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# A Randomized Comparative Trial of the Haemostatic Effect of Tranexamic Acid and Ethamsylate in Major Gynaecological Surgeries

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## ABSTRACT

**Objective:** Major gynaecological surgeries like abdominal myomectomy and hysterectomy are often associated with bleeding, this could affect patient's outcome during anaesthesia, by either increasing the perioperative morbidity and or mortality. The aim of our study is to compare the haemostatic effect of tranexamic acid and ethamsylate in patients undergoing epidural anaesthesia for major abdominal gynaecological surgeries.
**Methods:** Ethical clearance for this prospective randomized double-blind controlled study was obtained from the Ethics and Research Committee of a tertiary health institution in Nigeria (FMC/OW/HREC/245). Written informed consent was obtained from each of the patients scheduled for abdominal myomectomy or hysterectomy on elective basis, before being enrolled into this study. We recruited 90 patients and randomize them to either Group A (n=30) to received intravenous Tranexamic acid 15mg/kg, Group B (n=30) to receive intravenous Ethamsylate 12.5mg/kg or Group C (n=30) to receive Placebo (normal saline), 30 minutes before the induction of epidural anaesthesia. All data were entered into a data collection form and analysed with the statistical package for social sciences (SPSS) 21. Parametric data was analysed using two-tailed analysis of variance (ANOVA) for independent groups. A p-value of <0.05 was considered significant.
**Results:** A total of 90 patients were recruited into this study and they all completed the research. The duration of surgery was significantly longer in Group A (162.67±52.49 min), compared with Group B (151.87±55.31 min) and Group C (126.57±45.67 min), p=0.024. The comparison of the preoperative and postoperative Hb in Group A shows a decrease of 10.10%, and the difference was statistically significant, p=0.001. But when the preoperative and postoperative Hb were compared in Group B and Group C, the decrease in Hb significantly increased in Groups B (13.29%; p<0.0001) and Group C (14%; p<0.0001).
**Conclusion:** The administration of intravenous tranexamic acid before the induction of epidural anaesthesia for abdominal myomectomy or hysterectomy reduced the intraoperative and postoperative blood loss more, compared to the administration of intravenous ethamsylate or placebo, however with no clinical significance or apparent side effect.

***Keywords:*** Tranexamic acid, ethamsylate, haemostasis, surgical blood loss

## INTRODUCTION

Major gynaecological surgeries like abdominal myomectomy and hysterectomy are often associated with bleeding, this could affect patient's outcome during anaesthesia, by either increasing the perioperative morbidity and or mortality, especially in regions where there is limited resources and lack of blood transfusion programme and protocols [1]. Also, these patients often present late to the hospital in most developing countries, at times with

huge uterine fibroid or advanced uterine neoplasm, and this also makes the anaesthesia, which could be general or regional anaesthesia very challenging[2, 3].

Blood transfusion is associated with some adverse effects ranging from transfusion-associated infections, immune related and coagulopathic complications. Some individual refuses blood transfusion for religious and or personal reasons. This indicates that there is a need to identify a suitable mechanism to provide adequate care for patients at risk of perioperative blood loss.

Researchers have evaluated several methods of reducing blood loss, which includes anaesthetic, surgical and pharmacological techniques with positive findings[4, 5, 6]. Modig et al[4] observed in their study that epidural and spinal anaesthesia for various type of surgeries offered advantages over general anaesthesia by decreasing blood loss and transfusion requirements. Some surgical techniques that have proved valuable in reducing blood loss and risk of transfusion during surgery include the use of topical haemostatic agents (surgicel), vascular ligation, liquid nitrogen spray (cryosurgery), electrocautery, photoablation or photocoagulation, and radiofrequency[5]. The efficacy of tranexamic acid and ethamsylate in terms of reducing the risk of allogenic transfusion in major gynaecological surgeries have been evaluated separately by some authors with variable findings[7,8,9,10]. However no study has compared the therapeutic effect of tranexamic acid and ethamsylate in major abdominal gynaecological surgeries during epidural anaesthesia.

