

Prophylactic use of temporary uterine packing combined with topical tranexamic acid reduces blood loss and transfusion requirements in patients undergoing cesarean section: A double-blind, randomized controlled trial

Ahmed A. Taha^{a*}, Nahla W. Shady^a, Hany F. Sallam^a, Moussa M Ahmed^b

^aObstetrics and Gynecology Department, Faculty of Medicine, Aswan University, Aswan, Egypt.

^bObstetrics and Gynecology Department, Faculty of Medicine, Sohag University, Sohag, Egypt.

Abstract

Background: since antiquity post-partum haemorrhage (PPH) has been a terrible event for obstetricians. It accounts for 34% of maternal deaths in Africa and developed countries. It complicates 6% of cesarean delivery (CD) and still raising and correlates with increased frequency of caesarean sections, many uterotonic agents have successfully used alone or in combinations for prevention of such catastrophic, but the most effective medication is still up for controversy.

Objective: To compare the efficacy and safety of temporary uterine packing combined with topical tranexamic acid (TA) as adjunct for reducing blood loss following an elective cesarean delivery with intravenous tranexamic acid and placebo in women who have at least one risk factor for postpartum hemorrhage.

Patients and methods: A double-blind, randomized clinical trial (: NCT03706339) conducted on 450 pregnant women at term (38–40 weeks) gestation scheduled for elective cesarean delivery, who were assigned to either intravenous TA, topical TA, or placebo(saline). The main outcome measures were blood loss at and 6 hours after cesarean delivery, the need for any additional oxytocic drugs, and TA-related side effects.

Results: There was a significant decrease in the intraoperative blood loss and total blood loss in both topical TA and IV TA groups compared to placebo group ($p=0.0001, 0.0001, 0.0001, 0.0001$). Also, the need to extra uterotonics was significant decrease in IV TA group, 9 (6%) patients compared to 33 (22%) patients in placebo group, and 24 (16%) patients in topical TA group, ($p=0.0001$ and 0.006) respectively. Finally, operative time, hospital stay, postoperative hemoglobin, and post-operative complication showed no significant difference between the three groups ($P= 0.276, 0.126, 0.853, 0.955, 1.00, 1.00$) respectively.

Conclusion: IV TA and temporary uterine packing combined with topical tranexamic acid is more effective than placebo in reducing total blood loss during and after cesarean delivery in women who have at least one risk factor for postpartum hemorrhage, but IV TA more effective.

Keywords: Tranexamic acid; Cesarean delivery; Postpartum hemorrhage.

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***Correspondence:** ahmedramydoc@gmail.com

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Introduction

Post-partum haemorrhage (PPH) which occurs in 20% of cases and is responsible for about one-fourth of all maternal deaths worldwide, continues to be the most common complication despite different techniques used to stop excessive haemorrhage after CD, leading to higher rates of maternal morbidity and mortality. According to estimates, primary PPH happens in two to six percent of parturient worldwide is responsible for 34% of maternal deaths in Africa (Say et al., 2014; Ujjiga et al., 2014).

Since there has been an increase in the prevalence of caesarean deliveries (CD) in various places throughout the world, CD rates can reach 25–30%, and therefore the average blood loss during a CD (1000 mL) is double that of a vaginal delivery (500 mL) (Kandil, 2018).

An unexpected excessive blood loss after delivery may occur all sudden to a parturient and remain one among the leading causes of obstetric morbidity and mortality throughout the worldwide. Timely management strategies are urgently needed wherever women deliver. Despite significant advancements in obstetric care, 125,000 women die from blood loss related to delivery annually within the world (Say et al., 2014).

While plasminogen activators and fibrin degradation products rise due to the activation of the fibrinolytic system after placental delivery, fibrinogen and fibrin are rapidly broken down. The fibrinolytic enzyme plasmin increased bleeding by speeding up the breaking of blood clots during this activation, which can last up to 6–10 hours postpartum (Shakur et al., 2017).

It is generally accepted to utilize tranexamic acid (TA) to treat postpartum

haemorrhage. The modality and method of application, the appropriate duration for infusion, and in particular the dose of TA applied—which is typically different in each work—raise concerns about potential dangers of its use (Li et al., 2018).

