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Research Article

Tranexamic Acid in Management of Normal Vaginal Delivery Post-Partum Bleeding Issues

Elsayed Hamdi Noureldin*

Obstetrics and Gynecology Department, Faculty of Medicine; Zagazig University. Zagazig, Egypt

***Corresponding author**: Dr Elsayed Hamdi Noureldin, Lecturer of Obstetrics and Gynecology, Obstetrics and Gynecology Department, Faculty of Medicine, Zagazig University. Zagazig, Egypt. Email: elsayed_hamdi2002@yahoo.com

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Abstract

Background: *Postpartum hemorrhage is a commonly encountered clinical scenario in which all obstetricians all over the globe undergo all possible preventive measures to prevent its occurrence. A prior research meta-analysis regarding postpartum hemorrhage, revealed and displayed the crucial value of early management of post-partum hemorrhage showing that Every 15-minute time delay in administration of tranexamic agent is correlated and linked with a decrease of around 10% in the benefit against bleeding-related mortalities.*

Aim: *To evaluate the usefulness of tranexamic acid in management and prevention of post-partum bleeding issues that could arise after vaginal delivery*

Methodology: *A randomized, placebo controlled research trial, using two parallel research groups 500 research study subjects in each. cases scheduled to undergo vaginal delivery have been randomly categorized to be administered tranexamic acid or placebo immediately after delivery, along with the administration of a uterotonic drug. Tranexamic acid and placebo have been prepared at the same site each containing a 10-ml vial of the trial regimen*

Results: *Statistical comparative analysis as regards outcomes in both research groups in which there was statistical significant difference as regards Blood loss (ml), median (IQR), Primary outcome, no. (%),clinically significant postpartum hemorrhage, no. (%) (p values =0.007,0.038,0.027 consecutively) denoting that tranexamic acid research group had lower blood loss, postpartum hemorrhage in a statistically significant manner, whereas there was no statistical significant difference between both research groups as regards Additional uterotonic agent for excessive bleeding, no. (%),Severe postpartum hemorrhage, no. (%), Blood transfusion, Arterial embolization or surgery for postpartum hemorrhage, no. (%), Decrease hemoglobin >2 (g/dl), Decrease hematocrit >10% from pre no. (%),(p values =0.091, 0.572, 0.780, 0.422, 0.861, 0.585 consecutively).*

Conclusions: *Tranexamic acid is a useful agent in reducing postpartum hemorrhage and have a reasonably acceptable side effect profile that could be considered as a routine agent in practice.*

Introduction

Postpartum hemorrhage is a commonly encountered clinical scenario in which all obstetricians all over the globe undergo all possible preventive measures to prevent its occurrence [1,2,3].

Ecbolic agents such as oxytocin, methergine and prostaglandins are considered the main drugs used for prevention of post-partum hemorrhage particularly in cases of suspected atonic post-partum hemorrhage issues such as cases having over distended uterus such as twins and poly hydramnios. tranexamic acid as an anti-fibrinolytic agent is considered one of the promising drugs that could reduce the arousal of catastrophic levels of post-partum hemorrhage particularly after vaginal deliveries [4,5,6].

Prevention of postpartum hemorrhage relies on clinical care during antenatal care preventing and managing predisposing factors such as maternal anemia [7,8,9].

A prior research meta-analysis regarding postpartum hemorrhage, Revealed the crucial value of early management of post-partum hemorrhage showing that Every 15-minute time delay in administration of tranexamic agent is correlated and linked with a decrease of around 10% in the benefit against bleeding-related mortalities [10,11,12].

Several prior randomized, controlled research trials, involving cases having cesarean delivery, have revealed that the prophylactic intravenous administration of 1 g of tranexamic acid after childbirth reduced blood loss [13,14,15].

Aim of the work

To evaluate the usefulness of tranexamic acid in management and prevention of post-partum bleeding issues that could arise after vaginal delivery.

Methodology

"The study was conducted at AlZahraa hospital , Jeddah. KSA during the period from Dec. 2015 to Dec. 2018". A randomized, placebo controlled research trial, using two parallel research groups 500 research study subjects in each case scheduled to undergo vaginal delivery have been randomly categorized to be administered tranexamic acid or placebo immediately after delivery, along with the administration of a uterotonic drug. Tranexamic acid and placebo have been prepared at the same site each containing a 10-ml vial of the trial regimen (1 gm of tranexamic acid or placebo). The intravenous trial regimen has administered slowly intravenous (over a time period of 30 - 60 seconds) within 2 minutes after occurrence delivery, after the routine prophylactic intravenous injection of oxytocin at delivery of the anterior shoulder and clamping of the umbilical cord. All other aspects of managing the third stage of labor were identical in the both investigated research groups Adverse events have been assessed and evaluated in all the cases till discharge from hospital and by means of a telephone interview after 3 months postpartum.

