

Tranexamic Acid: Role in Prevention of Post Partum Hemorrhage

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ABSTRACT

Objective: The objective of the study was to compare the frequency of postpartum hemorrhage in patients given tranexamic acid along with active management of third stage of labor versus the control group in which active management of third stage of labor alone was done.

Study Design: Randomized controlled trial

Place and duration of study: This study was conducted in the Department of Obstetrics and Gynaecology, Unit II Sheikh Zaid Medical Hospital Rahim Yar Khan from January 2015 to October 2015.

Patients and methods: Eight hundred and twenty patients presenting in labor and fulfilling the inclusion criteria were included in this study. Patients were divided into two groups, cases and control. Each group had 410 patients. Cases were included those patients in which active management of third stage of labor was done, in addition they received intravenous 1gm tranexamic and control group received only active management of third stage of labor.

Results: As compared to active management of third stage of labor alone, addition of tranexamic acid was responsible for significant reduction in frequency of PPH and amount of blood loss(P value<0.05). Frequency of PPH was 7.3% in control group and 2.4% in tranexamic acid group.

Conclusion: It is concluded from our study that addition of tranexamic acid along with active management of third stage of labor is an efficient and safe method of reducing PPH.

Key words: Tranexamic acid, postpartum hemorrhage, active management of third stage of labor

INTRODUCTION

Postpartum hemorrhage (PPH) is a life threatening emergency situation. It is an important cause of maternal morbidity and one of the major killer of females of childbearing age group all over the world.¹ Prevalence of PPH is 34% in Pakistan according to WHO and 27% mothers died due to PPH who were having home deliveries (65%).² This prevalence is much higher in our country as compared to the figures in developed countries, where it is coated to be 2-11%. Postpartum hemorrhage is a common and occasionally life threatening complication of labor.³ It is the primary PPH which accounts for almost all cases of maternal death and is reported to occur in 2 to 20% of cases though reported incidence of maternal death (43%) with PPH occurring in 14% in one study done in Pakistan.⁴

Postpartum hemorrhage is defined as loss of greater than 500 ml blood followed by vaginal delivery of a baby and greater than 1000ml blood after lower segment Caesarean Section. However

these cut off values do not consider the pre-existing health condition and even blood loss of 200ml can be lethal for a woman with preexisting anemia or having medical disorder.⁵ Among 14 million mother having PPH each year, 2% mother died within an average interval of two hours from onset of bleeding till availability of help.^{4,5} Majority of deaths from PPH occur outside well equipped hospital, even expert and skilled obstetricians are unable to deal the women in dire condition of life and death without availability of life saving medicines and safe blood transfusion services.¹ Keeping in mind, the impact of PPH over maternal morbidity and mortality it is evident that if its incidence is reduced it is going to have marked reduction in maternal mortality. Patient morbidity also increases due to PPH. Majority of patients with PPH acquire blood borne infections, a hazard associated with multiple blood transfusions.⁶

In third stage after separation of placenta from the uterine wall, a cascade of physiological and hemostatic events occur aiming to reduce

bleeding: strong uterine contractions, increased platelets function, a massive release of coagulation factors and a simultaneous increase in fibrinolytic activity. As a result there is theoretical beneficial role of antifibrinolytic agents in the management of postpartum hemorrhage. Addition of tranexamic acid intravenously may be one of methods if added in third stage of labor management.

Tranexamic acid, an antifibrinolytic agent which is a synthetic derivative of amino acid lysine that works by reversibly inhibiting the activation of plasminogen factor thus stops fibrinolysis and reduces bleeding. It may boost up the patient's own hemostatic mechanism.⁷ It also reduces the requirement of blood transfusion by 39% as shown by meta-analysis of studies on surgical patients.^{1,8}

Tranexamic acid is commonly used in Gynaecology but antepartum hemorrhage due to placental abruption, placenta previa) has also been managed. Tranexamic acid seems to play important role in the management of bleeding during antenatal period as well.⁹ A few randomized controlled trials have shown role of tranexamic acid in the prevention of PPH following Caesarean section.^{10,11} One study evaluated the effect of tranexamic acid to prevent bleeding in the postpartum period after spontaneous vaginal delivery.¹² Postpartum hemorrhage is the leading cause of maternal mortality in developing countries like Pakistan. Third stage of labor is actively managed in routine practice and no recommendations for tranexamic acid (TA) use in PPH exist in Pakistan. Our study was aimed to determine the effectiveness of the addition of intravenous TA to a standard active management of the third stage of labor (which included prophylactic injection of 10IU of oxytocin at the delivery of anterior shoulder of baby, early cord clamping and controlled cord traction.). It can be an easily available and cost effective management of postpartum hemorrhage.

