A minimum interval of 30 min was observed between injections. Intraoperative vital signs were recorded every 5minutes. These include heart rate, blood pressure, arterial oxygen saturation and continuous electrocardiogram (ECG). The blood pressure was monitored every 2 minutes immediately after instituting the subarachnoid block for 15 minutes after the block, then every 5 minutes subsequently. Other intra-operative variables recorded included: the length of surgery; duration of Anaesthesia, no of fibroids enucleated, blood loss, no of units of blood transfused and anaesthetic and surgical complications. Hypotension defined as a systolic blood pressure less than 90mmHg was treated with Ephedrine in 3mg aliquots while bradycardia defined as a heart rate less than 60 beats/per minute was treated with atropine 0.01mg/kg intravenously. If required, metoclopramide (10 mg) was given for nausea. If this was ineffective, then ondansetron (4 mg) was given. All surgeries were performed by a Consultant Gynaecologist using a Foleys catheter as a tourniquet and applied to the base of the uterus. close to the insertion of the uterosacral ligaments. The tourniquet was released intermittently (at 30minutes intervals) during the surgery, reapplied after 2 minutes and finally removed after the repair of the uterus. Blood loss estimation was done by both volumetric (measuring the volumes in the cylinder and subtracting any other fluid used) and gravimetric (soaked swabs weighed by the electronic scale and blood loss estimated by subtracting the dry weight from the soaked weight and multiplied by 1.050 to convert to volume in mL). A blood transfusion was done following the loss of ≥ 20% of the patient's total blood volume or any blood loss causing a reduction in blood pressure of ≥ 20% from baseline and tachycardia of ≥ 20% of baseline values. A total number of units of blood transfused was noted. Side effects of tranexamic acid were monitored every 8 hours until 72hours postoperatively and managed if they occur. These included nausea, vomiting, diarrhoea and thrombosis (calf pain, oedema of the leg, superficial vein distension in calf, palpable cord on superficial veins in calf, chest pain, cough, haemoptysis and breathlessness). To ensure blinding, the postoperative assessment was not performed by the same physician who performed the pre-operative evaluation. At the end of the surgery, the epidural catheter was kept in place for 24hr for postoperative pain management. Subsequently, it was removed. Forty-eight hours postoperatively, blood was taken for postoperative haemoglobin estimation.
The main outcome measures for the study were the need for blood transfusion following the loss of ≥20% of the patient's total blood volume or any blood loss causing a reduction in blood pressure of ≥20% from baseline and tachycardia of ≥20% of baseline values, the total number of units of blood transfused, blood loss, and side effects of study drug (TXA) and complications resulting from TXA use.

RESULT

One hundred and thirty-one (131) patients completed the study; tranexamic acid group 66 and placebo group 65. One patient had an uncontrollable postoperative haemorrhage. This necessitated her having a total abdominal hysterectomy. She was thus disqualified from the study. This patient was later identified to be on the placebo. Baseline demographic and clinical characteristics of the women were comparable in the two groups for age, body mass index (BMI), uterine size and preoperative haemoglobin (Table 1).

Table 1: Demographic and clinical characteristics of the patients

	Group			
	Placebo Mean ±SD	Trane-xamic Mean ± SD	t-Stati-stic	p value
Age (years)	35.9±5.5	34.4±3.6	1.8153	0.072
BMI(Kg/m^2)	28.7±2.0	28.4±2.1	0.833	0.406
Uterine size	23.3±5.4	23.9±6.4	0.596	0.552
operative Hb	11.2±0.9	11.0±0.9	1.355	0.178

The mean age of the participants in the tranexamic acid group was 34.4±3.6 years and 35.9±5.5 years in the placebo group (p=0.072). The uterine size was comparable in both groups with the mean uterine size of 23.9±6.4 weeks in the tranexamic acid group and 23.3±5.4 weeks in the placebo group (p=0.552). The mean preoperative haemoglobin in the tranexamic acid group was 11.0±0.9 g/dl and in the placebo group

was 11.2±0.9g/dl (p=0.178). The mean baseline measurements of heart rate, mean arterial pressure, respiratory rate and arterial oxygen saturation (SPO2) were comparable in the two groups (p=0.767, 0.292, 0.962, 0.2123 respectively) [Table 2]. Also, the mean number of fibroids enucleated was comparable in the two groups, 14.8±9.3 and 15.5±6.1 in the placebo and tranexamic acid group respectively and this was not statistically significant (p=0.603) [Table 3]. Major blood loss > 1000 ml was recorded only among women in the placebo group [Table 4].