Tranexamic acid is a synthetic derivative of the amino acid lysine[11]. It binds the 5-lysine binding sites on plasminogen, and inhibits plasmin formation and displaces plasminogen from the fibrin surface. Thus, functioning as an anti-fibrinolytic agent. It can be used in the management of excessive bleeding. It is also thought to exert an anti-inflammatory effect by inhibiting plasmin-mediated activation of complement, monocytes, and neutrophils, and may improve platelet function. Tranexamic acid is a trans-stereoisomer of 4-(aminomethyl)-cyclohexane-carboxylic acid with a molecular weight of 157. The intravenous dosage is typically 0.5-1g by slow injection three times per day. Alternatively, the initial dose can be followed by an infusion of 25-50 mg/kg over 24 hours. It is excreted through the renal route in urine, thus necessitating dose reduction in patients with renal impairement[11].

Ethamsylate is a benzenesulfonate derivative, and it functions as a systemic haemostatic agent[12]. It exerts haemostatic action by improving platelet adhesiveness and restoring capillary resistance. It decreases bleeding time and increases platelet aggregation. It reduces capillary bleeding when platelets are adequate. The drug exerts anti-hyaluronidase action and improves capillary wall stability. It inhibits $PGI_2$ synthesis and correct abnormal platelet function. It can be given orally or parenterally, with oral dose of 250 – 500mg 8 hourly or intravenously 1 hour prior to surgery. It has a half-life of 8 hours, and it's excreted in urine[12].

This study was aimed to compare the haemostatic effect of tranexamic acid and ethamsylate in patients undergoing epidural anaesthesia for major abdominal gynaecological surgeries, and we hypothesized that there will be no mean difference in the postoperative haemoglobin concentration of the patients that received tranexamic acid or ethamsylate.

## PATIENTS AND METHODS

Ethical clearance for this prospective randomized double-blind controlled study was obtained from the Ethics and Research Committee of a tertiary health institution in Nigeria (FMC/OW/HREC/245). Written informed consent was obtained from each of the patients scheduled for abdominal myomectomy or hysterectomy on elective basis, before being enrolled into this study. We recruited ASA I, II or III, 30-60 years

old female patients, who were to have their surgery under epidural anaesthesia, and allocated them into Groups A (n=30), B (n=30) and C (n=30), by using a computer-derived random number sequence in an opaque envelope, to receive any of the study agents. The investigators were not aware of the group allotment until all the patients had been randomized. Sample size of 30 in each of the groups was derived using the formular for comparison of mean[13] and taking into consideration the standard deviations (SD) in Suryakumari et al study[14] (Tranexamic acid $SD_1$=0.15 and Ethamsylate $SD_2$ = 0.15).

Patients who refused to consent for the study, undergoing general anaesthesia, with evidence of uncontrolled clinically important neurological, renal, hepatic, cardiovascular, metabolic or endocrine dysfunction, on anticoagulants, allergic to the study agents or ASA class more than III were excluded from the study.

All the recruited patients were evaluated preoperatively in the Gynaecology ward to establish rapport, assess for anaesthesia and surgery fitness and obtain informed consent. The preanaesthetic plans, epidural anaesthetic technique, and postoperative rectal diclofenac insertion plans were explained to the patients and they were counselled on preoperative fasting; 2 hours for clear fluids, and 6 hours for solid foods.

Prior to patient's arrival in the theatre, a cockpit drill was done on the anaesthesia machine to ascertain its functionality. Airway maintenance devices, suction machine, oxygen and means of delivery, were checked to ensure availability and functionality. In the theatre, patients were identified and preoperative haemoglobin level documented. Using a multiparameter monitor (IMEC 10, manufactured by Shenzhen Mindray Bio-Medical electronics Company Limited, China), preanaesthetic pulse rate (PR), peripheral oxygen saturation ($SpO_2$), systolic (SBP), diastolic (DBP), mean arterial (MAP) blood pressures, respiratory rate (RR), peripheral body temperature, and electrocardiographic tracing were obtained. Intravenous access was secured with sized 16G or 18G cannula on the non-dominant arm. Group A (n=30) patients received intravenous Tranexamic acid 15mg/kg (Prexam, Precious Trust Ltd, Nigeria), Group B (n=30) received intravenous Ethamsylate 12.5mg/kg (Diacynone, Grams Pharmacy, Nigeria), while Group C (n=30) received Placebo (normal saline) 30 minutes before the induction of epidural anaesthesia. The study agents were made up to 20 ml with normal saline to avoid bias.

