Al-Azhar Med. J .(Surgery). *Vol. 50 (1), January, 2021, 443 - 452*
DOI: 10.12816/amj.2021.139736
https://amj.journals.ekb.eg/article_139736.html

ROLE OF TRANXEMIC ACID TO REDUCE AND PREVENT POSTPARTUM HEMORRAHGE IN LOW RISK WOMEN

By

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ABSTRACT

Background: To reduce maternal mortality and morbidity caused by bleeding, it is important to reduce the amount of bleeding during and after both normal vaginal delivery and lower segment cesarean section (LSCS). Tranexamic acid helps to reduce bleeding during and after both normal vaginal delivery and cesarean section.

Objective: To assess the safety and efficacy of Tranexamic Acid (TXA) in reducing blood loss during and after both NVD and elective CS.

Patients and Methods: The current study was conducted as controlled randomized trial on 200 women recruited from labor ward in Assiut Al -Azhar university Hospital. A total number of 100, 50 patients received tranexamic acid before induction of anesthesia in addition to oxytocin after delivery of the baby; in case of elective ceserian section the other 50 patients received tranxemic acid before second stage of labour in NVD the other 100 received only oxytocin after delivery in both NVD and CS.

Results: In the current study, there was significant difference between intervention and control groups as regards age. In the current study, no significant difference between intervention and control groups as regards gestational age at delivery (p<0721 in NVD, p<0.726 in CS). In the current study, no significant difference between intervention and control groups as regards preoperative hemoglobin (p 0.708 in NVD, p 0.107 in CS). Postoperative hemoglobin was significantly higher in intervention groups than control groups (p<0.001in NVD, p< 0.021 in CS). In the current study, no significant difference between preoperative and post-operative prothrombin time and INR between intervention groups and control groups both in NVD and CS. In the current study, there was significant difference in postoperative measurements (SBP and DBP) in all groups.

Conclusion: The use of tranexamic acid prior to cesarean section and vaginal delivery was significantly effective in reducing blood loss during cesarean section with no observed maternal or neonatal side effects.

Key words: Prophylactic tranexamic acid, blood loss, elective cesarean section, NVD.

INTRODUCTION

PPH and its complications are a significant cause of maternal mortality and morbidity, particulary in developing countries, accounting for about 25% of direct maternal deaths *(Geller et al., 2014* and *Novikova & Hofmeyr , 2015).*

Post-partum hemorrhage is defined as loss of > 500 ml within 24 hours of birth *(Li et al., 2017)*. The four main causes of PPH are uterine atony, genital birth

trauma, retained placental tissues and maternal coagulation disorders *(Dyer and Buiwick, 2013)*.

While uterine atony is responsible for the majority of primary post- partum haemorrhage, the surgical obstetrical causes such as injury of the cervix, vagina, paravaginal spaces, perineum and episiotomy comprise about 20% all primary PPH *(Henry and Carless 2012)*.

The occurrence rate of caesarean section (CS) has increased in both developed and developing countries, which would result in an increased risk of PPH. Although there has been a remarkable improvement in the prevention and treatment of PPH in recent years, deaths due to PPH remain relatively common in some parts of the world. To lower the occurrence rate of major morbidity and mortality due to PPH, it is very vital to reduce blood loss in CS and vaginal delivery though the incidence of early PPH (occurring within 24 hours of delivery) is lower in caesarean section than vaginal delivery, the former is a major surgery and causes greater blood loss. Hence, it is essential to prevent the blood loss effectively in a feasible way. Apart from obstetric, surgical and radiological interventions, pharmacologic management also plays an important role in this aspect. First line of therapeutic management for PPH is oxytocin *(Matteson et al., 2013)*.

Other modalities include intravenous ergometrine, intra-muscular carboprost and misoprostol. Prohaemostatic drugs such as tranexamic acid provide a complementary biochemical haemostatic effect to the well- proven uterotonics, especially oxytocin. Systemic anti-fibrinolytic agents are widely used in surgery. A systematic review of randomised controlled trials of anti-fibrinolytic agents in elective surgical patients identified 211 randomised controlled trials *(Movafegh et al., 2013)*.

