Reducing Blood Loss During Cesarean Myomectomy With Intravenous Versus Topical Tranexamic Acid: A Double-Blinded Randomized Placebo-Controlled Trial

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Citation

A A Taha, N W Shady, H F Sallam, M M Ahmed. *Reducing Blood Loss During Cesarean Myomectomy With Intravenous Versus Topical Tranexamic Acid: A Double-Blinded Randomized Placebo-Controlled Trial*. The Internet Journal of Gynecology and Obstetrics. 2023 Volume 27 Number 1.

DOI: 10.5580/IJGO.56699

Abstract

Objective: to evaluate the efficacy of intravenous versus topical tranexamic acid versus placebo for reducing blood loss for pregnant women with uterine leiomyomas who are undergoing CM.

DESIGN: A randomized, double-blind, clinical trial (ClinicalTrials.gov: NCT03505502).

Setting: Tertiary referral university hospital.

Methods: 120 pregnant women with uterine leiomyomas undergoing CM were randomly assigned to three groups: group I (placebo), group II (topical tranexamic acid) and group III IV tranexamic acid). The primary outcome was the estimation of intraoperative, postoperative, and total blood loss (ml). Mann Whitney test and Fisher's exact test were used for the analysis of the outcomes.

Results: Both Group II and Group III showed a significant reduction in intraoperative, postoperative, and overall estimated blood loss compared with Group I, (P=0.0001, 0.0001, 0.0001, 0.0001, 0.0001, 0.0001). The Postoperative hemoglobin was a significant decrease in group I compared to group II and III, (p=0.001 and 0.0001) respectively. The incidence of postpartum hemorrhage, the need for additional uterotonics, extra uterine artery ligation, and The incidence of blood transfusion were a significant increase in group I compared to group II and group III, respectively.

Conclusion: Intravenous and Topical Tranexamic acid application safe, reliable, and effective methods for the reduction of blood loss and the need for blood transfusion during CM.

INTRODUCTION

The prevalence of leiomyomas among pregnant women ranges from 0.1 to 10.7% depending on the gestational ages during the assessment, with leiomyomas more common among women of increasing maternal age (1). As cesarean delivery (CD)become more frequent and as many women delay pregnancy till older ages, The incidence rate of uterine fibroids will be increasing during CD (2).

Myomectomy during CD has traditionally been discouraged because of concerns about intraoperative bleeding, requiring hysterectomy, and concerns about increased postoperative complications (3).

Most obstetricians have been taught not to perform myomectomy during CD because of the risks of intractable bleeding, massive hemorrhage, and hysterectomy. In many situations, cesarean myomectomy is essential for the delivery of the fetus (4).

The more recent medical literature, however, indicates that cesarean myomectomies are probably safe if performed for justified indications, by experienced surgeons and by using meticulous tissue handling techniques who avoid unnecessary hysterectomies as well as serious and life-threatening complications. There is a benefit in performing a single operation indicated anyhow rather than two (5).

One important issue with myomectomy is controlling bleeding from the raw myoma beds after myomectomy (6).

In the literature, many studies report the use of Tranexamic Acid (TA) to reduce blood loss if given prophylactically at myomectomy. TA is an anti-fibrinolytic agent better known to gynecologists for oral use as a treatment of menorrhagia, and to trauma surgeons where it has been shown to reduce blood loss (7).

Safety concerns associated with intravenous administration of tranexamic acid include thrombosis, increased seizure risk, and renal impairment. Considering the safety concerns with intravenous administration, there has been a growing knowledge in the topical use of tranexamic acid for the prevention of blood loss associated with many surgical procedures(8). However, among the reported hemostatic strategies, the best strategy for CM was still unclear (9)

In our previous studies report the use of Tranexamic Acid (TA) to reduce blood loss if given prophylactically at hysterectomy and myomectomy (10,11).