Preloading was done with 10-15ml/kg of normal saline for all patients before instituting epidural anaesthesia in sitting position. The lower back was cleaned with povidone iodine and draped, Touffier's line which corresponds to $L_4/L_5$ interspace was identified as landmark and the chosen interspace was infiltrated with 3ml of 1% plain lidocaine. A Tuohy needle was then inserted and slowly advanced into the epidural space using loss of resistance to air technique, an epidural catheter was threaded about 6cm and secured, and patient returned to supine position. Following negative aspiration of cerebrospinal fluid (CSF) or blood, 3ml of lidocaine with epinephrine 1:200,000 was injected through the catheter as a test dose to confirm correct catheter placement. Aspiration of blood could necessitate repeating the procedure, however in case of aspiration of CSF; epidural block will be abandoned and patient excluded from the study, in order to avoid the risk of extensive spinal anaesthesia. Increase in heart rates after 5 minutes of test dose injection, could indicate intravascular injection, and thus necessitating readjustment of the epidural catheter. In view of negative response to epidural test dose injection, epidural anaesthesia was achieved by injecting 20ml of 0.25% bupivacaine (duracaine by Myungmoon Pharm Co. Ltd) over 3 minutes.

Sensory block was assessed every 5 minutes using methylated spirit-soaked

swab to test for sensory loss to cold, while motor block was assessed every 5 minutes using Modified Bromage's score (0 = Full flexion of knees and feet (no block); 1 = Just able to flex knees, full flexion of feet; 2 = Unable to flex knees, but some flexion of feet possible; 3 = Unable to move legs/feet). A sensory block up to the level of $T_6$ and modified Bromage score of 2 were judged adequate for surgery. Pain was assessed using a 10cm Visual Analogue Scale (VAS) and a VAS $\geq$ 3 was termed significant and was managed with intravenous pethidine 1mg/kg as rescue analgesic. Patient in whom sensory block level of $T_6$ was not achieved even after 30 minutes of loading dose of epidural injection, or who had a rise in heart rate and blood pressure due to surgical stimulation were classified as failed or inadequate block, or those who complained of pain within 1 hour of surgery and failed to respond to rescue medication, thus were excluded from the study and epidural anaesthesia combined with general anaesthesia.

Oxygen was administered throughout the period of anaesthesia and surgery via nasal prongs at 2-4 L/minute. The intraoperative SBP, DBP, and MAP was monitored every 5 minutes, while HR, arterial oxygen saturation ($SPO_2$), heart rhythm, peripheral temperature, and surgical blood loss were monitored continuously. Hourly urine output was also monitored to ascertain an output of greater than or equal to 0.5ml/kg/hr. For the purpose of this study, bradycardia was taken as decrease in heart rate of >25% from the baseline, and hypotension, a decrease of >20% SBP from the baseline or decrease of >25% MAP from the baseline.[15] Bradycardia and hypotension were managed with intravenous atropine 0.02mg/kg and ephedrine 0.2mg/kg respectively and these documented. Hypothermia was prevented and managed by giving warm fluids and keeping the theatre temperature at 25˚C. Anxiety was managed by giving intravenous midazolam 0.05mg/kg in accordance to patient's needs. Surgical blood loss was treated with crystalloid and or whole blood where necessary.

Other adverse effects such as urinary retention and shivering, were treated and documented. The sensory and motor blocks was assessed every 5 minutes to determine the maximum height of sensory block and degree of motor block. Thereafter assessed every 15 minutes to determine the time for two segment regression. The total epidural injection given was documented.

At the end of the surgery, rectal diclofenac suppository 1mg/kg was inserted for the patients for postoperative analgesia. All patients were transferred to the post anaesthesia care unit (PACU) for 4 hours monitoring by the PACU staff. The SBP, DBP, MAP, $SPO_2$, heart and respiratory rates, temperature, sensory and motor blocks regression, pain and sedation were monitored and recorded at 0 (on arrival in PACU), 15 and 30 minutes, 1, 2, and 4$^{th}$ hour following recovery. Pain was assessed with VAS scale (1-3 = no pain, 4 = mild/moderate pain, and ≥5 = severe pain). Patients with pain score ≥4 while in PACU will receive epidural injection of 0.1% bupivacaine and documented. Sedation was assessed with a 6-points Ramsey sedation score.