The lysine derivative TA, which has a relative molecular mass of 157, blocks the lysine-binding sites on the plasminogen molecules in order to indirectly exercise its antifibrinolytic effects. Because TA has a reversible and competitive action, inhibiting TA results in a lower affinity of plasminogen to bind to fibrin, which in turn results in a reduced activation of plasminogen to plasmin (Scher et al., 2021).

Since TA acts directly at active bleeding and clot formation sites and not within the circulation, its competitive mechanism of actions should be successful when administered topically. This prevents fibrin breakdown. It was previously believed that this successfully limits blood loss by achieving a higher therapeutic concentration at the site of bleeding (Jia and Junqing, 2019).

Lechien et al.(2021) postulate that It is yet unclear whether the effectiveness of topical tranexamic acid administration in CD for lowering blood loss in high-risk groups for postpartum haemorrhage is adequate to or but that of IV administration because to the shortage of trials comparing its use. On other hand In order to reduce the rate of post-partum haemorrhage, particularly in high-risk groups, the current research objectives need to consider the role for topical administration of TA.

The current study compares the efficacy intravenous versus temporary uterine packing combined with topical tranexamic with placebo in reducing blood

loss during and after caesarean delivery in women who have a minimum of one risk factor for postpartum hemorrhage. Our hypothesis that intravenous TA and temporary uterine packing with topical TA effective than placebo in reducing postpartum blood loss during CD.

Patients and Methods

A prospective, double-blinded, randomized placebo-controlled study (ClinicalTrials.gov: NCT03706339) was performed at the Obstetrics and Gynecology Department of a Tertiary University Hospital, Egypt, between November 1, 2018, and March 30, 2022. Women with full-term pregnancies who were scheduled to undergo an elective lower-segment cesarean and had a risk factor for postpartum hemorrhage were eligible for inclusion. Women who met the choice criteria of the study were invited to participate after signing an informed written consent. This trial was conducted and reported consistent with the CONSORT updated guidelines for reporting parallel group randomized trials (Schulz et al., 2010), and consistent with the revised recommendations of ClinicalTrials.gov for improving the standard of reporting randomized clinical trials.

Eligible Participants

Women who were scheduled for elective CD and had postpartum haemorrhage risk factors met the inclusion criteria for the study. Exclusion standards included: 1- the patients had a tranexamic acid allergy. 2- Patients with conditions including cardiac, preeclampsia, renal, hepatic, severe anaemia, thromboembolic illness, or diabetes Miletus, or those who use medications that may interfere with study drugs. 3- patients with defective placentas. 4- Patients who have any type of

pelvic pathology, such as severe endometriosis, uterine leiomyoma, severe pelvic adhesion, etc., require additional surgical intervention. 5. Patients who are unable to receive spinal anesthesia.

A total of 500 patients were asked to participate; 50 were rejected, 40 did not match the requirements, and 10 declined. The study therefore covered the remaining 450 patients. All participants got thorough medical history, general, and obstetric examinations. Body weight, height, and preoperative hemoglobin levels were also measured for each participant before an abdominal ultrasound was performed. Participants who met the eligibility requirements were informed about the study's purpose and any potential risks associated with tranexamic acid. After the individual was randomly assigned to one of three groups (the placebo group, normal saline NaCl 0.9%), the topical TA group, and the IV TA group), their informed written agreement was acquired (**Fig.1**).

Randomization

In accordance with a three-blocked randomization list that was coded (I or II or III) at a 1:1:1 ratio, patients were randomly assigned to one of three groups, each of which consisted of 120 patients. In order to create the three parallel groups, a computer-generated randomization mechanism was used. The assigned groups will be kept secret within serially numbered, opaque envelopes that won't be opened until recruitment. Prior to the onset of spinal anesthesia, patient assignments will be carried out by a third party who will not be actively involved in this investigation. The trial will be properly blinded; participants, outcome assessors, and the surgeon performing the procedure will all be unaware of the type and dosage of the medicine that will be utilized.