Table 2: Baseline haemodynamic variables

	Group			
	Placebo n=65 Mean ±SD	Tranexamic n=66 Mean ±SD	t-statistic	P-value
†SBP	123.9±9.6	124.5±9.0	0.355	0.723
†DBP(	73.6±4.5	72.2±1.7	2.296	0.024*
†MAPg)	92.4±5.0	91.6±2.8	1.054	0.292
***PR	72.5±3.0	72.6±3.1	0.298	0.767
**RR	14.0±1.9	14.0±1.9	0.044	0.965
SPO_2 (%)	98.4±0.8	98.3±0.8	1.251	0.213

Table 3: Mean number of fibroid enucleated from the two groups

	Group				
	Placebo n=65 Mean ±SD	Tranexamic n=66 Mean ±SD	Mean difference	t-statistic	P-value
No. of fibroid	14.8±9.3	15.5±6.1	0.716	0.519	0.603

Table 4: Comparison of intraoperative blood loss between the two groups

	Group				
Blood loss(ml)	Placebo n=65 n(%)	Tranexamic n=66 n(%)	Total n(%)	χ^2	P-value
< 500	11(16.9)	48(72.7)	59(45.0)	49.119	<0.001*
500-1000	32(49.2)	18(27.3)	50(38.2)		
>1000	22(33.8)	0	22(16.8)		
Blood loss (ml)	807.5±366.6¥	415.4±173.2¥	*na*	7.809¶	<0.001*
Range	350-1900	50-800			
Median	840	400			

There were 22 cases of excessive blood loss (>1000ml), and all of these were in the placebo group. There was a statistically significantly lower mean blood loss in the tranexamic acid group 415.4±173.2 (median=400, range=50–800 ml) compared to 807.5±366.6 (median=840, range 350–1900) ml in the placebo group (p < 0.001) [Table 4].Table 5 shows the need for blood transfusion in the two groups. The maximum number of blood units transfused in the placebo group was 4 units, compared to 1 unit in the tranexamic acid group. Amongst women in the placebo group, 21.4% received 2-4 units of blood while no woman in the tranexamic acid group required more than 1 unit of blood.

Table 5: Comparison of blood transfusion between the two groups

	Group				
	Placebo n=65 n(%)	Tranexamic n=66 n(%)	Total n(%)	χ^2	P-value
Need for Blood transfusion				54.328	<0.001*
Yes	47(72.3)	6(9.1)	53(40.5)		
No	18(27.7)	60(90.9)	78(59.5)		
Number of blood unit transfused					
0	18(27.7)	60(90.9)	78(59.5)	57.371	<0.001*
1	19(29.2)	6(9.1)	25(19.1)		
2-4	28(43.1)	0	28(21.4)		

Table 6: Comparison of mean duration of surgery between the two groups

	Group				
	Placebo n=65 Mean±SD	Tranexamic n=66 Mean±SD	Mean difference	t-statistic	P-value
Duration of surgery (minutes)	162.4±60.8	117.7±25.9	44.657	5.456	<0.001*

There was a statistically significant increase in the number of women who received a blood transfusion in the placebo group 47 (72.3%) compared to the tranexamic acid group 6 (9.1%) ($p < 0.001$) [Table 5, Figure III. The duration of surgery was noted to be longer in the placebo group 162.4 ± 60.8minutes compared to the tranexamic acid group 117.7 ± 25.9minutes ($p < 0.001$) as assessed by the t-test statistic [Table 6].