All complications were recorded and promptly treated by the attending anaesthetist. Before discharge from PACU to the gynaecological ward, patients achieved a modified Bromage score of ≤1. Patient's follow up was continued in the ward post-operatively. Epidural catheter was removed aseptically at the 24th hour post insertion, after epidural injection of 10 ml of 0.1% bupivacaine for postoperative analgesia. Blood was drawn and send to the laboratory for postoperative haemoglobin level evaluation. The primary outcome was to compare the mean postoperative haemoglobin in the first 24 hours among the groups. The secondary outcomes were to compare the proportion of blood loss using the difference between the preoperative and postoperative haemoglobin among the

groups, as well as evaluate the side effects of the study agents.

All data were entered into a data collection form and analysed with the statistical package for social sciences (SPSS) 21. Tables and figures were used to present the result, and expressed as mean, median (interquartile range), proportion (number of patients), and standard deviation. Chi-squared test was used to analyze the nominal data. Age, weight, height, pain score, duration of surgery, preoperative and postoperative haemoglobin level, baseline blood pressures, and highest blood pressures were analysed with student's t-test. Parametric data was analysed using two-tailed analysis of variance (ANOVA) for independent groups. A p-value of <0.05 was considered significant.

## RESULT

A total of 90 patients were recruited into this study and they all completed the research; 30 patients each in Groups A, B and C respectively. Table I shows the patient characteristics. The mean age (p=0.117), weight (p=0.283) and BMI (p=1.00) were similar among the groups, but the mean height was significantly lower (p=0.009) in Group C (1.58±0.05 m) compared to Groups A (1.62±0.07 m) and B (1.63±0.09 m). The ASA I, II and III distribution was similar among the groups (p=0.297).

The duration of surgery was significantly longer in Group A (162.67±52.49 min), compared with Group B (151.87±55.31 min) and Group C (126.57±45.67 min), p=0.024, but the duration of anaesthesia, total epidural injection and time of ambulation were similar among the groups (p=0.590, p=0.099 and p=0.852 respectively) as shown in Table II.

**Table I – Comparison of Patient's Characteristics**

| VARIABLE | GROUP A (N=30) | GROUP B (N=30) | GROUP C (N=30) | P VALUE |
|---|---|---|---|---|
| AGE (YR) | 42.53±10.84 | 46.70±11.41 | 41.13±9.74 | 0.117 |
| WEIGHT (KG) | 71.10±14.39 | 71.87±11.41 | 67.33±8.80 | 0.283 |
| HEIGHT (M) | 1.62±0.07 | 1.63±0.09 | 1.58±0.05 | 0.009* |
| BMI ($KG/M^2$) | 27.19±5.51 | 27.25±4.95 | 27.15±4.14 | 1.000 |
| ASA I/II/III (NUMBER) | 4/19/7 | 5/15/10 | 4/24/2 | 0.297 |

*

**Table II – Comparison of Surgical Characteristics among Groups**

| VARIABLE | GROUP A (N=30) | GROUP B (N=30) | GROUP C (N=30) | P VALUE |
|---|---|---|---|---|
| DURATION OF SURGERY (MINUTE) | 162.67±52.49 | 151.87±55.31 | 126.57±45.67 | 0.024* |
| DURATION OF ANAESTHESIA (MINUTE) | 175.23±57.00 | 168.57±57.09 | 158.83±70.63 | 0.590 |
| TOTAL EPIDURAL INJECTION (ML) | 26.77±10.06 | 23.92±10.77 | 21.73±4.97 | 0.099 |
| TIME OF AMBULATION (HOUR) | 9.93±9.19 | 9.73±7.90 | 8.90±4.05 | 0.852 |