The results showed that tranexamic acid reduced the risk of blood transfusion by 39%. Tranexamic acid is an analogue of lysine that inhibits fibrinolysis by competitively binding to plasminogen. It prevents the lysis of formed clot by inhibiting activation of plasminogen and plasmin. It is ten times more potent than Amino- caproic acid *(Movafegh et al., 2013)*.

Tranexamic acid has been shown to reduce uterine blood loss in non-surgical aspect. A study done on women with menorrhagia has showed significant reduction in mean menstrual blood loss in those treated with tranexamic acid *(Perel et al., 2013)*.

A randomized controlled trial assessed tranexamic acid for the treatment of PPH and it showed that a high dose of tranexamic acid reduces blood loss in women with PPH *(Prata et al., 2013)*.

Several randomised controlled trials have analysed the prophylactic role of tranexamic acid and have shown significant results in reducing blood loss. Tranexamic acid might reduce the need for hysterectomy, reduce the risk of severe anaemia and avoid the need for blood transfusion. Hence, this could contribute significantly to the goal of reducing maternal mortality *(Kolev and Longstaff 2016)*.

The present work aimed to assess the safety and efficacy of Tranxemic acid on

the amount of blood loss after both CS and vaginal delivery of patints at low risk of PPH.

PATIENTS AND METHODS

This study was conducted at the Department of Obstetrics & Gynecology in Assuit Al- Azhar University Hospital.

Ethical committee approved the study protocol and an informed consent was obtained from every participant prior to commencing the study.

The study was conducted on two hundred women undergoing cesarean section and vaginal delivery and divided into:

Group 1: Tranexamic acid was given prior to surgery in study group in addition to the routine care {10 units of oxytocin added to the intravenous drip soon after baby delivery}. Tranexamic acid injection was prepared by diluting 1g TA in 200 ml of normal saline. TA was administrated as intravenous infusion (over 15minutes), at least 20 minutes prior to skin incision.

Group 2: Control group of cesarean section had routine care alone.

Group 3: TA was given prior to vaginal delivery (before 2nd stage of labor) at the same route in group1.

Group 4: Control group of vaginal delivery had routine care alone.

Inclusion Criteria:

Primi para pregnant woman with singletone pregnancy of age group in range of 20 up to 35 years.

Exclusion Criteria:

Polyhydraminos, macrosomia, preeclampsia, abnormal placenta, thrombophilia, anaemia, coagulopathy, cardiovascular, renal or liver diseases contraindication to any drug used in this study protocol. previous ceserian sections and multigravida, presence of varicosities at lower segment of the uterus, and intra operative complications like injury of uterine artery during ceserean section, or presence of tears at lateral vaginal walls, cervix or perineum during vaginal delivery.

All patients were subjected to full history taking, clinical examination (clinical criteria) and laboratory investigations (Complete blood count haemoglobin before and after surgery, liver functions, kidney functions and random blood sugar).

Blood loss was measured in both groups following placental delivery until the end of surgery. Blood collected in suction container was noted. Soaked mops and operation table perineal sheet was weighed by electronic scale before and after surgery. Hemoglobin and hematocrit value before and after surgery were estimated and the percentage of difference was compared.

Statistical Analysis:

Recorded data were analyzed using the statistical package for the social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean ± standard deviation (SD). Qualitative data were expressed as frequency and percentage.

The following tests were done:

- Independent-samples t-test of significance was used when comparing between two means.

- Paired sample t-test of significance was used when comparing between related samples.

P-value was considered significant when P-value<0.05.

RESULTS

No significant difference between intervention and control groups both in CS and NVD according to residence, BMI, and gestational age at delivery. There war significant difference according to age between intervention and control groups **(Table 1)**.