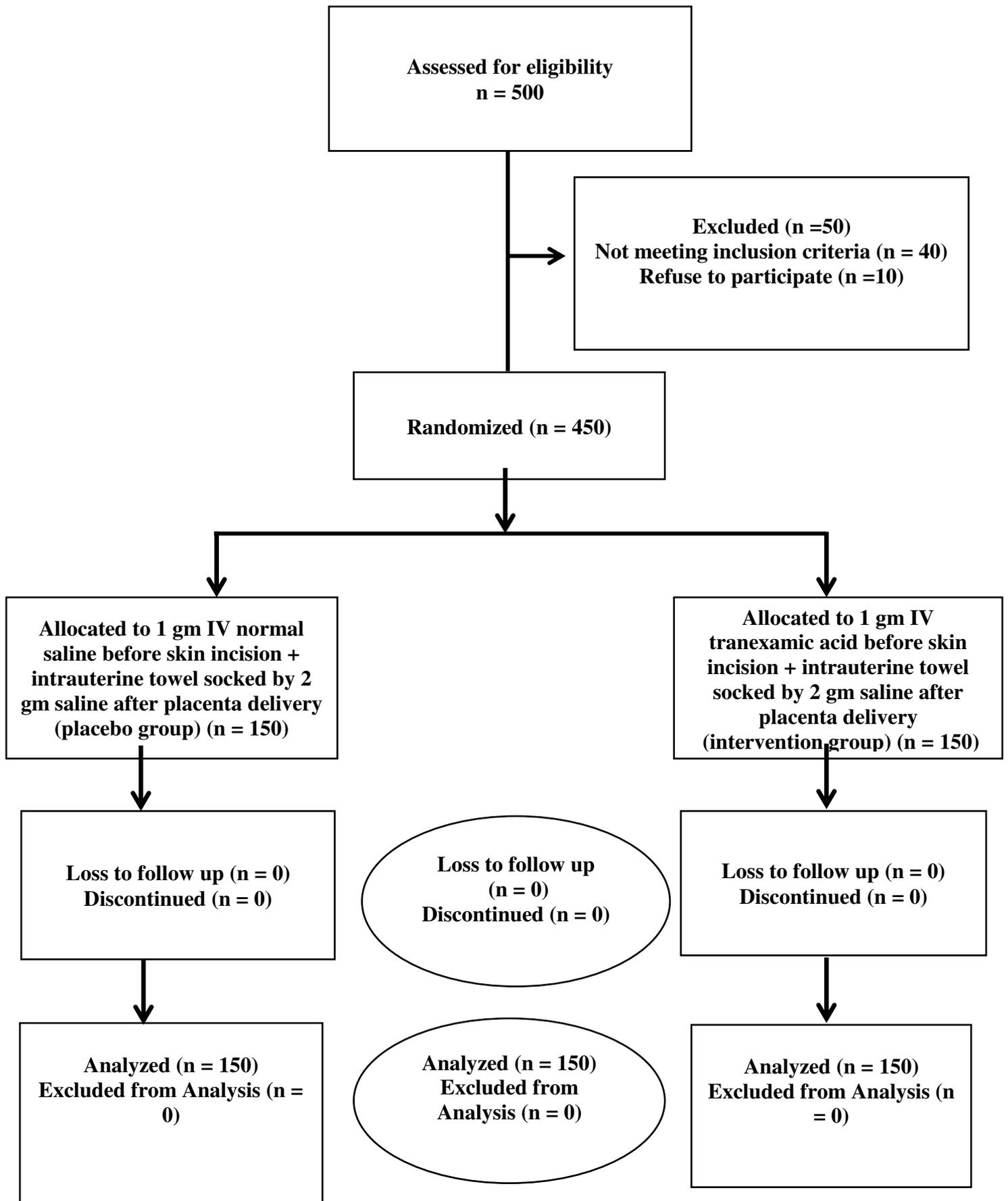


Fig.1. Study flow chart

Intervention

Eligible participants were allocated to one of the three groups 15 minutes before induction of spinal anesthesia.

1-Group I: (received 110 ml IV normal saline before skin incision + towel soaked with 60 ml saline inserted intrauterine at the placental bed after placenta delivery for five minutes) (placebo to IV and topical TA).

2-Group II: (received 110 gm IV normal saline before skin incision + towel soaked with 2 gm tranexamic acid (4 ampoules of kapron 500 mg 5 ml. Amoun company) diluted in 50 ml of sodium chloride 0.9%), it is inserted intrauterine at the placental bed after placenta delivery for five minutes) (topical TA+ placebo to IV TA).