**Table III – Comparison of the Preoperative and Postoperative Haemoglobin among Groups**

| VARIABLE | GROUP A (N=30) | GROUP B (N=30) | GROUP C (N=30) | P VALUE |
|---|---|---|---|---|
| **PREOP HG (G/DL)** | 11.31±1.24 | 11.36±1.37 | 11.18±1.65 | 0.887 |
| **GROUP A VS B** | | | | 0.888 |
| **GROUP A VS C** | | | | 0.741 |
| **GROUP B VS C** | | | | 0.656 |
| **POSTOP HB (G/DL)** | 10.17±1.13 | 9.85±0.92 | 9.64±1.16 | 0.160 |
| **GROUP A VS B** | | | | 0.393 |
| **GROUP A VS C** | | | | 0.028* |
| **GROUP B VS C** | | | | 0.705 |

Table III shows that the preoperative Hb was similar among Groups A, B and C (p=0.887). But, the postoperative Hb was much reduced in Group C (9.64±1.16 g/dL), compared to Group B (9.85±0.92 g/dL) and Group A (10.17±1.13 g/dL), however, the difference was not statistically significant, p=0.160. Also, when the postoperative Hb was matched among the groups, it was found that the comparison of Groups A versus B and Groups B versus C were respectively similar (p=0.393 and p=0.705),

but comparison of Groups A versus C was statistically significant, p=0.028.

Table IV shows the intragroup analysis between the preoperative and postoperative Hb changes. The comparison of the preoperative and postoperative Hb in Group A shows a decrease of 10.10%, and the difference was statistically significant, p=0.001. But when the preoperative and postoperative Hb were compared in Group B and Group C, the decrease in Hb significantly increased in Groups B (13.29%; p<0.0001) and Group C (14%; p<0.0001).

The distribution of the gynaecological diagnosis and major gynaecological surgeries are shown in Figure 1 and 2. Shivering was more in Group C (33.3%), compared to Groups A (16.7%) and B (16.7%) (Figure 3). Other complications observed in this study are shown in Figure 3.

**Table IV – Intragroup Comparison of the Preoperative and Postoperative Haemoglobin**

| GROUP | PREOP HB (G/DL) | POSTOP HB (G/DL) | % DIFFERENCE | P VALUE |
|---|---|---|---|---|
| **A (N=30)** | 11.31±1.24 | 10.17±1.13 | 10.10 | 0.001* |
| **B (N=30)** | 11.36±1.37 | 9.85±0.92 | 13.29 | <0.0001* |
| **C (N=30)** | 11.18±1.65 | 9.64±1.16 | 14.00 | <0.0001* |