Research outcomes

The primary outcome was postpartum hemorrhage occurrence, clinically defined as estimated blood loss of at least 500 ml, as measured with the collector bag, in all the cases during immediate postpartum clinical surveillance within the room of delivery. Other research outcomes involved adverse clinical events correlated to tranexamic acid e.g. nausea, vomiting, photopsia (sensation of seeing lights, flashes of color), or dizziness within the room of delivery.

Statistical Analysis

Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 23. Data were presented as mean and standard deviations for quantitative data with parametric distribution and median with inter-quartile range for quantitative data with non parametric distribution and numbers and percentages for qualitative data. The comparison between two groups was done using independent t-test for parametric data, Mann-Whitney test for non parametric data and Chi-square test for qualitative data while Fisher exact test was used instead of Chi-square test when the expected count was found less than 5 in any cell. Relative risk was calculated to assess the effect of tranexamic acid on post partum hemorrhage. The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant at the level of < 0.05.

Results

Table 1 Reveals that there is no statistical significant difference between both research groups (tranexamic acid and placebo research groups) as regards Age (years), mean ± SD , BMI before pregnancy, mean ± SD , Primiparous Any uterine scar, Previous cesarean delivery, History of postpartum hemorrhage, Gestational diabetes, Gestational hypertensive disorder, Hospitalization during pregnancy >24 hours, Induction of labor, Epidural analgesia, Oxytocin during labor , Duration of active phase of labor (hours), median (IQR), Operative vaginal delivery, Episiotomy, Perineal tear, Infant's birth weight ≥4000 g, Prophylactic oxytocin at delivery, Interval between delivery and administration of trial regimen, median (IQR), Controlled traction of umbilical cord, Duration of use of collector bag, mean ± SD (p values=0.229, 0.869, 0.899, 0.896, 0.782, 0.487, 0.678, 0.816, 0.795, 0.696, 0.508, 0.847, 0.514, 0.869, 0.705, 0.702, 0.819, 0.363, 0.641, 0.847, 0.202 consecutively).

Table 2 Reveals statistical comparative analysis as regards outcomes in both research groups in which there was statistical significant difference as regards Blood loss (ml), median (IQR), Primary outcome, no. (%),clinically significant postpartum hemorrhage, no. (%) (p values =0.007,0.038,0.027 consecutively) denoting that tranexamic acid research group had lower blood loss, postpartum hemorrhage in a statistically significant manner, whereas there was no statistical significant difference between both research groups as regards Additional uterotonic agent for excessive bleeding, no. (%), Severe postpartum hemorrhage, no. (%),Blood transfusion, Arterial embolization or surgery for postpartum hemorrhage, no. (%), Decrease hemoglobin >2 (g/dl), Decrease hematocrit >10% from pre no. (%), (p values =0.091, 0.572, 0.780, 0.422, 0.861, 0.585 consecutively).

Table 3 Reveals comparative statistical analysis between tranexamic acid and placebo research groups as regards adverse events and follow up findings in which there was statistical significant difference between both research groups as regards Vomiting or nausea being higher among the tranexamic acid research group (p value<0.001), on the other hand there was no statistical significant difference between both research groups as

regards Photopsia, Dizziness, Systolic ≥140 mm Hg, Diastolic ≥90 mm Hg (p values=0.391, 0.275, 0.618, 0.718 consecutively). concerning follow up findings there was no statistically significant difference as regards any thromboembolic event, Seizure, Readmission after discharge, Anticoagulant therapy at and after discharge (p values=0.411, 0.990, 0.683, 0.818 consecutively).

