



Journal of Contemporary Medicine
and Dentistry

www.jcmad.com

ISSN [P-2347-4513]
ISSN [O-2349-0799]
Year: 2021, Volume: 9
Issue: 3, p:47 – 51


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Role of Tranexamic Acid in Reducing Blood Loss in Vaginal Delivery

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Abstract

Background: Postpartum hemorrhage is the most common cause of morbidity and mortality. Recognition of PPH and management is based on achieving adequate uterine tone and maintaining maternal hemodynamic stability. Several drugs are available for the management of PPH. We in the current study tried to evaluate the efficacy of Tranexamic acid in reducing blood loss during normal labor. **Methods:** Based on the inclusion and exclusion criteria n=100 females were included in the current study. Administration of 10 IU injection Oxytocin I.V was given to mother as soon as the delivery of anterior shoulder of the baby followed by injection of Tranexamic acid 500 mg slow IV infusion for 5 minutes in the study group. 10 IU injection Oxytocin I.V was followed by placebo injection of normal saline 5 ml was given in the control group. **Results:** The mean fall in hemoglobin was 1.67 gm% in the study group and 2.15 gm% in the control group. The mean fall in hematocrit was 1.92% in the study group and 4.04% in the control group. The post-delivery hemoglobin and hematocrit were significantly reduced in the control group compared to the study group. The number of cases in the study group that required blood transfusion was n=3(6%) and the number of cases in the control group requiring the blood transfusion was n=8(16%). **Conclusion:** Within the limitations of the current study, it can be concluded that among the women with vaginal delivery who received prophylactic oxytocin and tranexamic acid reduced the blood loss from the time of delivery to 2-hour post-partum. The need for additional uterotonics and maternal blood transfusion is significantly reduced in the study group compared to the control group.

Keywords: Tranexamic Acid, Postpartum hemorrhage (PPH), Vaginal delivery

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Date of Acceptance: 10/09/2021

Introduction

Postpartum hemorrhage (PPH) is the leading direct cause of maternal death. WHO suggests that PPH occurs in 10.5% of postpartum women, which equates to nearly 14 million women annually [1, 2] PPH accounts for one-third of all maternal deaths, with 99% of these deaths occurring in low- and middle-income countries (LMICs) in women who give birth outside of a hospital setting. [2, 3] PPH is a leading cause of maternal death accounting for over 30% of maternal deaths in Africa and Asia. [4] Furthermore, it is a substantial source of

maternal morbidity and can have long-term effects on a woman's health. [4] Maternal hemorrhage can occur in the antepartum, intrapartum, or postpartum period. The WHO defines postpartum hemorrhage (PPH) as blood loss of 500 ml or more from the genital tract after delivery, although some studies define PPH as blood loss greater than or equal to 1000 ml as this has greater clinical significance. [4] Similar definitions do not exist for antepartum hemorrhage (APH) or intrapartum hemorrhage (IPH). Studies have shown that most maternal deaths occur due to uterine rupture, uterine atony, retained placenta, and genital tract trauma including cesarean section. [5, 6] Typically,

oxytocin is used as the initial medication for PPH management then other uterotonics are administered if oxytocin fails to stop bleeding, then hemostatic recombinant activated factor VIIa and the antifibrinolytic tranexamic acid have been used. [7] Tranexamic acid may be used to treat PPH, in case of high-risk factors such as placenta previa and lacerations from instrumental delivery, which may not respond to uterotonics. Tranexamic acid is a synthetic derivative of the amino acid lysine, and it serves as an antifibrinolytic by reversibly binding four to five lysine receptor sites on plasminogen This inhibits plasmin formation and displaces plasminogen from the fibrin surface. It may also directly inhibit plasmin and partially inhibit fibrinogenolysis at higher concentrations. Tranexamic acid is also thought to exert an anti-inflammatory effect by inhibiting plasmin-mediated activation of complement, monocytes, and neutrophils and may improve platelet function in certain circumstances. [8-10] Tranexamic acid has roughly eight times the antifibrinolytic activity of an older analog, ε-aminocaproic acid. Tranexamic acid also directly inhibits the activity of plasmin with weak potency (IC50 = 87 mM), and it can block the active site of urokinase plasminogen activator (uPA) with high specificity (Ki = 2 mM) among all the serine proteases. [11, 12] With this background we in the current study tried to evaluate the efficacy of parenteral tranexamic Acid, 500 mg, slow IV in reducing blood loss during normal labor.