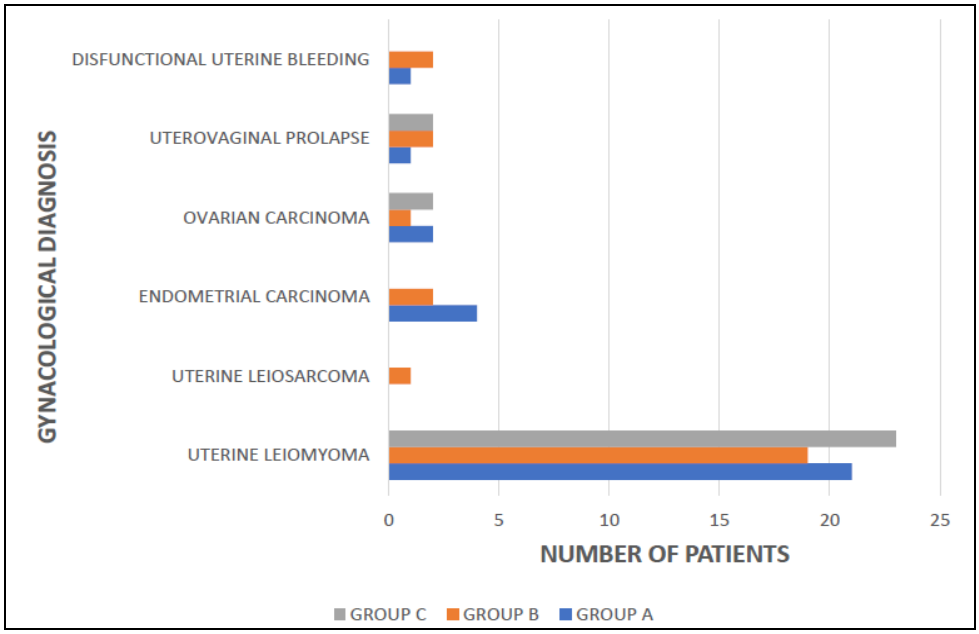


**Figure 1 – The Distribution of the Gynaecological Diagnosis Among the Groups**

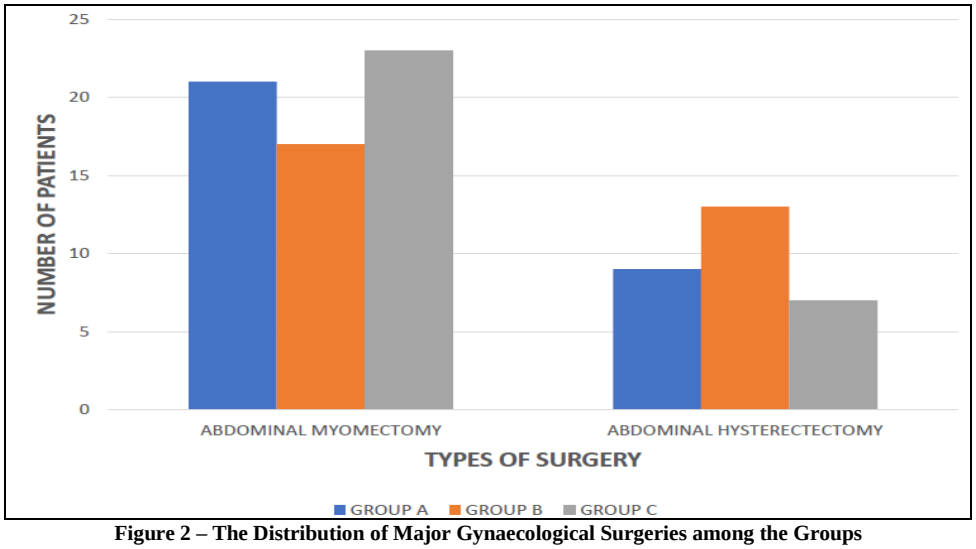


**Figure 2 – The Distribution of Major Gynaecological Surgeries among the Groups**

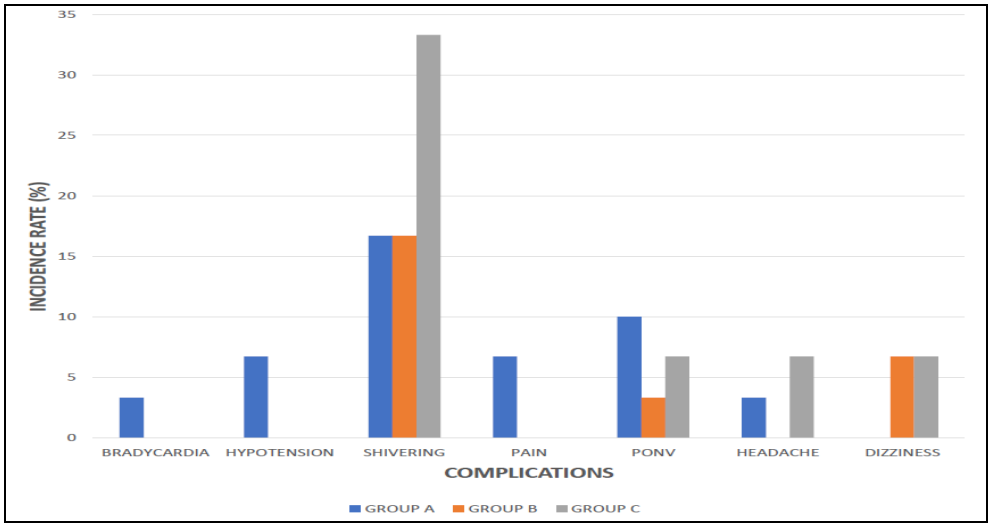


**Figure 3 – The Distribution of the Complications among the Groups**

## DISCUSSION

Our study compared the haemostatic effect of intravenous tranexamic acid (TXA) and ethamsylate (ETH) in major gynaecological surgeries and demonstrated that the administration of intravenous TXA before the induction of epidural anaesthesia for major gynaecological surgery reduced the intraoperative blood loss more, compared to when ETH or placebo was administered.