	Tranexamic acid group No. = 500	**Placebo group No. = 500**	**Test value**	**P-value**	**Sig.**
Age (years), mean ± SD	29.89 ± 4.32	30.22 ± 4.35	1.204•	0.229	NS
BMI before pregnancy, mean ± SD	24.19 ± 3.31	24.15 ± 4.32	0.164•	0.869	NS
Primiparous	267 (53.4%)	264 (52.8%)	0.016*	0.899	NS
Any uterine scar	32 (6.4%)	31 (6.2%)	0.017*	0.896	NS
Previous cesarean delivery	29 (5.8%)	27 (5.4%)	0.076*	0.782	NS
History of postpartum hemorrhage	25 (5.0%)	30 (6.0%)	0.481*	0.487	NS
Gestational diabetes	54 (10.8%)	50 (10%)	0.172*	0.678	NS
Gestational hypertensive disorder	10 (2.0%)	9 (1.8%)	0.054*	0.816	NS
Hospitalization during pregnancy >24 hr	31 (6.2%)	33 (6.6%)	0.067*	0.795	NS
Induction of labor	101 (20.2%)	106 (21.2%)	0.152*	0.696	NS
Epidural analgesia	488 (97.6%)	491 (98.2%)	0.438*	0.508	NS
Oxytocin during labor	287 (57.4%)	290 (58.0%)	0.037*	0.847	NS
Duration of active phase of labor (hours), median (IQR)	2.41 (1.61 – 4.2)	2.39 (1.51 – 3.9)	1.121ǂ	0.514	NS
Operative vaginal delivery	91 (18.2%)	89 (17.8%)	0.027*	0.869	NS
Episiotomy	115 (23.0%)	110 (22.0%)	0.143*	0.705	NS
Perineal tear	279 (55.8%)	273 (54.6%)	0.146*	0.702	NS
Infant's birth weight ≥4000 g	41 (8.2%)	43 (8.6%)	0.052*	0.819	NS
Prophylactic oxytocin at delivery	496 (99.2%)	493 (98.6%)	0.827*	0.363	NS
Interval between delivery and administration of trial regimen, median (IQR)	1 (1 – 2)	2 (1- 2)	0.894ǂ	0.641	NS
Controlled traction of umbilical cord	213 (42.6%)	216 (43.2%)	0.037*	0.847	NS
Duration of use of collector bag, mean ± SD	28.38 ± 4.54	29.25 ± 4.63	1.276•	0.202	NS

Data was presented as numbers and percentages, otherwise was indicated
BMI: Body mass index; IQR: Inter-quartile range
•: Independent t-test; * Chi-Square test; ǂ: Mann-Whitney test

Table 1: Characteristics of the two studied groups.

	Tranexamic acid group No. = 500	Placebo group No. = 500	P-value	Relative Risk ratio (95% CI)
Blood loss (ml), median (IQR)	230 (180 – 1130)	470 (220 – 1354)	**0.007•**	---
Primary outcome≠, no. (%)	41 (8.2%)	61 (12.2%)	**0.038***	**0.672 (0.462 to 0.979)**
Clinically significant postpartum hemorrhage, no. (%)	37 (7.4%)	54 (10.8%)	**0.027***	**0.630 (0.418 to 0.950)**
Additional uterotonic agent for excessive bleeding, no. (%)	35 (7.0%)	50 (10.0%)	0.091*	0.700 (0.463 to 1.059)
Severe postpartum hemorrhage§, no. (%)	13 (2.6%)	16 (3.2%)	0.572*	0.813 (0.395 to 1.671)
Blood transfusion	6 (1.2%)	7 (1.4%)	0.780*	0.857 (0.290 to 2.533)
Arterial embolization or surgery for postpartum hemorrhage, no. (%)	2 (0.4%)	4 (0.8%)	0.422*	0.500 (0.092 to 2.718)
Decrease hemoglobin >2 (g/dl)	76 (15.2%)	78 (15.6%)	0.861*	0.974 (0.729 to 1.303)
Decrease hematocrit >10% from pre no. (%)	14 (2.8%)	17 (3.4%)	0.585*	0.824 (0.410 to 1.653)

Data was presented as numbers and percentages, otherwise was indicated
The primary outcome was postpartum hemorrhage, defined as blood loss of at least 500 ml
§ Severe postpartum hemorrhage was defined as blood loss of at least 1000 ml.
* P-value of Chi-square test or Fisher exact test; •: Mann-Whitney test; Bold indicate significant

Table 2: Comparison between the two studied groups regarding outcomes.