Table 7 shows the side effects of tranexamic acid assessed. Amongst the participants, 5 women complained of nausea, 3 (4.5%) in the tranexamic acid group and 2 (3.1%) in the placebo group (OR = 0.7, CI = 0.1 – 4.1) which was not statistically significant ($p = 0.661$). Also, 2 women vomited, 1 (1.5%) in the tranexamic acid group and 1 (1.5%) in the placebo group (OR = 1.0, CI = 0.1 – 16.6) which was not statistically significant. There was no incidence of the thromboembolic event noted in

DISCUSSION

This randomized placebo-controlled trial assessed the efficacy of intravenous tranexamic acid in reducing the need for perioperative blood transfusion when used as an adjunct haemostat to pericervical tourniquet during open abdominal myomectomy. Baseline demographic and clinical characteristics of the women were comparable in the two groups for age, body mass index (BMI), uterine size, the total number of fibroids enucleated and preoperative haemoglobin. The study shows that intravenous tranexamic acid reduced the volume of blood loss and the need for blood transfusion compared to placebo, amongst women undergoing open abdominal myomectomy. More women in the placebo group received a homologous blood transfusion and this was statistically significant. Amongst women in the placebo group, 21.4% received 2-4 units of blood while no woman in the tranexamic acid group required more than 1 unit of blood. Postoperative haemoglobin was higher among women that received intravenous tranexamic acid, compared to the placebo group. There was a drop in haemoglobin between pre and post-myomectomy in both groups, however, the reduction in haemoglobin was greater in the placebo group compared to the tranexamic acid group.

Though symptoms of nausea and vomiting (which necessitated the use of IV metoclopramide) were noted. There was no incidence of a thromboembolic event. Uterine fibroid which is a common reason for gynaecological consultation in most Nigerian hospitals is diagnosed in 25% of women of the reproductive age group.[14,15] This is reflected in

this study in which the women fell within the reproductive age group.

This study demonstrated a significantly lower blood transfusion rate among the tourniquet group. In addition, not only was the number of patients requiring transfusions less, the total number of transfusions required for each patient was significantly less in the tranexamic acid group compared to the control group. Seventy-two per cent (72%) of the women in the placebo group needed blood transfusion compared to nine per cent (9%) in the tranexamic acid group. Study participants who did not receive tranexamic acid during myomectomy had a significantly higher chance of being transfused than those who received tranexamic acid. This finding follows the trend observed in the literature that intravenous tranexamic acid reduces the need for blood transfusion during myomectomy when compared with a placebo.[1,9,16] In a randomized controlled trial on myomectomy-associated blood loss in patients with multiple myomas, Shaaban et al[7] found that the need for blood transfusion was significantly reduced in the tranexamic acid group 13 (19.7%) compared to the placebo group 23 (34.8%). In another randomized controlled trial on reducing blood loss during open myomectomy with intravenous versus topical tranexamic acid, Nahla et al[16] reported a transfusion rate of 6 (17.1%) in the intravenous tranexamic acid group compared to 19 (54.3%) in the placebo group. In addition, the transfusion rate in this present study was relatively high (40.5%) when compared to the studies by Nahla et al[16] and other cohorts of studies (Vargas, 5.8% minimally invasive myomectomy group, 13.8% abdominal myomectomy group; Shaaban, 27.3%; Sinha, 18.1%; and Zhao, 5.7%).[6,7,16] However, the criteria for blood transfusion were not stated in these studies for purposes of comparison and to ensure the standard. Despite guidelines from professional organizations, there are wide variations in blood transfusion practices among physicians as they fail to adhere to simple transfusion algorithms. Reasons for the lack of adherence to blood transfusion practice guidelines are multiple but stem mainly in part from a lack of agreement with guideline recommendations. Thus the overall use of allogeneic RBC transfusions in clinical practice remains relatively high and still varies widely among many centres and practitioners.[17, 18] There was also more blood loss in the placebo group in this study compared to the study by Shaaban et al[7]. This may have also contributed to more blood transfusion rate in the placebo group compared to the Shaaban et al[7] study. Considering the inherent dangers associated with blood transfusion, the cost and the scarcity of the product, techniques that limit the necessity for blood transfusions should be encouraged all the time.

