

Original Research

Effectiveness of the use of intravenous tranexamic acid and pericervical tourniquet in decreasing peri-operative blood loss following open abdominal myomectomy: A randomized controlled trial.

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Abstract

Background: Uterine fibroid is the most common gynaecological tumour, with a prevalence of 20% to 50% of women over 30 years. Abnormal uterine bleeding is one of the most common modes of presentation with menorrhagia. Open abdominal myomectomy is the most common treatment option in our environment. It is associated with a significant degree of blood loss, with consequent blood transfusion. Thus, the need for interventions to reduce blood loss during the procedure. This study assessed the effectiveness of intravenous tranexamic acid in reducing blood loss when used as an adjunct to peri-cervical tourniquet during open abdominal myomectomy.

Methodology: This study was conducted at Barau Dikko Teaching Hospital, Kaduna. It comprised thirty-six consenting patients scheduled for elective open abdominal myomectomy, randomly assigned to receive either intravenous tranexamic acid or placebo immediately after securing intravenous access in the theatre. All the patients had a peri-cervical tourniquet applied intraoperatively. The volume of intraoperative blood loss, blood transfusion rate and the total number of units transfused, haemodynamic changes associated with blood loss, and the complications associated with the use of tranexamic acid were evaluated during the first 72 hours following the surgery.

Results: A total of thirty-six women who met the eligibility criteria were studied between June 2023 and December 2023. The mean age of the participants in the tranexamic acid group was 37.82 ± 5.89 years and 39.74 ± 5.17 years in the placebo group ($p = 0.307$). Most of the women 35 (97.2%) presented with symptoms of menorrhagia. Major blood loss > 1000 ml was recorded more among women in the placebo group than those who received tranexamic acid. There was a statistically significant reduction in the mean blood loss in the tranexamic acid group 947.65 ± 451.88 compared to 1320.53 ± 563.28 . ($p = 0.037$).

There was an increase in the number of women who received a blood transfusion in the placebo group 7 (36.8%) compared to the tranexamic acid group 4 (23.5%) ($p = 0.387$). Tranexamic acid resulted in a decrease in the risk of perioperative blood loss by 30%, RR 0.7 95% CI (2.19-2.59) and packed cell volume was significantly lower in the control group postoperatively (P value = .001). There was no significant side effect noticed in both groups.

Conclusion: Tranexamic acid reduces blood loss during and after myomectomy for patients with uterine fibroids and the need for blood transfusion is reduced in patients who had intravenous tranexamic acid as an adjunct to the application of a tourniquet.

Keywords: Tranexamic Acid; Blood Loss; Abdominal Myomectomy.

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Introduction

Uterine fibroid, also called uterine leiomyoma, or simply myoma is a benign tumor of the uterus. It is the commonest neoplasia of the uterus and autopsy studies indicate that between 20-50% of women over 30years old have uterine fibroids of various sizes.¹ The commonest presenting symptom is abnormal uterine bleeding, with heavy and prolonged bleeding.^{2,3} Women with myomas are more likely to report a “gushing” type of bleeding and higher tampon use than women without myomas.⁴

Management of uterine fibroid can be medical or surgical. Options for surgical treatment include hysterectomy and myomectomy which can be carried out via hysteroscopy, laparoscopy, or as an open abdominal procedure with open abdominal myomectomy being the most used procedure especially when conservation of the uterus is desired.^{1,5}

Hemorrhage during myomectomy could be a great challenge as this increases the need for perioperative blood transfusion.^{5,7,8} In a study of 91 women who underwent open abdominal myomectomy for uterine size greater than 16 weeks, the operative blood loss ranged between 50 to 3000 ml and 12% of the women were transfused with homologous blood.⁹ A similar study on 58 women also reported blood loss of 159 to 2500mL while 12.8% of the women received homologous blood transfusion.⁷

In a Cochrane review, several interventions to reduce blood loss have been explored and these include the use of vasopressin analogues, antifibrinolytic agents, gonadotrophin-releasing hormone analogues, oxytocin, misoprostol, and peri-cervical tourniquet.^{2,13} This study has drawn conclusions from a single agent versus placebo and none has utilized adjunct techniques against methods considered standard protocol in developing countries such as Nigeria that mainly use peri-cervical tourniquets to reduce blood loss. In addition, Peri-cervical tourniquets are always used to avoid blood loss and are considered standard practice by most gynaecologists during open abdominal myomectomy at Barau Dikko Teaching Hospital.

Tranexamic acid (TA), is an antifibrinolytic agent that reversibly inhibits the activation of plasminogen, thus inhibiting fibrinolysis and reducing bleeding. Tranexamic acid is a synthetic derivative of the amino acid lysine that exerts its anti-fibrinolytic effect through the reversible blockade of lysine binding sites on plasminogen molecules thereby reducing blood loss.³⁰ TA has been used to reduce blood loss and the need for homologous blood transfusion in cardiac surgery, liver transplantation, and orthopaedic surgical procedures.¹⁴ It is cheap and readily available.