Table (1): Personal data of the studied groups

Groups / Parameters	NVD		P-value	LSCS		P-value
Age: (years)	**Control (n= 50)**	**Intervention (n= 50)**		**Control (n= 50)**	**Intervention (n= 50)**	
Mean ± SD						
Range	22.12 ± 2.71	25.40 ± 4.74	0.000	24.12 ± 4.86	22.36 ± 2.93	0.0307
Residence: No. (%)	20.0-34.0	20.0-35.0		20.0-35.0	20.0-35.0	
Rural						
Urban	37 (74.0%)	41 (82.0%)	0.334	30 (60.0%)	35 (70.0%)	0.295
BMI	13 (26.0%)	9 (18.0%)		20 (40.0%)	15 (30.0%)	
Mean ± SD						
Range	26.78 ± 2.48	26.65 ± 2.76	0.805	26.92 ± 3.08	26.10 ± 2.01	0.118
Gestational age at delivery (weeks)	23.0-31.0	23.0-33.0		21.0-33.0	23.0-30.0	
Mean ± SD						
Range	38.38 ± 1.05	38.32 ± 0.55	0.721	38.80 ± 0.81	38.74 ± 0.90	0.727
	36.0-40.0	38.0-40.0		38.0-40.0	37.0-40.0	

Independent t- test.

No significant difference between intervention and control groups both in CS and NVD according to PT and INR. There was no significant difference between control and intervention groups both in CS and NVD preoperative. There is significant difference between groups postoperati according to Hb level **(Table 2)**.

Table (2): Comparison between intervention and control groups according to Hb level, PT, and INR

Groups / Parameters	NVD		P-value	LSCS		P-value
Pre-operative Hb:	**Control (n= 50)**	**Intervention (n= 50)**		**Control (n= 50)**	**Intervention (n= 50)**	
Mean ± SD						
Range	11.24 ± 1.07	11.32 ± 1.11	0.708	11.67 ± 1.10	11.32 ± 1.08	0.112
Post-operative Hb:	10.0-13.5	10.0-13.8		10.1-13.4	10.0-13.8	
Mean ± SD						
Range	9.25 ± 1.04	10.24 ± 1.24	0.001	9.47 ± 1.22	10.29 ± 1.11	0.021
P-value[2]	8.9-12.2	8.9-12.9		8.8-12.2	9.0-12.8	
Pre-operative PT:	0.000*	0.019*		0.000*	0.000*	
Mean ± SD						
Range	11.89 ± 0.53	11.98 ± 0.76	0.503	12.15 ± 0.82	12.41 ± 0.96	0.153
Post-operative PT:	11.0-13.0	11.0-13.7		11.0-14.0	11.0-14.0	
Mean ± SD						
Range	11.84 ± 0.55	11.88 ± 0.80	0.749	12.14 ± 0.83	12.36 ± 0.94	0.219
P-value[2]	11.0-13.0	11.0-14.0		11.0-14.0	11.0-14.0	
Pre-operative INR:	0.090	0.569		0.021*	0.207	
Mean ± SD						
Range	1.12 ± 0.08	1.11 ± 0.10	0.581	1.16 ± 0.07	1.11 ± 0.07	0.112
Post-operative INR:	1.0-1.2	1.0-1.3		1.0-1.2	1.0-1.2	
Mean ± SD						
Range	1.10 ± 0.08	1.11 ± 0.09	0.558	1.15 ± 0.07	1.13 ± 0.07	0.156
P-value[2]	1.0-1.2	1.0-1.3		1.0-1.2	1.0-1.2	
	0.132	0.420		0.828	0.340	

Independent t- test, Paired t- test.

No significant difference between control and intervention groups both in CS and NVD according to preoperative systolic and diastolic blood pressure measurements. There was significant difference between control and intervention groups according to 1-hour postoperative in NVD groups **(Table 3)**.