3-Group III (received 1 gm tranexamic acid (2 ampoules of kapron 500 mg 5 ml. Amoun company) IV before skin incision + towel soaked with 60 ml saline inserted intrauterine at the placental bed after placenta delivery for five minutes) (IV and placebo to topical TA). Following delivery, patients in all groups received an intravenous bolus of 5 IU oxytocin (Syntocinon, Novartis, Basel, Switzerland), 1 mL (0.2 mg) intramuscular ergometrine (Methergin, Novartis, Basel, Switzerland), and 20 IU oxytocin in 500 mL lactated Ringer's solution (infused at a rate of 125 mL/h). Fluid monitoring was performed through rate of infusion and urine output. A complete blood count test was performed 24 hours after delivery.

The uterine tone was assessed consistent with a five-point scale, where 1 = atonic, 2 = partial but inadequate contraction, 3 = adequate contraction, 4 = well contracted and 5 = alright contracted by the operating obstetrician immediately after delivery of

the placenta then every 5 min until abdominal closure began. Additional oxytocic therapy was given if the uterine tone was inadequate, or the cesarean delivery become hemorrhagic.

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 vaginal blood loss during the first 24 hours post-operative by calculating the difference in weight (in grams) between the dry and the soaked vaginal pads (1 gram = 1 ml). Then the estimated total blood loss was calculated by the addition of intraoperative and postoperative blood loss.

Study Outcome

The primary outcome was the estimation of blood loss during and after cesarean delivery.

The secondary outcome measures included the need for any additional oxytocic drugs, postoperative Hemoglobin concentration, the incidence of postpartum hemorrhage, operative time, and incidence of side effects (nausea, vomiting, and diarrhea).

Sample size

The sample size was calculated based on the first outcome (blood loss in women after cesarean delivery), taking mean blood loss with the utilization of oxytocin alone without TA as 596 mL with a typical deviation of 38mL (**Abdel-Aleem et al., 2013**). Assuming that TA effective in reducing blood loss by 205mL, 150 participants in each group will have > 90% power at 5% significance to detect such a difference (Epi-info: Centers for Disease

Control and Prevention, Atlanta, GA, USA).

Statistical Analysis

Utilizing version 16 of the Statistical Package for Social Sciences (SPSS), data were entered and statistically analyzed. Numbers and percentages were used to describe qualitative data. To compare the groups, a Chi-square test was utilized. The proper means (SD) or medians were used to characterize quantitative data. The Kolmogorov-Smirnov test was used to determine their normalcy. Using independent samples t-test, groups were compared within the normally distributed variables. For group comparisons within the non-normally distributed variables, the Mann Whitney test was applied. Odds ratios were calculated along with their 95% confidence interval. It was statistically significant if "p-value 0.05".

Results

Although we requested 500 patients to take part in the trial, only 450 did so since 50 patients were turned away due to inclusion criteria not being met by 40

patients and 10 patients refused to participate. Three groups with a total of 150 patients each were randomly assigned to the participants. Group I: (1000 ml IV normal saline received prior to skin incision + After the placenta has been delivered, the placental bed is covered with a towel soaked in 60 ml saline for five minutes); Group II: (1 gm IV normal saline received prior to skin incision + towel soaked with 2 gm tranexamic acid (4 ampoules of kapron 500 mg 5 ml. Amoun company) diluted in 50 ml of sodium chloride 0.9%), it is inserted intrauterine at the placental bed after placenta delivery for five minutes). Group III (received 1 gm tranexamic acid IV before skin incision + towel soaked with 2 gm saline inserted intrauterine after placenta delivery for 5 minutes).

The demographic criteria between the three studied groups showed that no significant difference with respect to their age, weight, Height, body mass index (BMI), parity, gestational age, initial hemoglobin and indication of CS, (Table 1).