This study seeks to establish its effectiveness in further reducing blood loss when used along with a peri-cervical tourniquet during open abdominal myomectomy.

Purpose of the study

To determine the effectiveness of intravenous tranexamic acid in reducing blood loss when used as an adjunct to peri-cervical tourniquet during open abdominal myomectomy; To determine the volume of blood loss during open abdominal myomectomy; with the addition of tranexamic acid as an adjunct to peri-cervical tourniquet and with peri-cervical tourniquet alone; To determine blood transfusion rate and the total number of units transfused with the addition of tranexamic acid as an adjunct to peri-cervical tourniquet and with peri-cervical tourniquet alone; To determine the hemodynamic changes associated with blood loss in the 2 groups and To determine the side effects associated with the use of tranexamic acid.

Methodology

This was a double-blind randomized placebo-controlled study [RCT Number; Cochrane South Africa PACTR202404508588938] conducted at Barau Dikko Teaching Hospital Kaduna. Patients were recruited

from the gynaecology clinic into the ward prior to surgery. The study population involved patients aged 18-50years scheduled for elective open abdominal myomectomy with uterine size between 12 and 24 weeks at Barau Dikko Teaching Hospital. This population was chosen because patients with uterine size greater than 24weeks may require general anesthesia which can interfere with blood loss. Patients with recurrent fibroids, bleeding disorders-morbidities, or previous pelvic surgeries were excluded.

Research tools/materials: All the gauze and abdominal packs used for the study were prepared by the researcher and weighed with a Digital Detecto brand of electronic Kitchen weighing scale before sterilization. This weighing scale is built to provide fast, stable, and error-free weighing results.

Sample size determination.

The formula for calculating sample size for randomized control trial, for one-tailed superiority trial i.e. use of both tourniquet and TXA, will be used.³².

$$N = \frac{(Z\alpha+Z\beta)^2P(1-P)}{(P_T-P_S)^2}$$

assuming a 95% confidence interval,

N = The desired sample size per group

Z α , the critical value of normal distribution at a level of significance of 95%

Z β statistical power at 80% =0.84

P is pooled prevalence = P_T+P_S/2

P_T prevalence of the outcome in the previous study=0.25

P_S prevalence of comparator in the previous study=0.12 (32)

$$N = \frac{(1.96+0.84)^2 \times 223.34(1-224.34)}{(303.06-145.61)^2}$$

$$N = \frac{2.8^2 \times 50095}{(157.45)^2}$$

$$N = \frac{392744.8}{24790}$$

$$N = 15.84$$

Approximating to the nearest ten: N = 16

Allowing for the loss of patients to protocol violation, a 10% increase was made to the calculated sample size bringing the total number of patients to 38. Calculate at 16 x 10/100 = 1.6 which is approximately 2. Therefore, sample size = 16+2 which is equal to 18

Each study group was allocated 18 patients given a total of 36All the patients were recruited during preoperative evaluation in the ward and clinic. Following the patient’s eligibility, detailed information about the study was explained to the patient including the study duration, and a written informed consent

was signed by the patient. Patients who withdrew their permission for the study for any reason were still given the standard care for the procedure.

Blinding and randomization were done by an assistant, who is not the researcher. Patients were randomly assigned to one of two study groups by the pharmacist using opaque sealed envelopes containing randomized numbers. These numbers were identified and used to place patients into one of two groups. Both the anesthetic and the surgeon were blinded, as the drugs were reconstituted at the pharmacy and sent to the theater in a 20ml syringe, then administered to the patient before the surgery.

Treatment group (A); patients in this group received intravenous tranexamic acid 1g immediately after securing intravenous access in the theatre.

Placebo group(B); patients in this group received a placebo (20mL of normal saline) also after intravenous access.

Procedure

The researcher and assistant reviewed all patients the night before surgery. History and examination were done to determine fitness for elective surgery, rule out exclusion criteria, and provide information to the patient on the perioperative course, technique of anesthesia, and allay anxiety. The study was explained to the patient and written informed consent was obtained.

Demographic data was obtained from the patient's case file which included age, weight, height, presenting symptoms, and uterine size. These were recorded on a preformed data collection form. A review of the relevant laboratory investigations was conducted which included Full blood count, bedside bleeding time, and urinalysis. The preoperative haemogram and platelet count were recorded.