	Tranexamic acid group No. = 500	Placebo group No. = 500	P-value*	Relative Risk ratio (95% CI)
In the delivery room				
Vomiting or nausea	41 (8.2%)	14 (2.8%)	**<0.001**	**2.929 (1.617 to 5.304)**
Nausea	29 (5.8%)	13 (2.6%)	**0.014**	**2.231 (1.174 to 4.241)**
Vomiting	21 (4.2%)	7 (1.4%)	**0.011**	**3.000 (1.287 to 6.994)**
Photopsia	15 (3.0%)	20 (4.0%)	0.391	0.750 (0.389 to 1.448)
Dizziness	13 (2.6%)	8 (1.6%)	0.275	1.625 (0.680 to 3.886)
Systolic ≥140 mm Hg	138 (27.6%)	131 (26.2%)	0.618	1.053 (0.859 to 1.292)
Diastolic ≥90 mm Hg	132 (26.4%)	127 (25.4%)	0.718	1.039 (0.843 to 1.282)
Completed interviews at 3 months	**476**	**468**		
Any thromboembolic event	2/476 (0.42%)	4/468 (0.85%)	0.411	0.492 (0.091 to 2.671)
Seizure	1/476 (0.21%)	1/468 (0.21%)	0.990	0.983 (0.062 to 15.674)
Readmission after discharge	15/476 (3.15%)	17/468 (3.63%)	0.683	0.868 (0.438 to 1.717)
Anticoagulant therapy at and after discharge	15/476 (3.15%)	16/468 (3.42%)	0.818	0.922 (0.461 to 1.843)

*Data were presented as numbers and percentages and compared using Chi-square test
*P-value of Chi-square test or Fisher exact test; Bold indicate significant

Table 3: Comparison between the two studied groups regarding adverse events and follow up findings.

Discussion

Tranexamic acid an antifibrinolytic agent that is well known to reduce bleeding events and severity in obstetric practice, however almost always it is considered the safest practice to avoid postpartum hemorrhage is to administer ecbolic agents**.** [16,17,18].

A growing research interest supported by some international guidelines have shown that tranexamic acid agent could be a useful adjuvant to ecbolics to avoid clinical scenarios of postpartum hemorrhage, it was also, revealed and displayed by prior research groups that tranexamic acid agent prevents catastrophic levels of post-partum bleeding when administer at a proper timing after delivery [19,20,21].

A prior research study similar to the current study in approach and methodology have revealed and displayed that cases delivering vaginally receiving prophylactic oxytocin, the usage of tranexamic acid made postpartum hemorrhage occurrence statistically significantly lower in comparison to placebo research group those research findings in comparison to the current study findings show great harmony and similarity [22,23,24].

Another prior research study have revealed and displayed among its findings that vomiting or nausea as side effects from bleeding reducing agents are statistically significantly higher among the research group administered tranexamic acid in comparison to other agents on the other hand it is revealed that nausea and vomiting although occurring more with tranexamic acid agent it is not in a clinically severe level [25,26].

Interestingly a prior research team of investigators following up cases that were administered tranexamic agent as a preventive agent for post-partum hemorrhage in conjunction to ecbolics have shown that there was no statistically significant difference in comparison to placebo research group as regards of thromboembolic events within 3 months after administration of the management protocol ,those research findings have shown great similarity and harmony to the current study findings denoting that tranexamic acid as an agent used in conjunction to ecbolic agents have a reasonable safety profile with acceptable levels of side effects that do not jeopardize maternal safety [1,5,7].

Another research team of investigators have compared and contrasted the usage of tranexamic acid to placebo in cesarean deliveries have displayed among their research findings a high level of efficacy in reducing bleeding events besides the even when post-partum hemorrhage occurred the levels of bleeding were not catastrophic and didn't require further intervention. Those research findings denote that tranexamic acid could have molecular level mechanisms that support hemostasis and reduce blood loss in manner making it a valuable agent in obstetric practice therefore if implemented in clinical guidelines could reduce maternal mortalities from bleeding issues [3,9,15,20].

Conclusions and recommendations for future research

Tranexamic acid is a useful agent in reducing postpartum hemorrhage and have a reasonably acceptable side effect profile that could be considered as a routine agent in practice .However the influence of tranexamic acid in reducing bleeding in traumatic deliveries should be investigated in future research studies besides future research should put in consideration other variables that could affect the bleeding within the post-partum period such as racial and ethnic differences besides the BMI variability among the cases .Future research studies are required to be multicentric in fashion to verify the current study findings.

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