Table 1. Demographic Criteria of pregnant women in the study groups

Parameters	Group I (n = 150)	Group II (n = 150)	Group III (n = 150)	Significance
Age (year)	30.94 ± 4.71	31.61 ± 4.99	31.29 ± 4.65	0.620
<ul style="list-style-type: none"> • Weight (kg) • Height (cm) • BMI 	69.12 ± 6.36 162.94 ± 3.98 26.03 ± 2.16	69.31 ± 6.75 162.98 ± 4.27 26.06 ± 2.07	69.65 ± 7.44 162.91 ± 4.32 26.20 ± 2.29	0.798 0.989 0.760
Parity (median) (Minimum – maximum)	3 (0 – 6)	3 (0 – 6)	3 (0 – 6)	0.835
Gestational age (weeks)	38.5 ± 1.05	38.43 ± 1.13	38.42 ± 1.18	0.804
Initial Hemoglobin	10.74 ± 0.82	10.65 ± 0.78	10.68 ± 0.73	0.595

Indication of CS (%)				
• Repeated CS	79(52.7)	84(56)	84(56)	0.959
• Breech	23(15.3)	21(14)	17(11.3)	
• Twin	17(11.3)	18(12)	22(14.7)	
• Macrosomia	20(13.3)	18(12)	16(10.7)	
• Patient request	11(7.3)	9(6)	11(7.3)	

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

There was a significant decrease in the intraoperative blood loss and total blood loss in both group II and group III compared to group I ($p=0.0001, 0.0001, 0.0001, 0.0001$) as the median intraoperative blood loss in group I was (654 ml) while (457 ml) in group II and (400 ml) in group III, and the median total blood loss in group I was (810 ml) while (630 ml) in group II and (550 ml) in group III. Also, there was a significant decrease in the intraoperative

blood loss and total blood loss in group III compared to group II, ($p= 0.0001$ and 0.0001). The mean postoperative blood loss for group I was (162.1 ± 35.72), group II was (156.27 ± 35.55) and group III was (149.53 ± 37.51), and this showed that there was a significant decrease in the post-operative blood loss in group III compared to group I, ($p= 0.003$) while no significant decrease between group II and group I, ($p=0.162$) or between group III and group II, ($p=0.109$), (Table 2).

Table 2. Blood loss in the study groups

Blood loss	Group I (n = 150)	Group II (n = 150)	Group III (n = 150)	Significance
Intraoperative	654(400-1200)	457 (240-1100)	400 (200-1000)	0.0001* 0.0001* / 0.0001* / 0.0001*
Postoperative	162.1 ± 35.72	156.27 ± 35.55	149.53 ± 37.51	0.011* 0.162 / 0.003* / 0.109
Total blood loss	810 (510-1400)	630 (330-1310)	550 (290-1170)	0.0001* 0.0001* / 0.0001* / 0.0001*

* 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.

The incidence of post-partum hemorrhage was significant decrease in group III, 8 (5.3%) patients compared to group I, 25 (16.7%) patients and group II, 21(14%) patients, ($p=0.002$ and 0.011) respectively. Also, the need to extra uterotonics was significant decrease in

group III, 9 (6%) patients compared to 33 (22%) patients in group I, and 24 (16%) patients in group II, ($p=0.0001$ and 0.006) respectively. However, neither the incidence of post-partum hemorrhage nor the need to additional uterotonics showed significant difference between group II and

group I ($p=0.522$ and 0.185) respectively. Uterine artery ligation was significant decrease in group III as it done to 3 (2%) Patients compared to 12 (8%) patients in each of both group I and group II, ($p= 0.017$). Also group III showed a significant decrease in the incidence of blood transfusion ,3 (2%) patients compared to 12(8%) patients in group I, and 13 (8.7 %) patients in group II. ($P= 0.017$ and 0.01) respectively. However, no

significant difference between group II and group III with respect to both extra uterine artery ligation and the incidence of blood transfusion. ($p=1.000$ and 0.835) respectively. Finally, operative time, hospital stay, postoperative hemoglobin, and post-operative complication as nausea, vomiting and diarrhea showed no significant difference between the three groups ($P= 0.276, 0.126, 0.853, 0.955, 1.00, 1.00$) respectively, (Table 3).