On arrival in the theatre, the anaesthetist ensured 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 baseline values recorded. Intravenous access with a 16-gauge cannula was secured and (15ml/kg) Normal saline solution was given to all patients prior to the procedure and spinal anesthesia was given. An aseptically prepared solution of 1g tranexamic acid in 20ml or 20ml normal saline (placebo) was administered immediately after securing the intravenous access at the time of skin incision (midline sub umbilical)

A Consultant Gynaecologist and senior registrars did all surgeries. Foleys catheter size 16 was used as a tourniquet and applied at the base of the uterus to occlude the uterine, as well as the ovarian arteries during the surgery, and blood loss was monitored. The tourniquet was applied and finally removed after the repair of the uterus. A suction machine at 80mmhg was used to collect blood loss estimation was done by both volumetric (measuring the volumes in the cylinder and subtracting any other fluid used) and gravimetric (soaked swabs were weighed by the electronic scale and blood loss was estimated by subtracting the soaked weight from the dry weight and multiplied by 1.050 to convert to volume in ML) methods.⁹ Blood transfusion was done following the loss of $\geq 20\%$ of the patients' total blood volume or any blood loss causing a reduction in blood pressure of $\geq 20\%$ from baseline and tachycardia of $\geq 20\%$ of baseline values. The total number of units of blood transfused was noted.

At the end of the surgery, patients were transferred to the recovery room and monitored for an hour before being taken to the ward. Side effects of tranexamic acid were monitored every 8hours until 72hours postoperatively by the researcher and the assistant and managed if they occurred. These include nausea, vomiting, diarrhea, and thrombosis (calf pain, oedema of the leg, superficial vein distension in the calf, palpable cord on superficial veins in the calf, chest pain, cough, hemoptysis, and breathlessness).

Data analysis: All data were analyzed using a statistical package for Social Science version 24. The basic demographic data such as age, BMI and clinical characteristics of the patients were analyzed using two-

sample t-tests to determine the difference between the two groups placebo and tranexamic acid. The frequency and percentages of the presenting symptom were analyzed using chi-square.

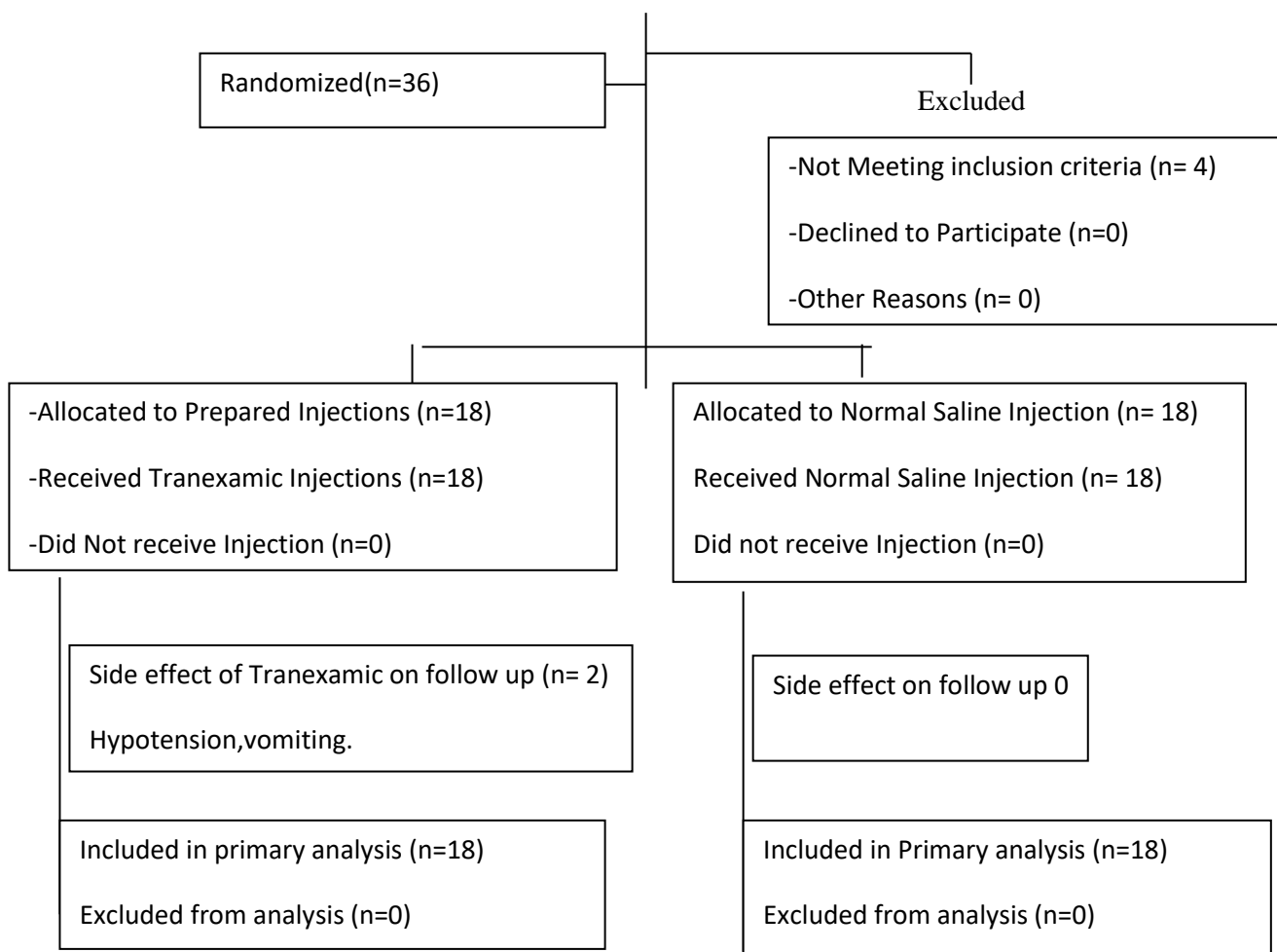
The volume of blood loss and transfusion rate between the two groups was compared using both chi-square and two sample t-tests. The post-operative PCV was analyzed using the two-sample t-test to determine the difference between the two groups. The hemodynamic changes associated with blood loss were compared with two sample t-tests and the side effects of tranexamic acid were determined using Chi-square statistic. A p-value of <0.05 was considered statistically significant.