Several techniques have been used to reduce the loss of blood during surgery. These include the use of Bonney's clamp, injection of vasopressin in the uterine muscle, pre-operative administration of GnRH analogue or misoprostol and the use of the tourniquet.[1] The tourniquet is by far the cheapest and most accessible for our environment. The conventional Foley's urethral catheter is easily adapted for this purpose.[1] All the participants in this study had pericervical tourniquet applications. This is standard practice in our institution. The use of a peri-cervical tourniquet as the Foley's catheter to occlude the uterine blood supply has been shown to reduce blood loss and blood transfusion requirements during myomectomy.[1,19,16] Considering the inherent dangers associated with blood transfusion, techniques that limit the necessity for blood transfusions such as the use of tourniquets should be encouraged. The use of a tourniquet helps to provide a clear operating field which is a cardinal principle of surgery. This is more so for myomectomies where haemorrhage is a major challenge. A clear and bloodless operating field allows the surgeon the opportunity to remove virtually every visible piece of fibroid and thus reduce the length of surgery. Myomectomy without uterine blood vessel occlusion results in so much haemorrhage that it is not recommended for uterine sizes greater than 12 weeks.[20] Using a combination of tranexamic acid plus tourniquet as was done in this study was more efficacious in reducing blood loss and blood transfusion when compared to studies that used only tranexamic acid. [9, 16]

Blood loss during myomectomy is primarily incurred while operating on the uterus and can be affected by factors like; uterine size, the number of fibroids removed, the rank of the surgeon and the technique of anaesthesia. [21-23] Thus, it was ensured that all surgeries were performed by a consultant gynaecologist using combined spinal epidural anaesthesia. The mean uterine size and number of fibroids enucleated in both groups were comparable. As a result, they had no effect on blood loss and blood transfusion in this study.

The efficacy of intravenous tranexamic acid as demonstrated in this study is per the results

of previous studies that compared intravenous tranexamic acid to placebo, reporting a lesser blood loss with tranexamic acid when compared to placebo.[7,8,19,16,24] The use of intravenous tranexamic acid resulted in less intraoperative blood loss, 415.4±173.2ml (median=400) in the tranexamic acid group compared with 807.5±355.6ml (median=840) in the placebo group. This is similar to the finding by Shaaban et al[7] in 2015 that evaluated the efficacy of tranexamic acid in reducing blood loss during and after open abdominal myomectomy for patients with three (3) or more uterine fibroids. The tranexamic acid group showed a lower amount of blood loss (407ml) when compared to the placebo group (677ml) with a p-value < 0.01. In the Shaaban et al[7] study treatment with tranexamic acid resulted in a decrease in the risk of perioperative blood loss by 40%. Similarly, two different studies by Nahla et al [16] and Caglar et al [9], found that intravenous tranexamic acid reduced blood loss during open abdominal myomectomy. In the study by Nahla et al[16], blood loss was noted to be less (721.71±211.78) in the group that received intravenous tranexamic acid compared to 1080±126.07 in the placebo group.[20] Similarly, in the study by Caglar et al[9], the authors reported that intravenous tranexamic acid decreased the perioperative blood loss during excision of myoma in the tranexamic acid group (804±482 ml) compared to the placebo group (1047±617 ml).[24] However, the volume of blood loss in the two studies above (both in the tranexamic acid and placebo group) is higher when compared to the finding of this present study. This is probably due to the application of peri-cervical tourniquet in both groups in this present study. The use of a pericervical tourniquet is a common practice in our institution. [11] The use of a pericervical tourniquet as the Foley's catheter to occlude the uterine blood supply has been shown to reduce blood loss during myomectomy.[1,19] Also, myomectomy without uterine blood vessel occlusion results in so much haemorrhage that it is not recommended for uterine sizes greater than 12 weeks.[20]

The duration of surgery was noted to be longer in the placebo group 162.4 ± 60.8minutes with higher blood loss compared to the tranexamic acid group 117.7 ± 25.9minutes (p < 0.001) as assessed by the t-test statistic. Our finding is similar to that of Shanthini et al[25] that evaluated the complications of abdominal and anaesthesia, and deliver postoperative analgesia. It is thus valuable in our environment where vaginal hysterectomy suggesting a possible association between blood loss and duration of surgery. On the contrary, most studies indicate that there is no association between blood loss and the duration of surgery as seen in our study.[12, 25,26] Intraoperative blood loss during open abdominal myomectomy varies, depending on the uterine size, number and location of myoma, skill of the surgeon, technique of anaesthesia and duration of surgery[12] Multiple fibroids, in more than one location (intramural, subserous, submucous) cause surgeons to spend more time thus resulting in more blood loss irrespective of the size of the fibroid. Though the mean number of fibroid enucleated in both groups was similar, their sizes and weight were not recorded and compared. The difference in the sizes and weight of the fibroids in both groups may have been responsible for the difference in the duration of surgery between the placebo and the Tranexamic acid group.