Anaesthesia for major gynaecological surgery remains a challenge in the developing countries due to increased blood loss from large gynaecological lesions and late patient presentation (fear of surgery and poor socioeconomic status), with strong choice of retaining their uterus and possibility of being able to bear children after surgery[3]. Thus, our institution incorporated the use of tourniquet as part of the management protocol for abdominal myomectomy, to reduce blood loss during the surgery. Tourniquet was used for all the patients that had abdominal myomectomy, irrespective of the group allotment.

Haemostatic effect of TXA and ETH were evaluated in this study by comparing the preoperative haemoglobin to the postoperative haemoglobin of the patients. We observed that the postoperative hemoglobin was higher in the study groups than the control group, but this was of no clinical significance (p=0.160). This is similar to the study conducted by Suryakumari et al[14] in obstetric patients, they observed that postoperative blood loss was similar and lower in both the TXA and ETH groups compared to the control group. It has been clinically established that intravenous TXA reduces surgical blood loss and mortality due to bleeding without any obvious safety issues in surgical patients and as well reduces the need for blood transfusion[16, 17]. However, much work has not been done in evaluating the haemostatic effect of intravenous ETH in major gynaecological surgeries[18].

We observed that when we compared the postoperative haemoglobin of the patients that received intravenous TXA and placebo, the difference in postoperative haemoglobin was significantly high (p=0.028), indicating that blood loss was much reduced in the TXA group, compared to the control group. This is consistent with the observation of Topsoee et al[8] and Shaaban et al[19]. Topsoee et al[8] reported that the administration intravenous TXA reduces intraoperative and postoperative blood loss and the need for reoperations due to postoperative bleeding in relation to abdominal hysterectomy. Shaaban et al[19] evaluated patients that had myomectomy, and noted that the administration of TXA reduced surgical blood loss. This is also similar to Opoku-Anane et al study[7], that noticed reduced blood loss in patients that

received intravenous TXA was given during abdominal myomectomy. Abdul et al[20] reported that the use of TXA provided adjunctive effect to tourniquet in reducing intraoperative blood loss during abdominal myomectomy compared to when tourniquet was used alone.

The place of tranexamic acid in controlling blood loss have generated so much research in the field of medicine. The Corticosteroid Randomisation After Significant Head injury (CRASH) -2 trial[21] and CRASH-3 trial[22] showed that early administration of tranexamic acid significantly decreases mortality in surgical or trauma patients with haemorrhage. The results of the World Maternal Antifibrinolytic (WOMAN) trial[23] contributes to strengthening the place of tranexamic acid in postpartum hemorrhage management. They found that tranexamic acid decreased death due to bleeding in women and reduces laparotomy for bleeding after Cesarean section and vaginal delivery, if given within 3 hours of giving birth. In 2017, World Health Organisation updated their guidelines for the use of tranexamic acid in treatment of postpartum hemorrhage. They outlined that tranexamic acid should now be included in the treatment regimen for postpartum haemorrhage along with other drugs, irrespective of the cause of hemorrhage[24].

Our study showed that blood loss during abdominal myomectomy and hysterectomy was much reduced in patients that received TXA compared to those that received ETH, however, the result was not clinically significant (p=0.393). This validates Patel et al[25] finding in non-surgical women with menorrhagia. They noted that TXA and ETH improved health-related quality of life in women with menorrhagia by reducing blood loss, with TXA demonstrating superior haemostatic effect over ETH. There is dearth of literature on haemostatic effect of ETH on gynaecological surgeries; Alanwar et al[18] reported in 2020, that no previous clinical trial has investigated the role of ETH in either prophylaxis or treatment of hemorrhage during surgery, that their study was the first to do so. However, they evaluated the combination of TXA and ETH in Cesarean delivery, and noted that the study drugs significantly reduced intraoperative and postoperative blood loss.

Patients in this study that received intravenous ETH were observed to have similar postoperative haemoglobin with those that received placebo (p=0.705). This is consistent with the observation of Smith et al[26], that compared the haemostatic effect of intravenous ETH with a placebo and reported that ETH did not reduce the blood loss during gynaecological surgery under epidural anaesthesia. However, our result contrast the findings of Garay et al[9] and Harrison et al[10], that evaluated the therapeutic efficacy of ethamsylate in uterine bleeding and demonstrated that blood loss was reduced. But it was in menorrhagia management.