Relationships for qualitative variables were assessed using the chi-square coefficient.

Ethical consideration

Ethical approval was obtained from the hospital Health Research Ethics Committee of Barau Dikko Teaching Hospital NUMBER(BDTH/2022/119/VOL1). A comprehensive information sheet was given to the patients to read and understand the motive of the study, following which written informed consent was obtained from all the patients to participate in the study using a structured consent form. All data collected in this study was treated as confidential and only used for the purpose of carrying out this study.

Consort Flow



Result

The study was a randomized controlled trial that involved a total of 36 women who met the eligibility criteria, studied between June 2023 and December 2023. Of the 36 participants who completed the trial, the treatment group was 18, and the control group was 18.

Baseline demographic data and clinical characteristics of the women were comparable in the two groups for age, body mass index (BMI), uterine size, and preoperative packed cell volume (Table 1). The mean age of the participants in the tranexamic acid group was 37.82 ± 5.89 years and 39.74 ± 5.17 years in the placebo group. The mean body mass index in the tranexamic acid group was $24.79 \pm 6.07 \text{kg/m}^2$ and the placebo group was $23.85 \pm 3.82 \text{kg/m}^2$. The uterine size was comparable in both groups with a mean uterine size of 22.4 ± 0.56 weeks in the tranexamic acid group and 23.2 ± 0.48 weeks in the placebo group at a 95% confidence interval.

The mean baseline measurements of systolic and diastolic blood pressure, mean arterial pressure, Pulse rate, and arterial oxygen saturation (SPO₂) were comparable in the two groups ($p = 0.034, 0.610, 0.203, 0.020, 0.681$). Most of the women 35 (97.2%) presented with symptoms of menorrhagia. Other presenting symptoms include infertility 29 (80.5%), pressure symptoms 7 (19.4%), and dysmenorrhea 3 (8.3%). Most of the women 35 (97.2%) presented with symptoms of menorrhagia, illustrated in Table 2. There was a statistically significant reduction in the mean blood loss in the tranexamic acid group 947.65 ± 451.88 (median = 840, range = 550 – 2420ml) compared to 1320.53 ± 563.28 (median = 1280, range 249 – 2200ml) in the placebo group ($p 0.037$), Decrease in risk of perioperative blood loss by 30% with Relative risk reduction of 0.7 and confidence interval of (2.19-2.59) Major blood loss > 1000 ml was recorded more among women in the placebo group than those who received tranexamic acid ($p 0.037$) [Table 3. There was also a statistically significant decrease in the mean postoperative packed cell volume ($P < 0.001$) in the treatment group compared to the control group. [Table 4] There was an increase in the number of women who received two or more units of blood transfusion in the placebo group (66.7%) compared to the tranexamic acid group (33.3%) ($p=0.016$) [Table 5].

The result showed that the entire sample experienced a drop in packed cell volume between pre- and post-myomectomy, the reduction was greater in the placebo group compared to the tranexamic acid group. [Table 6. Amongst the participants, none of those in the placebo group reported any side effects however in the tranexamic group there was one report of low blood pressure and one report of vomiting which was not statistically significant ($p=0.306$)