Table 3. Operative and postoperative outcome in the study groups

Variables	Group I (n = 150)	Group II (n = 150)	Group III (n = 150)	Significance
Post hemoglobin	9.83 ± 0.71	9.88 ± 0.73	9.87 ± 0.75	0.853
Operative time	56.07 ± 17.98	57.1 ± 17.61	55.0 ± 14.13	0.276
Hospital stays	4.23 ± 0.58	4.21 ± 0.58	4.11 ± 0.53	0.126
Post-partum hemorrhage (%)	25 (16.7)	21 (14)	8 (5.3)	0.007* 0.522 / 0.002* / 0.011*
Additional Uterotonics (%)	33 (22)	24(16)	9 (6)	0.0001* 0.185 / 0.0001* / 0.006*
Need Blood Transfusion (%)	12 (8)	13 (8.7)	3 (2)	0.031* 0.835 / 0.017* / 0.01*
Uterine artery ligation (%)	12 (8)	12 (8)	3 (2)	0.041* 1.00 / 0.017* / 0.017*
Nausea (%)	8 (5.3)	7 (4.7)	8 (5.3)	0.955
Vomiting (%)	4 (2.7)	4 (2.7)	3 (2)	1.000
Diarrhea (%)	4 (2.7)	4 (2.7)	5 (3.3)	1.000

*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 that the first double-blind randomized placebo-controlled trial comparing the temporary uterine packing combined with topical tranexamic acid as adjunct for reducing blood loss following an elective caesarean delivery with IV TA and placebo.

In the better of our knowledge for the use temporary uterine packing combined with topical tranexamic acid as adjunct for reducing blood loss following an elective caesarean delivery, no studies were recognized.

The outcomes demonstrated that the intravenous TA could essentially decreases both the intraoperative and total

blood loss, the need of transfusion after CD, the incidence of postpartum hemorrhage and therefore addition of extra additional uterotonics compared with topical application of TA and placebo. Also, the temporary uterine packing with topical TA is more effective than placebo for decreasing blood loss during CD but no statistical difference as regard to Number of cases with postpartum hemorrhage or the need of uterotonic. The degrees of plasminogen activators increased half an hour after the start of surgery, according to previous major research (Lechien et al., 2021). As a result, the hypothetical basis may help to elucidate the expected effectiveness of TA for minimizing loss for surgical operations with a focus on CD and its potential usage as a uterotonic adjunct in reducing blood loss during CD. By preventing plasmin from acting as an enzyme to break down fibrin, TA provides an alternative method to help maintain hemostasis.

Regarding the use of TA in CD, it was confirmed by many previous trials. (Abdel-Aleem et al., 2013 ; Sentürk et al., 2013 ; Ahmed et al., 2015). One study (Abdel-Aleem et al., 2013) reported that IV TA use was associated with a significant decrease in intraoperative blood loss, another trial reported that the use of IV TA during CD effectively reduces the blood loss during CD compared with placebo (Sentürk et al., 2013).

During delivery, when the placenta separates from the uterine wall, sequential changes occur and decrease hemorrhage, including strong myometrial contractions, increased platelet activity, and a huge release of coagulant factors; at an equivalent time, however, fibrinolytic activity increases (Ghosh et al., 2014). Finally, further suggests that TA by its

anti-fibrinolytic activity could be effective in PPH (Brenner et al., 2019).

A systematic review and meta-analysis conducted to assess the efficacy and TA in decrease hemorrhage and reduce transfusion needs for patients undergoing CD. They conclude that intravenous TA for patients undergoing CD was effective and safe (Ducloy-Bouthors et al., 2011).

A recent Cochrane review showed that timely administration of TA in patients with postpartum hemorrhage following delivery by any route resulted in not only reduced total blood loss but also decreased maternal mortality thanks to hemorrhage (relative risk RR 0.81; 95% CI: 0.65 – 1.00) (Li et al., 2017).

In the WOMAN study, a total of 20,060 women with a clinical diagnosis of postpartum hemorrhage were randomized to receive tranexamic acid (1 g intravenously, followed by a second dose if bleeding persisted after 30 minutes or resumed within 24 hours of the primary dose) or a matched placebo. Within 42 days following randomization, the primary outcome was either death from all causes or hysterectomy, with bleeding-related death serving as the primary secondary outcome. (RR = 0.81, 95% CI 0.65-1.00; p = 0.045) Tranexamic acid significantly decreased bleeding-related deaths while having no adverse effects on thromboembolic events or sequelae (Shakur et al., 2017 ; Beaumont et al., 2018).