MATERIALS AND METHODS

This study was conducted in the Department of Obstetrics and Gynaecology, Unit II Sheikh Zayed Medical Hospital Rahim Yar Khan from January 2015 to October 2015. Informed consent from the patients obtained for taking part in the study and using their data in research. Cases were all laboring mothers who received an intravenous injection of 1 gram Tranexamic acid along with active management of third stage of labor, while control group in which third stage of labor was

managed actively alone. Detailed history was taken, examination and investigation were carried out. Socio-demographic data such as age, parity, antenatal care was gathered. Blood loss after delivery was estimated by counting number of soaked pads and blood was collected in kidney. Third stage of labor was managed actively. Placental delivery was done by controlled cord traction.

The data analysis was done by using SPSS (statistical package for social sciences) version 15. Descriptive statistics was calculated. Frequency and percentage of PPH among cases and control were calculated. Mean and standard deviation calculated for age, parity, gestational age and blood loss. Association of postpartum hemorrhage with age and parity was also noted.

RESULTS

Study was conducted out in the Emergency Department of Obstetrics and Gynaecology unit II, Sheikh Zayed Medical Hospital, Rahim Yar Khan. Total 820 patients were included in the study. They were further divided in two groups (410 patients in each group).

Group A received 1 gram injection tranexamic acid intravenously along with active management of third stage of labor and Group B received active management of third stage of labor alone.

Mean age was 27.7 ± 3.8 years for control group and 28.2 ± 3.7 for cases. Minimum age for control group was 18 years and maximum age was 38 years. For cases these figures were 20 years and 40 years respectively. (Table 1) Most of the cases and control had two or more children. Mean gestational age in control group was 38.7 ± 1.08 and in cases it was 38.7 ± 1.03 . Maximum gestational age was 41 weeks in both control group and cases while minimum was 36 weeks in control group and 37 weeks in cases. (Table 1)

There was reduction in blood loss in group-Ai.e cases. Mean blood loss in cases was 395 ± 55.5 ml with minimum value 285 ml and maximum 645ml as compared to control group in which mean blood loss was 415 ± 80.3 ml with minimum and maximum values of 280 ml and 800 ml respectively. (Table 2)

Ten patients experienced blood loss more than 500 ml in group Ai.e cases while 30 patients in the control group experienced blood loss more than 500 ml. The frequency of PPH was 30 (7.3%) in control group and 10 (2.4%) in cases respectively. (Table 3)

While taking into account frequency distribution of age and blood loss in cases 2 patients (0.4%) who had PPH was in age group 21-25 years, 2 patients (0.4%) in age group 26-30 years and 06 patients (1.4%) was in age group 31-35 years which is statistically significant. In control group 6 (1.4%) patients with PPH were in age group 21-25 years, 10 patients (2.3%) belong to age group 26-

30 years and 14 patients (3.3%) were from age group 31-35 years. (Table 5)

Comparing the frequency distribution of parity and blood loss in different age groups in cases and control group is shown in **table 5**. There was no relation found between PPH and increasing parity.

Table 1

Group	Number	Minimum	Maximum	Mean	Standard deviation
Controls Age	410	18	38	27.77	3.873
Parity	410	01	07	2.52	1.299
Blood loss	410	280	800	415.51	80.32
Gestational age	410	36.00	41.00	38.00	1.089
Cases Age	410	20	40	28.27	3.704
Parity	410	01	07	2.56	1.275
Blood loss	410	285	645	395.53	55.579
Gestational age	410	37.00	41.10	38.77	1.039

Table 2: Blood loss

Groups	N	Mean	Std. Deviation	Minimum	Maximum
Control	410	415.51	80.325	280	800
Tranexamic acid group	410	395.53	55.579	285	645
Total	820	405.52	69.708	280	800

Table 3: Frequency distribution of Postpartum hemorrhage among cases and controls

		Postpartum hemorrhage		Total	
		No	Yes		
Groups	Control	Count	380	30	410
		% within Groups	92.6%	7.3%	100.0%
	Tranexamic acid group (cases)	Count	400	10	410
		% within Groups	97.5%	2.4%	100.0%
Total		Count	780	40	820
		% within Groups	95.1%	4.8%	100.0%

Table 4: Frequency distribution of age

Groups	Age					Total
	15-20	21-25	26-30	31-35	>35	
Control blood loss <500ml not PPH	2	82	178	96	22	380
Blood loss >500ml PPH	0	06	10	14	0	30
Total	2	88	188	110	22	410
Cases blood loss <500ml not PPH	0	64	194	122	20	400
Blood loss >500ml PPH	0	02	02	06	0	10
Total	0	66	196	128	20	410

Table 5: Frequency distribution of parity and blood loss among cases and controls