No morbidity or mortality recorded at the end of the study

Table 1: Sociodemographic, baseline clinical, and laboratory characteristics of the patients

| | Group | | t-Statistic | P-value |
|-------------------------|--------------------|-----------------------|-------------|---------|
| | Placebo Mean±SD | Tranexamic Mean±SD | | |
| Age (years) | 39.74±5.17 | 37.82±5.89 | 1.038 | 0.307 |
| BMI(Kg/m ²) | 23.85±3.82 | 24.79±6.07 | -0.558 | 0.580 |
| Uterine size(weeks) | 23.2±0.48 | 22.4±0.56 | 0.464 | 0.645 |
| Preoperative PCV | 32.37±2.39 | 32.82±2.51 | -0.558 | .580 |
| SBP (mmHg) | 127.00±13.91 | 138.12±16.22 | -2.214 | 0.034 |
| DBP (mmHg) | 82.74±7.19 | 84.35±11.40 | -0.515 | 0.610 |
| MAP (mmHg) | 97.49±8.92 | 102.20±12.68 | -1.299 | 0.203 |
| PR (beats/minute) | 84.87±8.11 | 92.71±10.99 | -2.450 | 0.020 |
| SPO ₂ (%) | 97.00±1.94 | 97.29±2.31 | -0.415 | 0.681 |
| Preoperative PCV | 32.37± 2.39 | 32.82± 2.51 | -0.56 | 0.58 |

Table 2: Different Presenting symptoms of the patients before surgery

| | Group | | Total |
|-------------------|---------------------------|------------------------------|-------|
| | Placebo n= 18(50.0) | Tranexamic n= 18(50.0) | |
| Menorrhagia | 18(50.0) | 17(47.2) | 35 |
| Pressure Symptoms | 1(14.3) | 6(85.7) | 7 |
| Infertility | 15(51.7) | 14(48.3) | 29 |
| Dysmenorrhea | 2(66.7) | 1(33.3) | 3 |

Table 3: Comparison of intraoperative blood loss between the tranexamic acid and placebo group

| Blood loss(ml) | Group | | RR (95% CI) | t-test | P-value |
|-----------------|---------------------------|------------------------------|------------------|--------|---------|
| | Placebo n= 18(50.0) | Tranexamic n= 18(50.0) | | | |
| < 500 | 2(100) | 0(0) | | 9.474 | 0.009 |
| 500-1000 | 5(27.78) | 13(72.22) | | | |
| >1000 | 12(75) | 4(25) | | | |
| Blood loss (ml) | 1320.53±563.28 | 947.65±451.88 | 0.7(2.19 – 2.59) | 4.724 | 0.037 |

*Significant at 0.05

Table 4: Comparison of postoperative packed cell volume between the tranexamic acid and placebo group

| Postoperative PCV | Group | | Total n36(100%) | t.test | P-value |
|-------------------|----------------------------|-------------------------------|--------------------|--------|---------|
| | Placebo n=18 n (50%) | Tranexamic n=18 n (50%) | | | |
| Mean | 25.00±2.81 | 29.71±2.02 | | 5.71 | <0.001 |

Table 5: Comparison of blood transfusion between the tranexamic acid and placebo group

| | Group | | Total= 36(100) | χ^2 | P-value |
|----------------------------------|---------------------------|------------------------------|----------------|-------------------|---------|
| | Placebo n= 18(50.0) | Tranexamic N= 18(50.0) | | | |
| Need for Blood transfusion | | | | | |
| Yes | 7(63.6) | 4(36.4) | 11(100) | .749 ^a | 0.387 |
| No | 12(48.0) | 13(52.0) | 25(100) | | |
| Number of blood units transfused | | | | | |
| 1 | 5(62.5) | 3(37.5) | 8(100) | .016 | 0.898 |
| 2-4 | 2(66.7) | 1(33.3) | 3(100) | | |

Table 6: Comparing intraoperative haemodynamic changes in tranexamic acid and placebo group.

| | Group | | t-statistic | P-value |
|-------------------|----------------------------|-------------------------------|-------------|---------|
| | Placebo n=18 Mean±SD | Tranexamic n=18 Mean±SD | | |
| SBP (mmHg) | 119.11±9.55 | 133.41±16.64 | -3.207 | .003 |
| DBP (mmHg) | 78.16±7.43 | 86.06±11.46 | -2.480 | .018 |
| MAP (mmHg) | 91.81±7.54 | 101.61±12.66 | -2.860 | .007 |
| PR (beats/minute) | 86.00±7.13 | 96.24±16.42 | -2.473 | .019 |
| SPO2(%) | 96.42±1.57 | 97.88±1.11 | -3.181 | .003 |

Discussion

This randomized trial assessed the effectiveness of intravenous tranexamic acid on perioperative blood loss. It also assessed and showed the need for blood transfusion compared to placebo, amongst women undergoing open abdominal myomectomy by about 30%. Also, postoperative packed cell volume was higher among women who received intravenous tranexamic acid, compared to their counterparts who received a placebo. The mean intraoperative systolic blood pressure, diastolic blood pressure, and mean arterial pressure were significantly increased when compared to the baseline in the placebo group than in the tranexamic acid group. However, symptoms of vomiting and reduced blood pressure were noted in the tranexamic group. There was no incidence of thromboembolic events.