Materials and Methods

This cross-sectional study was conducted in the Department of Obstetrics and Gynecology, Prathima Institute of Medical Sciences, Naganoor, Karimnagar. Institutional Ethical committee permission was obtained for the study. Written consent was obtained from all the participants of the study. Patients admitted to our hospital based on the inclusion and exclusion criteria were selected for the study.

Inclusion criteria

1. Primi and second gravid
2. More than 38 weeks of gestation
3. Spontaneous or induced labor

Exclusion criteria

1. Anemia
2. Twin pregnancy
3. Uterine fibroids history of previous PPH
4. Polyhydramnios, macrosomia
5. Abnormal placenta: placenta previa, placental abruption, placental adhesions
6. caused by repeated artificial abortions
7. Pre-labor Rupture of Membrane PROM.

The patients were randomly allotted to two groups by computer-generated random number and the groups were designated as Study Group 'S': Routine prophylactic 10 IU Inj. Oxytocin IV was given to the mother as soon as the delivery of the anterior shoulder of the baby followed by Inj. Tranexamic acid 500 mg slow IV i.e over 5 mints Control Group 'C': Routine prophylactic 10 IU Inj. Oxytocin IV was given to the mother as soon as the delivery of the anterior shoulder of the baby followed by a Placebo injection of normal saline 5 ml slow I.V All the patients were monitored with BP, heart rate, Respiratory rate. Pre-Delivery: CBC, coagulation profile (PT, APTT, INR), BT, CT, blood grouping and typing, HIV, HbsAg, RBS. BP was checked immediately after placental delivery and the first and second hour after delivery. The extent of PPH was measured by weight and volume. Immediately after delivery of the baby, when all the liquor was drained, the patient was brought to the edge of the table. A disposable, conical, graduated plastic collection bag is placed under the buttocks of the patient for the blood to get collected. The amount of blood collected in the blood drape is measured. Then the patient was given pre-weighed pads, which were weighed 2 hrs postpartum. In our study blood loss was measured by measuring the blood collected in the drape and by weighing the swabs before and after delivery. Total blood loss (ml) = blood in the drape (ml) + (swab weight post-delivery in gms. Swab weight predelivery in gms)/1.05. All the available data was uploaded on an MS Excel spreadsheet and analyzed by SPSS version 20 in windows format. The continuous variables were represented as mean and standard deviations. The categorical variable is depicted in percentage p-values <0.05 was considered significant.

Results

The mean age group of the study group was 26.5 ± 3.55 years similarly the mean age of the study group was 25.4 ± 4.5 years. The majority of the patients in both groups were between 21 – 25 years followed by 26 – 30 years as depicted in Table 1. The p-value was 0.523 hence no significant difference was found in the distribution of cases of both groups.

Table 1: Age-wise distribution of cases in the study

Age group	Study Group N (%)	Control group N (%)
< 20 years	05(10)	06(12)
21 – 25	28(56)	26(52)
26 – 30	10(20)	12(24)
> 30	07(14)	06(12)
Total	50(100)	50(100)

N=33 patients in the study group and n=30 patients in the control group were primigravidas. N=17 patients in the study group and N=20 patients in the control group were 2nd gravidae. The parity index was comparable in both groups. Antenatal booking was not different in both groups significantly. 6% of the patients in the study group and 4% of the patients were unbooked cases. The mean weight was 57.5 kg in the study group and 58.1 kg in the control group. The mean height was 152.5 cm in the study group and 153.5 cm in the control group. The average BMI was 24.25 kg/m^2 in the study group and 25.65 kg/m^2 in the control group. The mean fall in hemoglobin was 1.67 gm% in the study group and 2.15 gm% in the control group. The mean fall in hematocrit was 1.92% in the study group and 4.04% in the control group. The post-delivery hemoglobin and hematocrit were significantly reduced in the control group compared to the study group depicted in table 2.

Table 2: Changes in the Blood Indices

Blood indices		Study Group		Control Group		p-value
		Mean	SD	Mean	SD	
Hb gm%	Pre-delivery	12.45	1.26	12.50	1.03	<0.041
	Post delivery	10.78	1.32	9.05	1.05	
	Change	1.67	0.023	2.15	0.71	
PCV%	Pre delivery	35.50	3.15	36.32	3.67	<0.01
	Post delivery	33.62	3.35	32.82	3.92	
	Change	1.92	0.450	4.04	0.66	

The onset of labor in the study was analyzed, spontaneous labor was in n=47(94%) and

induced labor was in n=3(6%). Similarly, in the control group, spontaneous labor was in n=45(90%) cases and induced labor was in n=5(10%) cases. The mean duration of the 3rd stage was 4.40 mins in the study group and 4.52 mins in the control group. There was no influence of the drug in the duration of 3rd stage.