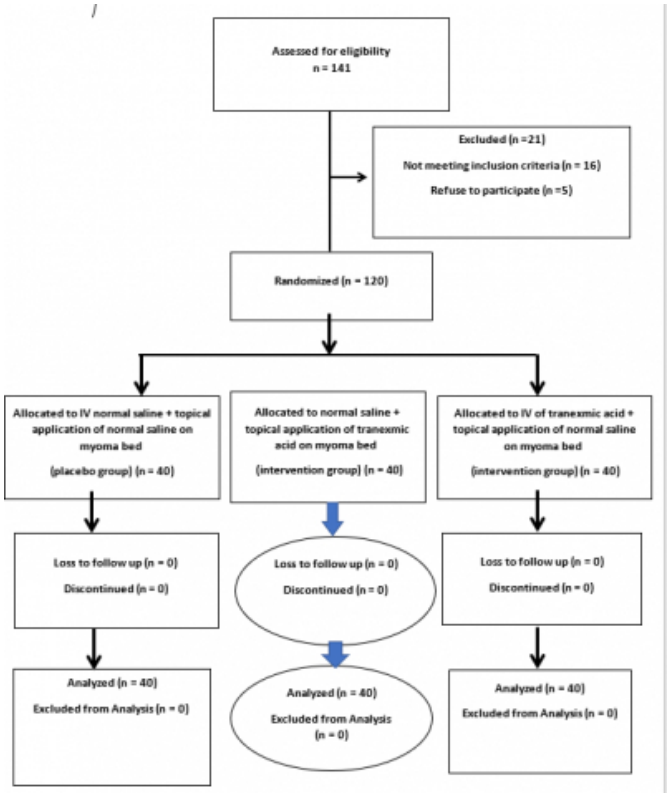
Given the positive impact of TA on hemostasis in other specialties, perhaps modifications to the intravenous TA dosing and administration regimens may translate to a positive impact on hemostasis during CM(12).

In the view of lack of knowledge and experience highlights to inform on the best practices for prevention of bleeding during CM our study aimed at evaluating the role of adjunctive IV versus Topical tranexamic acid application for prevention of hemorrhage in women with CM.

MATERIALS AND METHODS:

It was a clinically registered randomized, double-blind, clinical trial (ClinicalTrials.gov: NCT03505502) conducted in a tertiary university hospital. The ethical review board approved the study by a grant number of (Aswu/203/2/18). The study participants were either women who attended the outpatient gynecology clinic, seeking antenatal care, and discovered they had leiomyomas or women who attended a labor ward for emergent CS with leiomyomas then they scheduled to undergo cesarean myomectomy from 1st of January 2018 to 30th of June 2022. Women who met the selection criteria of the study were invited to participate after signing informed consent. This trial was conducted and reported according to the CONSORT updated guidelines for reporting parallel group randomized trials (13).

Figure 1



ELIGIBLE PARTICIPANTS

Study inclusion criteria were women who underwent myomectomy at the time of cesarean delivery. All the women fulfilled the following criteria: (1) documented fibroid uterus during the index pregnancy by antenatal ultrasound and conferment by intraoperative findings; (2) delivery by cesarean delivery; (3) no evidence of antenatal bleeding;(4) no other procedures at the time of CS besides myomectomy. Exclusion criteria were: 1-Patients with preeclampsia, cardiac, hepatic, renal, or thromboembolic disease. 2-patients with Cervical myoma, broad ligament myoma, and Myoma FIGO staging (1,2,7 and 8). 3-patients with placenta previa or antepartum hemorrhage. 4-patients had an allergy to tranexamic acid. Indications for possible cesarean myomectomy included: patients' desire, symptomatic myomas, and degenerative myoma.

141 patients were asked to participate,21 patients were excluded,16 patients not meeting inclusion criteria and 5 patients refuse to participate. therefor the remaining 120 patients were included in the study. All participants underwent detailed history, general, and obstetric examinations, body weight, and Hight were calculated and an abdominal ultrasound examination was undertaken for all participants. The participants who fulfilled the eligibility

criteria were explained about the study with the beneficial and possible adverse effects of tranexamic acid. Informed consent was obtained from them after that participants were randomized to 3 groups: group 1 [40 patients received 110 ml normal saline IV just before skin incision], group II [40 patients received 2gm topical tranexamic acid (4 ampoules of kapron 500mg 5 ml), and group III [40 patients received 1 gm tranexamic acid (2 ampoules of kapron 500 mg 5 ml. Amoun company) IV just before skin incision].