Five (5) women complained of nausea, 3 (4.5%) in the tranexamic acid group and 2 (3.1%) in the placebo group (OR=1.0, CI=0.1–16.6) but this was not statistically significant (p=0.661).). Also, two (2) women vomited, 1 (1.5%) in the tranexamic acid group and 1 (1.5%) in the placebo group (OR=1.0, CI=0.1–16.6). This was also not statistically significant. These symptoms were treated with 10mg of metoclopramide administered intravenously. There was no incidence of the thromboembolic event noted in any of the women in this study. In a randomized control trial on reducing blood loss during open myomectomy with intravenous versus topical tranexamic acid, Nahla et al[16] reported side effects of nausea, vomiting and diarrhoea. However similar to the findings in this study, these were not statistically significant (p=0.102, 0.87 and 1.00). There was also no incidence of a thromboembolic event. Although tranexamic acid administration has shown a risk for a complication like thrombosis and an embolism due to its antifibrinolytic effect, thromboembolic events were not reported in most of the studies.[7, 9,16]

All surgeries were done using the combined spinal epidural technique (CSE) to ensure uniformity of the anaesthetic technique. The use of CSE combines the benefit of rapidity, density, and reliability (definitive endpoint with the appearance of cerebrospinal fluid) that is characteristic of single-shot spinal anaesthesia with the flexibility of continuous epidural to vary the intensity of the block, control the duration of patients present late with huge uterine fibroid, refuse hysterectomy and have increased chances

of surgery being prolonged.[27] Evidence is also in favour of better perioperative outcomes with RA compared with GA in terms of deep vein thrombosis, myocardial events, and pulmonary complications. The CSE technique is safe, and cost-effective with minimal perioperative complications and can be used in resource-limited environments such as ours for abdominal myomectomy. Compared to general anaesthesia, the gauze and abdominal packs used for the study were weighed with a Digital Electronic Kitchen weighing scale before sterilization. This weighing scale is built to provide fast, stable and error-free weighing results.) and thus help reduce errors due

Strengths

This study has several strengths. Firstly the study design used was a randomized placebo-controlled trial according to the CONSORT statement. The study was also double-blinded such that neither the patients nor the researcher was not aware of the medication the patient was receiving Secondlythe surgeon, principal investigator and anaesthesiologists undertaking the procedure in the theatre were blinded to the intervention hence eliminating potential bias in theatre. Thirdly all surgeries were performed by fellowship-trained gynaecologists to ensure uniformity and thus eliminate bias imposed by the surgeon's experience and thus minimize the influence of skill. Lastly, the intraoperative anaesthetic technique was the same for all patients and this was the combined spinal epidural (CSE) anaesthetic technique. This eliminates the effect of the anaesthetic technique on blood loss and transfusion requirements. Blood loss is known to be less with regional compared to general anaesthesia.[29].

it is associated with reduced perioperative blood loss and blood transfusion requirement.[28, 29].

Limitation

The limitations of our study include the fact that the estimations of blood loss are often not precise; however, we used fairly objective methods (use of pre-weighed surgical mops and gauze.[2630] All

to this. Secondly, Long term complications also need to be documented with good patient follow-up.

CONCLUSION

Our current result suggests that TXA can effectively decrease the intraoperative volumes of blood loss and transfusion requirements with acceptable side effect when used as an adjunct hemostat to pericervical tourniquet in patients undergoing abdominal myomectomy. The Foley's catheter form of tourniquet is cheap, safe, readily available and effectively reduces blood loss and transfusion rates during myomectomy while not adding to the complications due to the operation. The percentage contribution of each method to blood loss reduction was not assessed in this study. This should be the subject of another study.

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