Groups	Parity			Total
	1-3	4-6	>6	
Control blood loss<500ml not PPH	312	50	18	380
Blood loss >500ml PPH	26	04	0	30
Total	338	54	18	410
Cases blood loss<500ml not PPH	318	70	12	400
Blood loss >500ml PPH	06	04	0	10
Total	324	74	12	410

DISCUSSION

According to WHO, 10.5% of all live births are complicated by obstetrical hemorrhage, which is a leading cause of maternal death. PPH was the most frequent cause in 14million reported cases of obstetrical hemorrhage. It results in 150,000 maternal deaths annually which form one quarter of the total maternal deaths.¹³The reported prevalence of PPH in Pakistan is 34% according to WHO.²PPH causes significant maternal morbidity, severe anemia, coagulation disorder, need of multiple blood transfusions, acute tubular necrosis, Sheehan syndrome and obstetrical hysterectomies.⁴

In the current study 820 patients (410 cases & 410controls) were enrolled.Demographic data of the patientsincluding age, parity, gestational age and blood loss was evaluated. Distribution of patients according to different age groups and duration of pregnancy evaluated.

In our study, cases were having mean blood loss of 395ml and 415ml in control group. There was a difference of 20 ml on average. Rezan A Kadir conducted a systematic review of five randomized controlled trials in which mean blood loss difference was 32ml in cases and control. These trials concluded that tranexamic acid reduces the blood loss after lower segment caesarean section and vaginal deliveries, and need for blood transfusions also reduces.⁹

The frequency of PPH in our study was 2.4 % in tranexamic acid group as compared to control group having frequency 7.3%. This is comparable with the study of G Kemal in which the frequency of PPH i.e blood loss>500ml was less 1.8% in experimental group and 6.8 % in the control group.¹⁰

Incidence of PPH was magnificently less in study (cases 31.1% versus 63.2% controls) done by Amr H Yehia in 2014.¹⁴

In another study conducted by Yang H, et al. frequency of PPH was lower 6.4% in the tranexamic acid when compared with controls. Average blood loss was also significant in the tranexamic acid. This showed that tranexamic acid is efficient and safe in reducing postpartum haemorrhage.¹⁵

In the study of Movafegh A, Eslamian L, et el. Mean blood loss was significantly lower in cases as compared to control group(262.5±39.6 vs 404ml±94ml).¹⁶ In Study of M. Heesen et al; included seven trials concluded significantly reduced blood loss after addition of tranexamic acid (WMD -140.29 ml, CI -189.64 to -90.93ml: P <0.00001).¹⁷In our study there was no association between increasing age, parity an gestational age with increased blood loss.In the study of Ferrer P, Roberts I, et al. the addition of tranexamic acid in third stage was helpful in the reductionof postpartum blood loss of 92ml.¹⁸

Postpartum hemorrhage is the leading cause of maternal mortality in developing countries like Pakistan. Maternal Mortality nonetheless remains a crucial indicator of the obstetrical care and health status of the mother. The most common causes of PPH are atonic uterine, placentationpathology, trauma of genital tract,retained placental and membranes, coagulopathies and arteriovenous malformations. Aggravating factors for PPH include past history, multiparity, increased BMI, induced or augmented labor, multiple pregnancy, polyhydramnios and good sizes baby. Majority of females with PPH have no identifiable risk factors.¹⁹Thats why it is important to prevent occurrence of PPH in all mothers. This prevention is especially important for countries like Pakistan where maternal deaths are attributed by PPH.Almost in all health care facilities third stage of labor is actively managed and no recommendations for tranexamic acid use in PPH

exist in Pakistan. So to emphasize this problem by adding tranexamic acid with third stage of labour can be an effective way to reduced postpartum hemorrhage in areas where surgical facilities are not available.

LIMITATIONS OF STUDY

There may be element of patients selection bias, as all the patients were from same hospital.

CONCLUSION

Theoretical data and results of different clinical trials indicate the tranexamic acid is effective in the prevention as well as for the treatment of PPH. Although the available results of majority of clinical trials is not of sufficient quality to reach any definitive recommendation, however it does suggest the tranexamic acid administration reduces postpartum blood loss. Although larger randomized controlled trials are required to support this finding further.

Healthy mothers are a promise for healthy nation. But unfortunately poor infrastructure, lack of appropriate training for health care providers, less investment for health and negative cultural norms are amongst multiple factors that have impact on the maternal health. Preconception evaluation, appropriate birth spacing, appropriate pregnancy planning, women education regarding importance of seeking antenatal care services need to be give attention and health care facilities should be available close to home. As majority of deliveries are conducted by traditional birth attendants, a comprehensive training program of the TBAs should be organized emphasizing on timely referral of high risk cases to appropriate facilities can help to reduce maternal complications.

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