Table (3): Comparison between preoperative and 1 hour postoperative systolic and diastolic blood pressure in intervention and control groups

Groups / Blood Pressure	NVD		P-value	LSCS		P-value
	Control (n= 50)	**Intervention (n= 50)**		**Control (n= 50)**	**Intervention (n= 50)**	
Pre-operative SBP:						
Mean ± SD	113.00 ± 7.89	114.40 ± 7.05	0.352	113.60 ± 7.76	112.40 ± 7.16	0.424
Range	100.0-130.0	100.0-130.0		100.0-130.0	100.0-120.0	
Post-operative SBP:						
Mean ± SD	104.00 ± 9.31	111.10 ± 7.51	0.001	109.00 ± 9.04	110.20 ± 8.45	0.494
Range	90.0-120.0	90.0-120.0		90.0-130.0	90.0-120.0	
P-value[2]	0.001*	0.001*		0.001*	0.003*	
Pre-operative DBP:						
Mean ± SD	73.80 ± 6.02	73.80 ± 5.67	1.000	71.40 ± 7.56	72.00 ± 7.56	0.692
Range	60.0-80.0	60.0-80.0		60.0-80.0	60.0-80.0	
Post-operative DBP:						
Mean ± SD	66.30 ± 6.04	71.50 ± 6.41	0.001	67.90 ± 7.15	70.40 ± 7.27	0.086
Range	55.0-80.0	60.0-80.0		55.0-80.0	55.0-80.0	
P-value[2]	0.000*	0.000*		0.000*	0.002*	

Independent t- test , paired t- test.

DISCUSSION

The increased frequency of PPH in the developing world is mainly due to expectant management because of lack of availability of medications used in the active management of the third stage *(Prata et al., 2013).*

During placental delivery, fibrinogen and fibrin are rapidly degraded, whereas plasminogen activators and fibrin degradation products increase due to activation of the fibrinolytic system. This activation can last up to 6-10 h postpartum causing more bleeding *(Kolev and Longstaff, 2016).*

Tranexamic acid competitively inhibits activation of plasminogen, thereby reducing conversion of plasminogen to plasmin (fibrinolysin), an enzyme that degrades fibrin clots, fibrinogen, and other plasma proteins, including the procoagulant factors V and VIII.

Tranexamic acid also directly inhibits plasmin activity, but higher doses are required than are needed to reduce plasmin formation. In vitro, the antifibrinolytic potency of tranexamic acid is approximately 5 to 10 times that of aminocaproic acid *(Pabinger et al., 2017).* It was used in gynecological bleeding and major trauma.

Thus, the current study was held to assess the efficiency of use of tranexamic acid in reducing blood loss in patients undergoing both ceserian section and vaginal delivery.

In this study, there wer 4 groups 2 study groups either CS or vaginal delivery each one contained 50 cases as well as 2 control groups either CS or vaginal delivery each one contained also 50 cases.

In the study of *Gungorduk et al. (2013)* There were 660 women who underwent elective CS were included in the study to determine the efficacy and safety of tranxemic acid in reducing blood loss during elective.

In the study of *Xu et al. (2013),* there were 174 primipara undergoing CS (88 given TA immediately before CS were compared with 86 others to whom TA was not given) to determine the efficacy of TA in reducing blood loss in patients after CS.

In our study, as regard personal data as (residence, BMI, and gestational age), there were no significant differences between intervention and control groups, but there was significant difference according to age.

In the study of *Xu et al. (2013),* the patients' characteristics in the two groups were similar, with no statistical difference between the two groups.

In our study, there was no significant statistical difference in the measurement of blood pressure preoperative and 1 hour postoperative between the groups. Postoperative hemoglobin was significantly higher in the intervention groups than in the control groups. Reduction in hemoglobin was significantly less in the study group than in the control group .

The previous study of *Movafegh et al., (2013)* showed that tranexamic acid significantly reduced the quantity of blood loss from the end of LSCS to 2 hours postpartum. It also significantly reduced the quantity of blood loss intraoperative. *Abdel-Aleem et al. (2013)* showed that tranexamic acid significantly reduced the blood loss in the study group.

In our study, no significant difference between preoperative and post-operative measurements of prothrombin time and INR between intervention groups and control groups in both NVD and CS.