RANDOMIZATION

Patients were randomized to three groups, each compromised of 40 patients according to a three-blocked randomization list which was coded (I or II or III) at a 1:1:1 ratio. The three parallel groups were prepared using a Computer-generated randomization system. The allocated groups will be concealed in serially numbered sealed opaque envelopes that will only be opened after recruitment. Patient allocation will be performed before the induction of anesthesia by an independent person, who will not otherwise be involved in this study. The trial will be appropriately blinded; the participants, outcome assessors, and the surgeon performing the procedure will be blinded to the medication type, which will be used.

INTERVENTION

Eligible participants were allocated to one of three groups after induction of spinal anesthesia and immediately before the operation and just before skin incision. They received 1-gram tranexamic acid (10 ml) in 100 ml saline infusion or placebo (110 normal saline) by slow intravenous injection at an approximate rate of 1 mL per min just before skin incision. Also, all patients received Prophylactic antibiotics in form of Cefazolin 2 g I.V, after that Pfannenstiel incision was done then the subcutaneous fat and abdominal fascia were opened crosswise, and the rectus muscle was opened on the midline, the parietal peritoneum was opened longitudinally, the visceral peritoneum was opened transversely and dissected downwards with the bladder and kept against symphysis pubis by a Doyen retractor, followed by transverse incision at lower uterine segment then delivery of The fetus &placenta. Then 20 unit oxytocin was infused.

After that Uterus was inspected for number, location, and staging of myomas, then CM was done for all myomas using the same cesarean incision where possible or utilizing other incisions, when necessary.

Intracapsular serosal enucleation of myomas was performed by gently dissecting between the myoma and the pseudo capsule (9). The myoma was grasped by Collins forceps and gently enucleated out. A gauze soaked with 2g tranexamic acid (20 ml) diluted in 100 ml of sodium chloride 0.9% or placebo (120ml of sodium chloride 0.9%.) used to compress the myoma bed for 5 minutes. To ensure a sufficiently high concentration, the tranexamic acid was diluted only to a volume sufficient to moisten a fairly large wound surface: 20 ml moisten at least 1500 cm2. Myoma bed was closed by 1 or 2 layers of interrupted vicryl sutures (Vicryl 1–0 polyglactin 910; Egycryl, Taisier CO, Egypt). At the end of the surgery, 1 intraperitoneal suction drain was routinely used in all patients the drains were removed on the second postoperative day unless otherwise indicated. Enucleated myomas were sent to histopathology. All operations were ever performed by the same obstetrician's team.

BLOOD LOSS ESTIMATION

Intraoperative blood loss was measured by adding the volume of the contents of the suction bottle after delivery of the baby and placenta and the difference in weight (in grams) between the dry and the soaked operation sheets and towels (1 gram = 1 ml.). Post-operative blood loss was measured through the intraperitoneal suction drain which measured every 12 hours and on removing the drain plus blood loss through the vagina during the first 24 hours post-operative. After that, the total blood loss was calculated by the addition of intraoperative and postoperative blood loss.

STUDY OUTCOME

The primary outcome was the estimation of intraoperative, postoperative, and total blood loss (ml). The secondary outcome measures included: operative time, a period for hospitalization, the incidence of postpartum hemorrhage, the need for additional uterotonics, uterine artery ligation, and blood transfusion. Also, Hemoglobin concentration was done in all patients preoperatively and 24 hours postoperative, and the change in concentration was noted. Any side effects such as fever, nausea, vomiting, and diarrhea were recorded.

SAMPLE SIZE

As blood loss is the primary outcome variable, it is used for calculation of sample size. The sample size was calculated based on published data in women undergoing cesarean delivery using a single 15 mg/kg preoperative dose of tranexamic acid which showed a statistically significant reduction in blood loss of 250 ml in women who received

tranexamic acid compared to placebo (14). The sample size 40 patients in each arm, was calculated to detect a mean 250 ml difference in estimated blood loss between groups with a power of 85% at the 5% significance level.