In our previous work we demonstrated that topical tranexamic acid is effective as IV TA for reduce blood loss during CD for placenta previa (Shady and Sallam , 2017).

Our study shows that the use of temporary uterine packing with topical

tranexamic acid helps reduce the blood loss during and immediately after the operation but less effective than IV TA. The mean difference between topical application of TA and placebo= 170ml, and the main difference between IV application of TA and placebo=250 ml. This difference in blood loss may reach statistical significance, but at the clinical view may be less significant to affect the general condition of the patients. In our locality, the prevalence of anemia is high, which may make the patients not tolerable with any small amount of blood loss during delivery. So, any intervention can save, even so, non-significant amount of blood during CD, of great benefit for the patients.

No study in the literature to our known compare the outcome of topical application of TA during CD, but many studies in the literature ensure about the efficacy of topical TA in orthopedic, cardiac and other surgical subspecialty. (Larsson et al., 2006).

In our study, there was no significant difference in the mean operating time between the three groups. According to numerous other research (Sentürk et al., 2013 ; Ahmed et al., 2015), the operating time for a caesarean section frequently ranges between 50 and 60 minutes.

One limitation of our study was a single-center study, and that we aren't used alkaline hematin method which may be a validated method for accurate measurement of blood loss but use a gravimetric method to live the quantity of blood loss. However, many trials, conclude that Estimation of blood loss employing a gravimetric method is an accurate and objective tool to

gauge intraoperative blood loss (Alshryda et al., 2014 ; Li et al., 2018).

Furthermore, study wasn't powered to assess the efficacy of tranexamic acid in prevention of severe PPH or to assess its safety especially thromboembolic complications

One of the strengths of our investigation was that a double-blind randomized examination adequately powered to compare the effect of intravenous TA and temporary uterine packing with topical TA versus placebo on the amount of perioperative blood loss.

Another quality of the investigation lies in its simplicity of use of TA, which don't need skills, can bring about a clinically significant decrease in intraoperative blood loss.

Conclusion

Topical tranexamic acid, IV tranexamic acid, and temporary uterine packing all work better than a placebo for reducing overall blood loss during and after caesarean birth in women who have at least one risk factor for postpartum hemorrhage, although IV tranexamic acid is more efficient.

Compliance with ethical standards

Conflict of interest :The authors declare that they have no conflict of interest.

Ethical approval : The study protocol was approved by the Ethics Committee of Aswan University Faculty of Medicine (Aswu/276/7/18). ClinicalTrials.gov

identifier: NCT03706339 . The study was in accordance with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: Informed consent was obtained from all individual participants included in the study.

Author's contribution: AT: review of literature, manuscript preparation, NS:

design, literature review, manuscript preparation. HS: conception and design, literature review, manuscript preparation. HS: manuscript preparation, M.A: review of literature, manuscript preparation.