The included patients were those who were term, singleton, going for NVD and elective cesarean section. Patients with major maternal medical problem, patients with bleeding tendency, patient with high risk of thrombo-embolism, ante-partum hemorrhage, abnormal site of the placenta, macrosomic baby, twin pregnancy and polyhydramnios were excluded.

We used placebo in the current study, and this agreed with the study of *Gungorduk et al. (2011)*.

Peitsidis et al. (2011) have found two cases of pulmonary embolism in tranexamic acid treated group.

CONCLUSION

The use of tranexamic acid prior to cesarean section is significantly effective in reducing blood loss during caesarean section with no observed maternal or neonatal side effects.

REFERENCES

1. **Abdel-Aleem H, Alhusaini TK, Abdel-Aleem MA et al. (2013):** Effectiveness of tranexamic acid on blood loss in patients undergoing elective cesarean section: randomized clinical trial. J Matern Fetal Neonatal Med 2013; 26 (17): 1705–1709.
2. **Dyer RA, Buiwick AJ, Carvalho B (2013):** Oxytocin for labour and caesarean delivery: implications for the anaesthesiologist. Current Opinion. Anesthesiology, 24(3): 255-61.
3. **Geller SE, Goudar SS, Adams MG, Naik VA, Patel A, Bellad MB et al. (2014):** Factors associated with acute postpartum haemorrhage in low-risk women delivering in rural India. International Journal of Gynecology and Obstetrics, 101(1): 94-99.
4. **Gungorduk K, Yıldırım G, Asıcıoğlu O, Gungorduk OC, Sudolmus S, Ark C. (2011):** Efficacy of intravenous tranexamic acid in reducing blood loss after elective cesarean section: a prospective, randomized, double-blind, placebo-controlled study. Am J Perinatol. 2011 Mar; 28(3):233-40.
5. **Henry DA, Carless PA, Moxey AJ, O'Connell D, Stokes BJ, Fergusson DA et al. (2012):** Antifibrinolytic use for minimizing perioperative allogeneic blood transfusion. The Cochrane Library, https://www.ncbi.nlm.nih.gov/pubmed/21249650.
6. **Kolev K, Longstaff C (2016):** Bleeding related to disturbed fibrinolysis. British journal of haematology, 175(1): 12-23.
7. **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): 215-221.
8. **Matteson KA, Rahn DD, Wheeler TL (2013):** Non-surgical management of heavy menstrual bleeding: A systematic review and practice guidelines. Obstetrics and Gynecology, 121 (3): 632.
9. **Mayur G, Purvi P, Ashoo G, Pankaj D (2007):** Efficacy of tranexamic acid in decreasing blood loss during and after cesarean section: a randomized case controlled prospective study. J Obstet Gynecol India, 57(3):227-30.
10. **Movafegh A, Eslamian L, Dorabadi A (2013):** Effect of Intravenous Tranexamic Acid Administration on Blood Loss During and After Cesarean Delivery. Obstetric Anesthesia Digest., 33(1):34-5.

11. **Novikova N, Hofmeyr GJ (2015):** Tranexamic acid for preventing postpartum haemorrhage (Review) Copyright © 2011 The Cochrane Collaboration. Published by JohnWiley & Sons, Ltd.

12. **Pabinger I, Fries D, Schöchl H, Streif W, Toller W (2017):** Tranexamic acid for treatment and prophylaxis of bleeding and hyperfibrinolysis. Wiener klinische Wochenschrift, 129(9-10):303-16.

13. **Peitsidis P, Kadir RA. (2011):** Antifibrinolytic therapy with tranexamic acid in pregnancy and postpartum. Expert Opin Pharmacother. 2011 Mar; 12(4):503-16.

14. **Perel P, Ker K, Morales Uribe CH, Roberts I. (2013):** Tranexamic acid for reducing mortality in emergency and urgent surgery. Cochrane Database Syst Rev 2013; 1: CD010245.

15. **Prata N, Bell S, Weidert K (2013):** Prevention of postpartum hemorrhage in low-resource settings: current perspectives. International journal of women's health, 5:737.