STATISTICALLY ANALYSIS:

Data were entered and statistically analyzed using the Statistical Package for Social Sciences (SPSS) version 16. Qualitative data were described as numbers and percentages. Chi-square test and Monte Carlo test were used for comparison between groups, as appropriate. Quantitative data were described as means (SD) or medians, as appropriate. They were tested for normality by the Kolmogorov-Smirnov test. In the normally distributed variables, a one-way ANOVA test with LSD post-hoc multiple comparisons was used for comparison between groups, as appropriate. In the non-normally distributed variables, the Mann Whitney test and Kruskal-Wallis test were used for comparison between groups, as appropriate. Odds ratios and their 95% confidence interval were calculated. "p-value ≤0.05" was statistically significant.

RESULTS:

Our study started with 141 patients who were asked to participate,21 patients were excluded,16 patients not meeting inclusion criteria and 5 patients refuse to participate. therefor the remaining 120 patients were randomized to 3 groups each group comprised 40 patients. Group I: (received 1 gm IV normal saline before skin in scion), Group II:(received 2 gm topical tranexamic acid application after myomectomy on the myoma bed) and Group III (received 1 gm tranexamic acid IV before skin incision).

There was no significant difference between the three groups concerning their age, weight, height, body mass index (BMI), parity, gestational age, initial hemoglobin, and an indication of CS. (Table 1). Also, there was no significant difference concerning number of the myomas, myoma stage, myoma site, and the size of the largest myoma. (Table 2).

Table 1

Table (1): preoperative Characteristics of pregnant women in the study groups: -

Parameters	Group I (n = 40)	Group II (n = 40)	Group III (n = 40)	Significance
Age (year)	29.5 ± 2.42	29.6 ± 2.68	29.83 ± 2.85	0.854
Weight (kg)	69.25 ± 7.76	69.43 ± 7.18	69.4 ± 7.77	0.994
Height (cm)	162.45 ± 4.19	163.58 ± 4.38	163.52 ± 4.6	0.436
BMI	26.2 ± 2.55	25.96 ± 2.74	25.94 ± 2.71	0.888
Parity (median) (minimum – maximum)	3 (0 – 4)	2 (0 – 5)	3 (0 – 5)	0.866
Gestational age (weeks)	37.4 ± 1.45	37.55 ± 1.34	37.5 ± 1.22	0.878
Initial Hemoglobin	9.97 ± 0.624	9.98 ± 0.623	10.03 ± 0.622	0.905
indication of CS (%)				
repeated cs	23(57.5)	21(52.5)	24(60)	
breech	8(20)	9(22.5)	6(15)	
CPD	2(5)	3(7.5)	4(10)	0.965
fetal destress	4(10)	5(12.5)	5(12.5)	
patient request	3(7.5)	2(5)	1(2.5)	

BMI (body mass index), CS (Cesarean Section), CPD (cephalopelvic disproportion)
Variables are presented as mean and standard deviation, median (minimum – maximum) and number (percentage).

Table 2

Table (2): Characteristics of myoma in the study groups: -

Parameters	Group I (n = 40)	Group II (n = 40)	Group III (n = 40)	Significance
No of myoma	3(1-4)	2(1-5)	2(1-4)	0.560
Myoma stage	5(4-6)	5(4-6)	5(4-6)	0.950
Myoma site (%):				
Upper segment	30(75)	28(70)	26(65)	0.621
Lower segment	10(25)	12(30)	14(35)	
Largest myoma	9.45 ± 2.61	9.78 ± 2.496	9.18 ± 2.51	0.573

Variables are presented as median (minimum – maximum), number (percentage)and mean and standard deviation.

Both Group II and Group III showed a great reduction in intraoperative and postoperative blood loss compared with Group I, (P=0.0001,0.0001,0.0001,0.0001), so the overall estimated blood loss in group II and III showed highly reduction compared with group I (P=0.0001,0.0001).

However, no significant difference in overall estimated blood loss either intraoperative or post-operative between group II and III,

(P= 0.623, 0.318, and 0.588 respectively). (Table 3)

Table 3

Table (3): primary outcome in the study groups: -

Blood loss	Group I (n = 40)	Group II (n = 40)	Group III (n = 40)	Significance
Intraoperative	725(320-1050)	510(190-1000)	500(200-1050)	0.0001* 0.0001* / 0.0001* / 0.623
postoperative	198.6 ± 40.98	111.63 ± 21.67	105.0 ± 21.72	0.0001* 0.0001*/ 0.0001*/ 0.318
Total blood loss	952.25 ± 186.7	620.5 ± 206.92	596.5 ± 199.04	0.0001* 0.0001*/ 0.0001*/ 0.588

* Statistically Significant Difference (Group I Versus Group II / Group I Versus Group III / Group II Versus Group III)

Variables are presented as median(minimum-maximum) and mean and standard deviation.