Uterine fibroids are diagnosed in 20-25% of women of reproductive age and 30-40% of women older than 40years.²² It was reflected in this study in which most of the women fell within the reproductive age group of 37 to 39years. Approximately 20-40% of women with fibroids experience significant symptoms and consult gynaecologist care.²³ The most common clinical symptoms include abnormal uterine bleeding, dysmenorrhea, pelvic pain, infertility, and recurrent pregnancy loss.^{6,23,24} In this study, menorrhagia was the commonest presenting symptom with 35 (97.2%) of the women who participated in the study presenting with menorrhagia. This finding is higher than the finding of the study by Ezeama et al,¹⁵ where 41.7% of the women with uterine fibroid presented with menorrhagia as the commonest presenting symptom.¹⁵ However, Geidam et al⁶ in their study on the indication and outcome of abdominal myomectomy in Northern Nigeria reported a relatively higher value (57.7%) of menorrhagia in women with uterine fibroid.⁶

The effectiveness of intravenous tranexamic acid demonstrated in this study is in accordance with the results of previous studies that compared intravenous tranexamic acid to placebo, reporting less blood

loss with tranexamic acid than placebo.^{13,25,26,27,28,29} In this study the use of intravenous tranexamic acid resulted in less intraoperative blood loss

In agreement with the result of this study, Shaaban et al²⁷ in 2015 evaluated the efficacy of tranexamic acid in reducing blood loss during and after open abdominal myomectomy for patients with three or more uterine fibroids.²⁷TA group showed a lower amount of blood loss (407 mL) when compared to the control group (677 mL; $P < .01$) with a reduction of risk of perioperative blood loss by 40%. In accordance with the above finding, this study also found that the tranexamic acid group had a lower amount of blood loss (947ml) as compared to the placebo group (1320ml) with a p-value of 0.037. Treatment with tranexamic acid resulted in a decrease in the risk of perioperative blood loss by 30%.

Also, in two different studies by Nahla et al²⁵ and Caglar et al²⁸, intravenous tranexamic acid has been found to reduce blood loss during open abdominal myomectomy. In the study by Nahla et al²⁵, 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.²⁵ Similarly, in the study by Caglar et al²⁸, the authors reported that intravenous tranexamic acid succeeded in decreasing perioperative blood loss during excision of myoma in the tranexamic acid group (804 ± 482 ml) compared to the placebo group (1047 ± 617 ml).²⁸ The volume of blood loss in the two studies above both in the tranexamic acid and placebo group are comparable to the findings of this present study. However, both studies had no application of pericervical tourniquet. Overall, results in the present study follow most of the trend observed in the literature that intravenous tranexamic acid reduces blood loss during abdominal myomectomy when compared with placebo.

On the contrary, Sammy et al¹⁰ in a study on the use of intravenous tranexamic acid as an adjunct haemostat to ornipressin during open myomectomy in 34 patients noted no significant difference in blood loss between the two groups with a median blood loss in the ornipressin group (n=17) and ornipressin plus a tranexamic acid group of 398ml and 251ml respectively ($p = 0.361$).¹⁰ However, the technique of anaesthesia, the rank of the surgeon, uterine size, location, and the number of fibroids enucleated were not mentioned in their study. Caglar et al²⁸ emphasized the importance of the above parameters in perioperative blood loss during myomectomy.²⁸

This study found twenty-eight percent (28%) of the women in the placebo group needed blood transfusion compared to nine percent (9%) in the tranexamic acid group. Study participants who did not receive tranexamic acid during myomectomy had a higher chance of being transfused than those who received tranexamic acid. This finding follows the trend observed in most literature that intravenous tranexamic acid reduces the need for blood transfusion during myomectomy when compared with a placebo. In a randomized controlled trial on myomectomy-associated blood loss in patients with multiple myomas, Shaaban et al²⁷ 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%). The transfusion rate in this study was relatively lower when compared to the studies by Nahla et al²⁵ and Shaaban et al²⁷. However, the criteria for blood transfusion were not stated in these two studies to ensure the standard.

The mean postoperative packed cell volume was significantly higher in the tranexamic acid group ($29.71 \pm 2.02\%$) compared to the placebo group ($25.0 \pm 2.80\%$). These results concur with the findings from other studies which showed that a decrease in haemoglobin was more for the participants in the placebo compared to those in the tranexamic acid group.^{13,25,27,28} In addition, the duration of surgery was noted to be longer in the placebo group (162.4 ± 60.8 minutes) compared to the tranexamic acid group (117.7 ± 25.9 minutes). This showed that tranexamic acid controlled the blood loss even though the duration of surgery was longer in the tranexamic acid group, it also follows the trend in literature.^{25,27,28}

In this study, the mean baseline systolic blood pressure, diastolic blood pressure and mean arterial pressure were significantly more reduced in the placebo group than the tranexamic acid group when

compared to the mean intraoperative values ($p = 0.003$, $p = 0.018$, and $p = 0.007$). The mean pulse rate was significantly lower in the placebo group compared to the tranexamic acid group ($p = 0.019$). None of the previous studies found in the literature on the use of tranexamic acid to reduce blood loss during myomectomy studied the haemodynamic (blood pressure, pulse rate, mean arterial pressure) changes associated with blood loss. Sudden blood loss of a moderate degree causes a fall in blood pressure, which is compensated to a certain extent by a baroreceptor-mediated rise in heart rate and vasoconstriction. This was reflected in this study as blood loss was associated with reduced blood pressure.