Table 3: Amount of Blood Loss

Blood loss in ml	Study Group		Control Group		p-value
	Mean	SD	Mean	SD	
Time of delivery to 30 mins	38.86	4.32	42.5	3.50	0.023*
30 mins to 2 hours	22.20	3.56	27.30	3.64	0.014*
Blood in GCB	135.33	30.38	213.10	41.67	0.032*
Total Blood loss	191.11	37.05	277.13	49.31	0.01*

* significance

The number of cases in the study group that required blood transfusion was n=3(6%) and the number of cases in the control group requiring the blood transfusion was n=8(16%). In the study group APGAR $\geq 8 / 10$ was found in n=47(94%) an APGAR $< 8 / 10$ n=3(6%) and in the control group the APGAR $\geq 8 / 10$ n=44(88%) and APGAR $< 8 / 10$ n=6(12%). The maternal complications in the study have been depicted in table 4. Additional uterotonics were required in n=3(6%) cases of the study group and n=7(14%) of the control group. The mean duration of hospital stay in the control group was 4.56 days and the mean duration of hospital study in the control group was 5.5 days.

Table 4: Maternal Complications

Maternal Complications	Study Group (n=50)	Control Group (n=50)
Headache	1 (2%)	1 (2%)
PPH	0 (0%)	3 (3%)
Nausea	2 (4%)	1 (2%)
Vomiting	1 (2%)	0 (0%)
Fever	1 (2%)	1 (2%)
Total	5 (10%)	6 (12%)

Discussion

As obstetric blood loss contributes to one-fourth of global maternal death, death resulting from PPH should be avoided. As the fibrinolytic system gets activated after placental delivery antifibrinolytic agents can be used to reduce obstetric blood loss. Tranexamic acid 500 mg slow intravenously was used prophylactically in our study to observe its efficacy in reducing blood loss during and after vaginal birth in the

study group. Tranexamic acid 500 mg slow intravenously was used prophylactically in our study to observe its efficacy in reducing blood loss during and after vaginal birth in the study group. In our study, the age group of patients included varied from 18 to 33 years. The maximum percentage of patients belong to the age group of 20-24 years. On average, 54% of the 100 population were between 21-25 years with a mean age of 23.3 years. Yang H et al.,^[13] in a similar study found the mean age was 23.5 years. mean age was 23.5 years. In this study N=33 patients in the study group and n=30 patients in the control group were primigravidas. N=17 patients in the study group and N=20 patients in the control group were 2nd gravidas. In a similar study Gungorduk K et al.,^[14] found primigravidas were 28% and second gravidas were 72%. The mean fall in hemoglobin was 1.67 gm% in the study group and 2.15 gm% in the control group. The mean fall in hematocrit was 1.92% in the study group and 4.04% in the control group. Peitsidis P et al.,^[15] in their systematic review of five randomized controlled trials in which mean blood loss difference was 32 ml in cases and control. They concluded that tranexamic acid reduces the blood loss after lower segment cesarean section and vaginal deliveries and the need for blood transfusions also reduces. The frequency of PPH was found in the control group with n=3(6%) of cases no case of PPH was detected in the study group. The result is comparable to G Kemal et al.,^[16] where they found the frequency of PPH (blood loss >500 ml) was in less than 1.8% of the experimental group and 6.8% of cases of the control group. In our study, there was a statistically significant reduction of blood loss in both periods, that is from time of delivery to 30 mins and from 30 mins to 2 hrs postpartum. Mean blood loss from the time of delivery to 30 mins was 174.19 ml in the study group and was 255.6 ml in the control group. Movafegh A, et al.,^[17] found the mean blood loss was significantly lesser in cases with tranexamic acid use as compared to the control group (262.5±39.6 vs 404.0 ml ± 94 ml). M Heesen et al.,^[18] in their seven trials concluded the use of tranexamic acid reduced the blood loss (WMD - 140.29 ml, CI 189.64 to 90.93 ml: P <0.00001). Tranexamic acid use is associated with complications such as nausea or vomiting hence

the number of cases reported with nausea and vomiting in our study were slightly more in the study group (table 4) as compared to the control group however none of the cases were severe and we managed easily.

Conclusion

Within the limitations of the current study, it can be concluded that among the women with vaginal delivery who received prophylactic oxytocin and tranexamic acid reduced the blood loss from the time of delivery to 2-hour postpartum. The need for additional uterotonics and maternal blood transfusion is significantly reduced in the study group compared to the control group.

Conflict of Interest: None

Source of support: Nil

Ethical Permission: Obtained

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