Postoperative hemoglobin was a significant decrease in group I compared to group II and III, (p=0.001 and 0.0001) respectively. The incidence of postpartum hemorrhage was a significant increase in group I, 18 (45%) patients compared to group II,3 (7.5%) patients, and group III, 2(5%) patients, (p=0.0001 and 0.0001). Also, the need for additional uterotonics was a significant increase in group I,22 (55%) patients compared to group II, 5(12.5%) patients, and group III,3(7.5%) patients, (p=0.0001 and 0.0001). Patients needed extra uterine artery ligation also a significant increase in group I, 9(22.5%) compared to 2(5%) patients in group II, and 1(2.5%) patient in group III, (p=0.023 and 0.007) respectively. The incidence of blood transfusion was increased in group I, 20 (50%) patients compared with 5 (12.5%) patients in group II, and 3 (7.5 %) patients in group III. (P= 0.0001 and 0.0001). However, no significant difference between group II and group III concerning postoperative hemoglobin, the incidence of postpartum hemorrhage, additional uterotonics, uterine artery ligation, and the incidence of blood transfusion. (p=0.778, 1.00, 0.712, 1.00 and 0.712 respectively).

There was a significant decrease in operative time in group I and group III compared with group II, (p= 0.0001 and 0.0001). Also, operative time was a significant decrease in group III compared to group I, (p=0.018). There was a significant decrease in hospital stay in group II compared to group I, (p=0.005). However no significant difference between group III compared to group II and group I about the hospital stay, (p= 0.201 and 0.119 respectively).

Finally, no significant difference between the three groups related to postoperative complications in the form of fever, nausea, vomiting, and diarrhea. (P= 1.00, 0.906, 1.00, and 0.620 respectively). (Table 4)

Table 4

Table (4): secondary outcome in the study groups: -

Variables	Group I (n = 40)	Group II (n = 40)	Group III (n = 40)	Significance
Post hemoglobin	8.43 ± 0.856	9.11 ± 0.923	9.17 ± 0.944	0.001* 0.001* / 0.0001* / 0.778
Operative time	58.48 ± 7.84	91.43 ± 7.931	56.73 ± 4.61	0.0001* 0.0001* / 0.018* / 0.0001*
Hospital stay	4.45 ± 0.815	3.95 ± 0.71	4.18 ± 0.813	0.019* 0.005* / 0.119 / 0.201
Post-partum hemorrhage (%)	18 (45)	3 (7.5)	2 (5)	0.0001* 0.0001* / 0.0001* / 1.00
Additional Uterotonics (%)	22 (55)	5(12.5)	3 (7.5)	0.0001* 0.0001* / 0.0001* / 0.712
Need Blood Transfusion (%)	20(50)	5 (12.5)	3 (7.5)	0.0001* 0.0001*/ 0.0001*/ 1.12
Uterine artery ligation (%)	9(22.5)	2(5)	1(2.5)	0.008* 0.023*/ 0.007*/ 0.712
Fever (%)	2(5)	3(7.5)	2(5)	1.000
Nausea (%)	2 (5)	3 (7.5)	4 (10)	0.906
Vomiting (%)	1 (2.5)	2(5)	2 (5)	1.000
Diarrhea (%)	1 (2.5)	1 (2.5)	3 (7.5)	0.620

*Statistically Significant Difference (Group I Versus Group II / Group I Versus Group III / Group II Versus Group III)

Variables are presented as mean and standard deviation and number (percentage).

DISCUSSION

This study is the first double-blind randomized placebo-controlled trial comparing the effectiveness of intravenous versus topical TA for diminishing loss for pregnant ladies with uterine leiomyomas who are experiencing CM. The outcomes demonstrated that the intravenous or topical utilization of TA could essentially decrease the intraoperative, post-operative, total blood loss, and blood transfusion necessities after CM. Also, no cases with deep venous thrombosis as well as aspiratory embolism were recognized.