Ethamsylate has also been used to decrease blood loss in various pathologies such as menorrhagia, gynaecological surgeries, hip surgeries, ophthalmology procedures and tonsillectomies with conflicting results[26-30]. Ramos-Sánchez et al[27] reported that when they compared preoperative hemoglobin levels of the patients that had total hip replacement surgery, they observed that ETH did not reduce blood loss in their study. Cuevas et al[28] observed that single intravitreal injection of ethamsylate significantly cleared sub-macular haemorrhage and resolved choroidal neovascular membrane, and thus improved the visual acuity of their patient with sub-macular haemorrhage with suggestive associated choroidal neovascular membrane. Deacock et al[29] observed that when ETH was given to the patients undergoing tonsillectomy surgery, it reduced blood loss to the magnitude that is directly proportional to the severity of the surgery. While Gary et al[30] noted that no useful reduction in blood loss was observed from the use of ETH in patients that had tonsillectomy.

Accurate determination of blood loss is difficult. Various methods of estimating surgical blood loss have their shortcomings and thus, should be used with caution. We predicted the blood volume (PBV) of our patients using the method described by Nadler et al[31], that acknowledges the patient's body weight (kg) and height (m) in its calculation: PBV = (0.3561 X Height$^3$) + (0.03308 X Weight) + 0.1833. However, our emphasis during the study was to evaluate the haemostatic effect of both TXA and ETH, using the level of haemoglobin (Hb) loss as our determining factor. Thus, using the Breecher et al[32] method; $Hb_{loss}$ = ($Hb_{preoperative}$ - $Hb_{postoperative}$), we were able to determine the haemoglobin difference among the groups. We observed that the haemoglobin loss was lesser in the patients that received TXA (10.10%), compared with the patients that received ETH (13.29%) or placebo (14%). In a retrospective study conducted by Celebi et al[33] that focused on evaluating the rate at which the TXA reduces blood loss during gynaecological surgery for cancer, noted that the amount of perioperative bleeding was reduced by 30%. The decrease incidence of blood loss observed in our study could be related to the technique of surgery. Sixty seven percent of the patients evaluated, had abdominal myomectomy and in addition to the use of either of the study drugs, tourniquet was applied around the lower uterine segment and below the uterine fibroids, to achieve mechanical vasoconstriction on the ascending uterine artery bilaterally. This was removed at achieving haemostasis. A study[19] showed that the use of tourniquet has an adjunctive effect to the use of haemostatic agent in reducing blood loss during abdominal myomectomy.

Only the patients that received TXA had pain, bradycardia or hypotension, those in either TXA or placebo group had headache and dizziness, but the incidence of shivering was more in the patients that received placebo. However, all the groups had nausea and vomiting. The patients that had complication were appropriately managed. Complications observed in this study became apparent after the induction or top ups of epidural anaesthesia. Neuraxial block can be complicated by bradycardia, hypotension, headache, nausea and vomiting[3]. Nevertheless, some gastrointestinal complications like nausea and vomiting have been reported with the administration of TXA or ETH[34]. In another study conducted by Hajmurad et al[35], they reported that there is concern of thrombotic complications with TXA administration. Clot anuria can occur, especially in solitary kidney patients. Thus, patients with risk of thrombo-embolic diseases or are on anticoagulant, were excluded from this study. Dose-dependent risk of seizures after TXA administration during cardiac surgery with cardiopulmonary bypass has also been documented as one of the major complications of TXA administration[36]. The seizures might be explained by the inhibitory effect of TXA on gamma-aminobutyric acid type A and glycine receptors, which are two major mediators of central nervous system inhibition, resulting in synaptic excitation and increase the risk of seizures.

We had the limitation of not analyzing the surgical blood loss in terms of volume and evaluating the volume of blood transfused. We believe that more studies should be done to relate the haemostatic effect of TXA and ETH to the volume of surgical blood loss and quantity of blood products transfused during the intraoperative and postoperative period. Thus, we concluded that the administration of intravenous tranexamic acid before the induction of epidural anaesthesia for abdominal myomectomy or hysterectomy reduced the intraoperative and postoperative blood loss more, compared to the administration of intravenous ethamsylate or placebo, however with no clinical significance or apparent side effect.

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**Ethical Approval:** Approved

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