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References

- **Abdel-Aleem H, Alhusaini T K, Abdel-Aleem, M A, Menoufy M, Gülmezoglu A M, et al. (2013).** Effectiveness of tranexamic acid on blood loss in patients undergoing elective cesarean section: randomized clinical trial. *The Journal of Maternal-Fetal & Neonatal Medicine*, 26(17): 1705-1709.
- **Ahmed M R, Sayed Ahmed W A, Madny E H, Arafa A M, Said M M, et al. (2015).** Efficacy of tranexamic acid in decreasing blood loss in elective caesarean delivery. *The Journal of Maternal-Fetal & Neonatal Medicine*, 28(9): 1014-1018.
- **Alshryda S, Sukeik M, Sarda P, Blenkinsopp J, Haddad F S, Mason JM, et al. (2014).** A systematic review and meta-analysis of the topical administration of tranexamic acid in total hip and knee replacement. *The bone & joint journal*, 96(8): 1005-1015.
- **Beaumont D, Pavord S, Gayet-Ageron A, Ker K, Mousa H A, Shakur H, et al. (2018).** Antifibrinolytic drugs for treating primary postpartum haemorrhage. *The Cochrane database of systematic reviews*, 2(2): CD012964.
- **Brenner A, Ker K, Shakur-Still H, Roberts I, et al. (2019).** Tranexamic acid for post-partum haemorrhage: What, who and when. *Best Practice & Research Clinical Obstetrics & Gynaecology*, 61: 66-74.
- **Ducloy-Bouthors A S, Jude B, Duhamel A, Broisin F, Huissoud C, Keita-Meyer H, Susen S, et al. (2011).** High-dose tranexamic acid reduces blood loss in postpartum haemorrhage. *Critical care*, 15(2): 1-10.
- **Ghosh A, Chaudhuri P, Muhuri B, Gungorduk OC, Sudolmus S, Ark C. (2014).** Efficacy of intravenous tranexamic acid before cesarean section in preventing post partum hemorrhage-a prospective randomized double blind placebo controlled study. *Int J Bio Med Res*, 5: 4461-4.
- **Jia J. (2019).** Combined use of intravenous and topical tranexamic acid in patients aged over 70 years old undergoing total hip arthroplasty. *Journal of orthopaedic surgery and research*, 14(1): 1-7.
- **Kandil M. (2018).** The sky rocketing rate of cesarean section in Egypt. *Glob Drugs Therap*, 3(4): 1-1.
- **Larsson C, Saltvedt S, Wiklund I, Pahlen S, Andolf E. (2006).** Estimation of blood loss after cesarean section and vaginal delivery has low validity with a tendency to exaggeration. *Acta obstetrica et gynecologica Scandinavica*, 85(12): 1448-1452.
- **Lechien A, Faraoni D, Van der Linden P. (2021).** Effective tranexamic acid concentration for 95% inhibition of tissue-type plasminogen activator-induced hyperfibrinolysis in full-term pregnant women: a prospective interventional study. *Blood Coagulation & Fibrinolysis*, 32(3): 186-193.
- **Li B, Miners A, Shakur H, Roberts I. (2018).** Tranexamic acid for treatment of women with post-partum

haemorrhage in Nigeria and Pakistan: a cost-effectiveness analysis of data from the WOMAN trial. *The Lancet Global Health*, 6(2): e222-e228.

- **Li C, Gong Y, Dong L, Xie B, Dai Z. (2017).** Is prophylactic tranexamic acid administration effective and safe for postpartum hemorrhage prevention?: A systematic review and meta-analysis. *Medicine*, 96(1).
- **Say L, Chou D, Gemmill A, Tunçalp Ö, Moller A B, Daniels J, Alkema L, et al. (2014).** Global causes of maternal death: a WHO systematic analysis. *The Lancet global health*, 2(6): e323-e333.
- **Scher C S, Kaye A D, Liu H, Perelman S, Leavitt S. (2021).** *Essentials of Blood Product Management in Anesthesia Practice*. Cham, Switzerland: Springer International Publishing.
- **Schulz K F, Altman D G, Moher D, et al, CONSORT Group*. (2010).** CONSORT 2010 statement: updated guidelines for reporting parallel group randomized trials. *Annals of internal medicine*, 152(11):726-732.
- **Sentürk M B, Cakmak Y, Yildiz G, Yildiz P. (2013).** Tranexamic acid for cesarean section: a double-blind, placebo-controlled, randomized clinical trial. *Archives of gynecology and obstetrics*, 287: 641-645.
- **Shady N W , Sallam H F. (2017).** Adjunctive IV tranexamic acid versus topical tranexamic acid application of the placental bed for prevention of postpartum hemorrhage in women with placenta previa: a randomized controlled trial. *International journal of reproduction, contraception, obstetrics and gynecology*, 6:12.
- **Shakur H, Roberts I, Fawole B, Chaudhri R, El-Sheikh M, Akintan , Loto O, et al. (2017).** Effect of early tranexamic acid administration on mortality, hysterectomy, and other morbidities in women with postpartum haemorrhage (WOMAN): an international, randomised, double-blind, placebo-controlled trial. *The Lancet*, 389(10084):2105-2116.
- **Ujjiga, T T A, Omolo J O, Aketch M O, Ochi E B, et al. (2014).** Risk factors associated with postpartum haemorrhage at Juba Teaching Hospital, South Sudan, 2011. *South Sudan Medical Journal*, 7(3): 52-56.