In the best of our knowledge for the utilization of TA in reducing blood loss during CM, no studies concerning the utilization of TA were recognized. Past principal research has detailed that the degrees of plasminogen activators expanded 30 minutes after the initiation of surgery. (12) Thus, the hypothetical basis could clarify an expected efficiency of TA for decreasing loss for surgical procedures with special concern with CM.

Given the positive impact of TA on hemostasis in other specialties, perhaps modifications to the intravenous and topical application of TA dosing and administration regimens may translate to a positive impact on hemostasis during myomectomy. (7) However, the ideal mode of administration is debatable. Limited literature has compared all the available modes of administration including intravenous (IV), topical irrigation, and retrograde through the drain. (9) Our study showed that no difference present between IV and topical application of TA in reducing hemorrhage during CM.

Bonney, (15) a pioneer in a uterine myomectomy, distributed his first description of CM in 1914. During CD in a 30□year□

old primipara ladies with numerous myomas, he evacuated six myomas, of which the biggest was "the size of a melon". In his comments, he underlined that "the unequivocally retractile condition of the uterine dividers is unconventionally good for enucleation since it decreases the hemorrhage from the cavities ". Following the CM, these women had three vaginal deliveries.

In 1989, Burton et al. (16) were most likely the first to report the system of myomectomy during pregnancy and CD. They assessed an 8-year involvement in the surgical management of leiomyomata during pregnancy. Five ladies experienced explorative laparotomy, six had a myomectomy during pregnancy, and three had a hysterectomy; one patient aborted after surgery. Thirteen other ladies had coincidental myomectomies at CD; one of these had an intraoperative drain. No other complications were accounted for.

Dimitrov et al. (17) led a forthcoming study in Bulgaria to assess myomectomy during CS as "a normal strategy". Their investigation group contained 21 cases that experienced myomectomies during CS and were contrasted with a control group of 162 successive CS without having experienced myomectomies. They found that myomectomy during CS expanded the blood loss by 10 %.

Ehigiegba et al (18), prospectively assessed the intra- and post-operative complications of cesarean myomectomies in 25 pregnancies. Anemia was apparent in 60 % of patients but only five patients (20 %) required blood transfusion. Three patients (12 %) had subsequent pregnancies, two of whom had normal vaginal deliveries and one underwent a repeat CS.

The CM has various advantages over non-CM. Incisions on the uterus are commonly littler because the uterus/tumor proportion is littler than in a non-pregnant uterus. Myomectomy itself is, in fact, simpler to perform, because of simpler recognizable proof of the cleavage plane. The flexibility of the pregnant uterus empowers the easy placement of stitches, while uterine contractions and physiological involution in the puerperium further decrease hemorrhage. (19) Our study showed that the addition of TA would be further prevented hemorrhage and hematoma formation at the CM site.

The CM has the advantage of two tasks in one (CD and myomectomy), in this manner forestalling both the dangers and expenses of reoperation. (20) In an examination from Taiwan, up to 40.9% of patients, who had just CS while likewise having myoma, required repeat surgery during follow-up of 6–38 months for suggestive myoma. (21)

Besides, CM gives side effect alleviation and improved personal satisfaction in affected ladies and takes out the dangers of myoma-induced complications in puerperium and resulting pregnancies. For CM, Kanthi et al. contrasted CM and abdominal myomectomy in ladies with a solitary fibroid. (22) The CM group included 33 patients with a normal myoma size of 66.9 ± 57.6 mm, of which 73% were subserous. The abdominal myomectomy group comprised of 32 patients with myoma size 96.4 ± 3.20 mm, of which 72% were intramural. Hemoglobin drop, as a mean result measure, just as the frequency of blood transfusion, did not vary among the groups. The authors inferred that the blood loss was comparative among CM and abdominal myomectomy in ladies with single fibroids, making CM a sensible alternative in such cases.