16. **Xu J, Gao W, ju Y, (2013):** Tranxemic acid for thew prevention of post- partum hemorrhage after ceserian section: adouble – blind randomized trial. Arch gynecol obstetric 2013, 287(3): 463-8.

دور حمض الترانيكسيميا لتقليل ومنع حدوث نزيف مابعد الولادة في السيدات ذوات الحمل منخفض الخطورة

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خلفيـة البحـث: يعـد نزيـف مـا بعـد الـولادة أحـد أهـم التحـديات التـي تواجـه أطبـاء التوليـد فـى كافـة أنحـاء العـالم ومـا قـد يترتـب عليهـا مـن مضـاعفات قـد تصـل إلـي حـد وفـاة الأم. مـن هنـا جـاءت أهميـة البحـث فـي سـبل تقليـل حـدوث فـرص النزيـف مـا بعـد الـولادة، خاصـة وأن تلـك المضـاعفات مسـئولة عـن مـا يقـرب مـن ربـع حـالات الوفيـات الناتجـة عـن الـولادة فـى الـدول الناميـة. وعلـي الـرغم مـن خطـورة نزيـف مـا بعـد الـولادة إلا أنـه توجـد سـبل عـدة يمكـن إسـتخدامها لمنعـه وتقليـل فـرص حدوثـه. وتعـددت الطـرق المسـتخدمة فـى ذلـك فمنهـا مـا يعتمـد علـى التـدخلات الجراحيـة المعتمـدة أثنـاء الـولادة ومنهـا مـا هـو عقـاقير مسـتخدمة لتقليـل حـدوث النزيـف. ويعتبـر حمـض الترانيكسـيميا أحـد العقـارات المسـتخدمة فـى تقليـل حـدوث النزيـف بشـكل عـام يعمـل عـن طريـق تقليل العوامل التي تزيد من سيولة الدم بالجسم وأثناء الولادة بشكل خاص.

الهـدف مـن البحـث: تقيـيم دور حمـض الترانكسـيميا فـي تقليـل حـدوث نزيـف مـا بعـد الولادة فى السيدات ذوات المخاطر المنخفضة.

المريضـات وطريقـة البحـث: وتـم عمـل هـذه الدراسـة علـي 200 حالـة مـن السـيدات فـى قسـم التوليـد وأمـراض النسـاء بجامعـة الازهـر فـرع أسـيوط، كمـا تـم عمـل تلـك الدراسـة علـي هـذه الحـالات بعـد تسـجيل موافقـة كتابيـة للحـالات ومعرفـة التـاريخ الإكلينيكـي الكامـل لهـا وخصوصـا التـاريخ الخـاص بالنسـاء والتوليـد، وتـم عمـل هـذه الدراسـة الإستكشـافية علـي السـيدات فـي المرحلـة العمريـة المتراوحـة بـين 20 الـي 35 سـنة وذلـك باسـتبعاد السـيدات ذوات الحمـل الخطـر، وايضـا اللاتـي يعـانين مـن امـراض مزمنـة غيـر مرتبطـة بالحمـل. وقـد تـم إعطـاء السـيدات عقـار حمـض

الترانيكسيميا (1000 جم) قبل الولادة سواء كانت ولادة طبيعية او قيصرية وملاحظة نسبة النزيف من عدمه.

نتائج البحث: لم يكن هناك فرق كبير بين مجموعات التدخل ومجموعات التحكم فيما يتعلق بنسبة الهيموجلوبين قبل العملية، بينما كانت نسبة الهيموجلوبين أعلى بشكل ملحوظ فى مجموعات التدخل من مجموعات التحكم، حيث وصلت قيمة الملائمة في الولادة الطبيعية اقل من 0,001 ووصلت قيمة الملائمة في الولادة القيصرية أقل من 0,021.

الاستنتاج: لحمض الترانيكسيميا تاثيرا واضحا وفعالا فى إنخفاض معدل النزيف اثناء الولادة وبعدها.