Amongst the participants in this study, one woman had vomiting in the tranexamic acid group, and one was found to have reduced blood pressure in the same group. There were no side effects found in the placebo group. There was no thromboembolic event 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 al²⁵ reported side effects of nausea, vomiting, and diarrhoea. However, these were not statistically significant ($p = 0.102$, 0.87 and 1.00), even though, nausea and vomiting are the common side effects of tranexamic acid. There was no incidence of thromboembolic events. Even though tranexamic acid administration has shown a risk for complications like thrombosis and embolism due to its antifibrinolytic effect, thromboembolic events were not reported in most of the studies.^{25,26,27,28}

All the participants in this study had pericervical tourniquet application, as it would not be ethical to conduct myomectomy without any standard measure to reduce blood loss as there exists a proven, effective, standard measure in use in this setting. The use of a peri-cervical tourniquet to occlude the uterine blood supply has been shown to reduce blood loss during myomectomy.^{5,13}

Being a hospital-based study, the small sample size and the study population may not accurately represent the population scenarios. This is a limitation of this study. In addition the involvement of Multiple surgeons in the surgeries may also no be replicable at other levels of healthcare.

Conclusion

Tranexamic acid reduces blood loss during and after myomectomy for patients with uterine fibroids and the need for blood transfusion is reduced in patients who had intravenous tranexamic acid as an adjunct to the application of a tourniquet. Treatment with tranexamic acid as an adjunct to pericervical tourniquet in myomectomy has a decreased risk of perioperative blood loss by 30%, RR 0.7 with insignificant side effects. We recommend the use of tranexamic acid as an adjunct to the use of tourniquet during open abdominal myomectomy to reduce the blood loss and burden of blood transfusion including the cost.

conflict of interest: There is no conflict of interest with the company or any collaboration with the manufacturers.

References

1. Kwawukume EY. Uterine Leiomyomas, In: Kwawukume EY, Emuveyan EE (Eds), Comprehensive Gynaecology in the Tropics. 1st Edition. Accra, Asante and Hitscher. 2005. 124-137.
2. George A, Catherine A, Philippe-Yves L, Nicholas L. The management of uterine leiomyomas. J Obstet Gynaecol Can 2015;37(2):157-178.
3. Aamir T K, Manjeet S, Janesh K G. Uterine fibroids: current perspectives. Int J Womens Health. 2014; 6: 95-114.
4. Wegienka G, Baird DD, Hertz-Picciotto I, et al. Self-Reported heavy bleeding associated with uterine leiomyomata. Obstet Gynecol. 2003; 101(3):431-437.