The CM bears the danger of significant hemorrhage, because of high uterine vascularization in pregnancy, with an announced frequency of intraoperative hemorrhage in CM going from zero to 35.3%. (23)

Therefore, perioperative hemorrhage and its outcomes are the most regularly described complications, and literature remembers reads for huge perioperative hemorrhage requiring: reoperation, hysterectomy, blood vessel embolization, or ligation, and blood transfusion. (23)

One important issue with myomectomy is controlling blood loss from the raw myoma beds after their removal. Blood loss is generally estimated from the suction aspiration, and from weighing swabs and drapes used during surgery. Several techniques to reduce blood loss have been studied and reported. A randomized trial comparing vasopressin and saline injected into the serosa before the uterine incision showed that vasopressin is extremely effective for decreasing blood loss. In this study, 50 % of patients receiving saline required transfusion, while none of those in the vasopressin group required transfusion (13 % vs 5 % decrease in hematocrit values) (24).

Three classifications of interventions have been identified that may diminish blood loss during myomectomy; these incorporate (I) mediations on uterine vessels such as laparoscopic uterine artery dissection, uterine artery embolization, paracervical mechanical tourniquet, and hormonal tourniquets, for example, vasopressin and terlipressin; (ii) uterotonics, for example, ergometrine,

oxytocin, misoprostol, and sulprostone; and (iii) myoma dissection procedures, which incorporate the utilization of laser, and synthetic dissectors, for example, sodium-2-mercaptoethanol sulfonate (mesna). (25,26)

TA is a regularly utilized hemostatic medication in clinical practice, which can seriously hinder the binding of plasmin to fibrin monomers and fibrin-interceded initiation of plasminogen. In any case, there were worries that TA may systemically affect expanding the danger of thrombosis without the simultaneous utilization of thromboprophylaxis regimen [27]. There were no cases of DVT or pulmonary embolism in our study. However, no long-term follow-up has been maintained.

There was no study in the literature address the role of IV TA during CM although a meta-analysis of the effect of prophylactic TA treatment in major benign uterine surgery showed that prophylactic treatment with TA in women undergoing myomectomy was associated with a reduction of intraoperative blood loss by 251 mL. (28)

There was no study in the literature address the role of topical TA during CM although Two case reports on the use of topical TA to control postoperative local bleeding in 2 women with clotting disorders who were undergoing gynecologic procedures. (29)

A 51-year-old woman with essential thrombocytopenia underwent an uneventful total abdominal hysterectomy and sapling-oophorectomy; however, the patient experienced a continuous loss of blood from drains There were no cases of DVT or pulmonary embolism in our study. However, no long-term follow-up has been maintained. placed in the peritoneal cavity and sub rectal space. After multiple failed attempts to stop the bleeding with pressure dressings, a pressure dressing soaked in 5 mL of TA (100 mg/mL) was applied. Bleeding decreased within a few minutes, and 2 additional applications were used over a 48-hour period, which allowed the patient to be discharged with no further complications on postoperative day 6. (29)

In the second case, a 75-year-old female with a history of severe factor XI deficiency underwent a vaginal hysterectomy and vaginal wall repair. Postoperatively, the vaginal vault oozed blood which could not be controlled with vaginal packs. The bleeding was better controlled once a vaginal pack soaked in 15 mL of TA (100 mg/mL) was applied, with a reduction in bleeding observed the following day. The patient was subsequently initiated on oral TA, given as 1 g daily for 7 days, and was discharged on a postoperative day 6 with no further complications. (29)

One limitation of our study was we are not used alkaline hematin method which is a validated method for accurate measurement of blood loss, but use instate a gravimetric method to measure the amount of blood loss. However, Marcel H et al 2004 in veterinary surgery compare gravimetric and colorimetric methods of quantifying surgical blood loss and conclude that Estimation of blood loss using a gravimetric method is an accurate and objective tool to evaluate intraoperative blood loss (30)

One of the strengths of our investigation was that a double-blind randomized examination gives the first proof that IV or topical TA a basic option preemptive intervention for diminished intraoperative blood loss and need of blood transfusion during CM. Another quality of the investigation lies in its simplicity that a basic effectively do-capable intervention can bring about a clinically significant decrease in intraoperative blood loss.

CONCLUSION

The results support the hypothesis that intravenous and topical TA application is a safe and reliable method to help decrease blood loss during and after the CM. This study indicates the use of topical TA in patients undergone CM is associated with decreased blood loss as intravenous TA.

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