5. Ikechebelu JI, Ezeama CO, Obiechina NJA. The use of tourniquet to reduce blood loss at myomectomy. *Niger J Clin Pract* 2010;13(2):154-158.
6. Geidam AD, Lawan ZM, Chama C, Bako BG. Indications and outcome of abdominal myomectomy in University of Maiduguri Teaching Hospital: Review of ten years. *Niger Med J*. 2011; 52(3): 193-197.
7. Frederick J, Hardie M, Reid M, Fletcher H, Wynter S, Frederick C. Operative morbidity and reproductive outcome in secondary myomectomy: a prospective cohort study. *Human Reproduction* 2002;17(11):2967-2971.
8. Okogbo FO, Ezechi OC, Loto OM, Ezeobi PM. Uterine leiomyomata in South Western Nigeria: a clinical study of presentations and management outcome. *Afr Health Sci*. 2011;11(2):271-278.
9. West S, Ruiz R, Parker WH. Abdominal myomectomy in women with very large uterine size. *Fertil Steril* 2006; 85:36-39, doi:10.1016/j.fertnstert.2005.05.073.
10. Sammy N, Timona O, William S. Intravenous tranexamic acid as an adjunct haemostat to ornipressin during open myomectomy. A randomized double-blind placebo-controlled trial. *Ann Surg Innov Res* 2005; 9:10.
11. Musallam KM, Tamim HM, Richards T, et al. Preoperative anaemia and postoperative outcomes in non-cardiac surgery: a retrospective cohort study. *Lancet* 2011; 378: 1396-407.
12. Rhode JM, Dimcheff DE, Blumberg N, et al. Healthcare-associated infection after red blood cell transfusion: a systematic review and meta-analysis. *JAMA* 2014; 311(13): 1317-1326.
13. Kongnyuy EJ, Wiysonge CS. Interventions to reduce haemorrhage during myomectomy for fibroids. *Cochrane Database of Systematic Reviews* 2014;(8): CD005355.DOI10.1002/14651858.CD005355.pub5.
14. Dunn CJ, Goa KL. Tranexamic acid: a review of its use in surgery and other indications. *Drugs* 1999; 57:1005-1032.
15. Ezeama CO, Ikechebelu JI, Obiechina NJ, Ezeama NN. Clinical presentation of uterine fibroids in Nnewi, Nigeria. *Ann Med Health Sci Res*. 2012;2(2):114-118.
16. Atombosoba AE, Lucky OL, Chukwuemeka AI, Israel J, Isa AI. Review of the clinical presentation of uterine fibroid and the effect of therapeutic intervention on fertility. *Am J Clin Med Res*, 2015;3(1), pp9-13. DOI:10.12691/ajcmr-3-1-2.
17. Taylor A, Sharma M, Tsirkas P, Sardo A, Setchell M, Magos A. Reducing blood loss at open myomectomy using triple tourniquets: A randomized controlled trial. *BJOG* 2005; 112: 340-345.
18. William NJ, Angela J, Marcin W. Tranexamic acid: a clinical review. *Anaesthesiol Intensive Ther* 2015; 47.4,339-350.
19. Katharine K, Phil E, Pablo P, Haleema S, Ian R. Effect of tranexamic acid on surgical bleeding: systematic review and cumulative meta-analysis. *BMJ* 2012;344 doi: <http://dx.doi.org/10.1136/bmj.e3054>.
20. Henry DA, Carless PA, Moxey AJ, O'Connell D, Stokes BJ et al. Anti-fibrinolytic use for minimizing perioperative allogenic blood transfusion. *Cochrane Database Syst Rev*. 2011;(1):CD001886. doi: 10.1002/14651858.CD001886.pub3.
21. Araoye MO, Subject selection, In: *Research methodology with statistics for health and Social sciences*. Ilorin: Nathadex; 2004: 115-121.
22. Stewart E, Cookson C, Gandolfo R, Schulze-Rath R. Epidemiology of uterine fibroid: a systematic review. *BJOG An Int J Gynaecol*. 2017; 124(10): 1501 – 12.
23. Erica E, Geraldine E, Eden R, Maureen B, Tanka D, Leeber S. Racial differences in fibroid prevalence and ultrasound findings in asymptomatic young women (ages 18-30): A pilot study. *Fertil Steril*. 2013; 99(7): 1951-1957.
24. Atashkhoei S, Fakhari S, Pourfathi H, Bilehjani E, Garabaghi PM, Asiaei A. Effect of oxytocin infusion on reducing the blood loss during abdominal myomectomy: a double-blind randomised controlled trial. *BJOG* 2016; 124: 292-298.

25. Nahla W, Hany F, Huda F. Reducing blood loss during open myomectomy with intravenous versus topical tranexamic acid: A double-blinded randomized placebo-controlled trial. *Middle East Fertil Soc J.* 23 (2018) 225-231.
26. Panagiotis P, Anna K. Tranexamic acid for the management of uterine fibroid tumours: A systematic review of the current evidence. *World J Clin Cases* 2014; 2(12): 893-898.
27. Shaaban M, Ahmed M, Farhan R, Dardeer H. Efficacy of Tranexamic Acid on Myomectomy-Associated Blood Loss in Patients with Multiple Myomas: A Randomized Controlled Clinical Trial. *Reprod Sci* 2016 07 29; 908-912.
28. Caglar GS, Tasci Y, Kayikcioglu F, Haberal A. Intravenous tranexamic acid use in myomectomy: A prospective randomized double-blind controlled study. *Eur J Obstet Gynaecol Reprod Biol.* 2008; 137(2): 227-231.
29. Opoku-Anane J, Vargas MV, Moawad G, Cherie M, Robinson JK. Use of Intravenous Tranexamic Acid During Myomectomy: A Randomized Double-Blind Placebo Controlled Trial. *J Minim Invasive Gynaecol.* 2015; 22(6S): S197.
30. Shahid A, Khan A. Tranexamic Acid in Decreasing Blood Loss During and after Caesarean Section. *J coll Physicians Surg Pak.* 2013; 23(7): 459-462.
31. Fletcher H, Frederick J, Hardie M, Simeon D. A randomized comparison of vasopressin and tourniquet as hemostatic agents during myomectomy. *Obstet Gynaecol* 1996; 87(6): 1014-8.
32. Baradwan S, Hafid B, Latifah HM, Gari A et al. Prophylactic tranexamic acid during myomectomy: A systematic review and meta- analysis of randomized controlled trials. *Obstet Gynaecol* 2022; 276:82-91