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ORIGINAL ARTICLE

Role of Tranexamic Acid in Reducing Blood Loss in Vaginal Delivery

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Abstract

Introduction Anti-fibrinolytic agents are used to reduce obstetric blood loss as the fibrinolytic system is known to get activated after placental delivery.

Objectives To evaluate the efficacy of parenteral tranexamic acid in reducing blood loss during normal labour and to compare it with the amount of blood loss in patients who received placebo in the third stage of labour.

Methodology Patients with spontaneous labour or planned for induction of labour and fulfilling the inclusion criteria were recruited for the study. In each patient, the pre-delivery pulse rate, blood pressure, Hb gm% and PCV% were noted. Labour was monitored carefully using a partogram. The study group received Inj. Oxytocin and Inj. Tranexamic acid. The control group received Inj. Oxytocin and Placebo injection. Immediately after delivery of the baby, when all the liquor was drained, the patient was

placed over a blood drape—a disposable conical, graduated plastic collection bag. The amount of blood collected in the blood drape was measured. Then the patient was given pre-weighed pads, which were weighed 2 h post-partum. The blood loss was measured by measuring the blood collected in the drape and by weighing the swabs before and after delivery.

Results The total number of patients studied was 100—equally distributed in both the groups. The age group of the patients and BMI were comparable. There was a significant increase in the pulse rate and decrease in blood pressure in the control group as compared with the study group. The post-delivery haemoglobin and haematocrit were significantly reduced in the control group as compared to the study group. The mean blood loss at the end of 2 h was 105 ml in the study group and 252 ml in the control group. There was a significant increase in the usage of uterotonics and also in the need for blood transfusion in the control group; 12 % of the patients in the control group had to stay for more than 3 days compared to 2 % in the study group.

Conclusion Tranexamic acid injection, an antifibrinolytic agent when given prophylactically after the delivery of the baby, by intravenous route appears to reduce the blood loss and maternal morbidity during normal labour effectively.

Keywords Blood loss · Maternal morbidity · Tranexamic acid

Introduction

Labour is a physiological process, but it is often associated with morbidity and mortality, the most common cause being blood loss [1]. Life-threatening obstetric haemorrhage occurs in approximately 1 per 1000 deliveries [2]. The most recent Practice Bulletin from the American College of Obstetrics and Gynaecology estimates a total of 1,40,000 maternal deaths per year or one woman every 4 min [3]. There are a number of drugs available for the management of PPH with the most recent ones being the anti-fibrinolytics and recombinant factor VIIa [4] with restricting factors being high costs and difficulties in procuring or storing the medication.

Postpartum haemorrhage (PPH) remains a leading cause of maternal mortality, especially in developing countries. In confidential enquiries into maternal deaths in South Africa (2005–2007, Confidential enquiries 2006), 383 maternal deaths due to PPH were reported and the majority of these were considered to be preventable [5]. Of these deaths, 67 (17.5 %) were caused by uterine atony, where uterotonics were required to control the bleeding. Other cases of maternal death from PPH were due to uterine rupture (37 in women with previous caesarean sections and 43 in women without previous caesarean sections), retained placenta (88), inversion of uterus (7) and other genital tract trauma including caesarean section (141) [6].

The great majority were, thus, not due to uterine atony, and attempts to address the problem need to go beyond the use of uterotonic drugs. Because of the difficulty of randomized trials in women presenting with PPH, the use of tranexamic acid for preventing PPH in high-risk women could be regarded as a proxy for assessing its use for treating PPH. In particular, high-risk factors which may not be responsive to uterotonics, such as placenta praevia and lacerations from instrumental delivery, may respond to tranexamic acid [7].

The changes in the fibrinolytic components during and immediately after placental delivery are consistent with fibrinolysis occurring as a response to local fibrin deposition. The plasma fibrinogen level decreases during the third stage of labour and after placental delivery, and the level of fibrin/fibrinogen degradation products in the serum increases 1 h after child birth and remains raised in the early puerperium [8]. Hence, anti-fibrinolytics will be effective in reducing blood loss by interacting with the fibrinolytic mechanism [8, 9]. This study observes the blood loss reduced by tranexamic acid, an antifibrinolytic agent during third stage of labour.

Materials and Methods

Hundred pregnant women who were admitted in the antenatal ward or labour ward of JSS Medical College and Hospital, Mysore, for safe confinement at term were included in this study. Fifty patients were randomized in study group (receiving both Inj. Oxytocin and Inj. Tranexamic acid) and 50 patients in control group (receiving Inj. Oxytocin and Placebo).

Study Outcome To evaluate the efficacy of parenteral tranexamic acid in reducing blood loss during normal labour and to compare it with the amount of blood loss in patients who received placebo (5 ml of normal saline) in the third stage of labour

Primary Outcomes:

1. Reduction in blood loss after parturition.
2. Changes in the blood indices in both the groups.

Secondary Outcomes:

1. Requirement of maternal blood transfusion.
2. Usage of any extra uterotonics.
3. Maternal and foetal complications.
4. Duration of hospital stay.

Study Design Prospective randomized placebo-controlled study.

Study Population All women with singleton term pregnancies, fulfilling the inclusion criteria and planned for vaginal delivery were enrolled into the study.

Study Period 1October 2014 to 31 March 2015.

Informed Consent All the patients and the attenders gave written informed consent.

Inclusion criteria:

- Primi and second gravida
- More than 38 weeks of gestation
- Spontaneous/induced labour

Exclusion criteria:

- Haemoglobin <8 gm%
- Twin pregnancy
- Polyhydramnios
- Macrosomia
- Previous h/o PPH
- Fibroid complicating pregnancy
- Medical co-morbidities complicating pregnancy
- Placenta previa
- Abruptio placenta
- PROM—patients referred from periphery with PROM were excluded as the chances of chorioamnionitis were more due to repeated internal examinations
- Prolonged and obstructed labour

Patients who were admitted in the ward with spontaneous labour or were planned for induction of labour and fulfilled the inclusion criteria were recruited for the study.

Block randomization was done with blocks of 2, 4 and 6 with 30, 30 and 40 %, respectively, using RALLOC software. Concealed envelopes were used for randomization.

In all the patients, detailed medical and obstetric history was taken. In each patient, the pre-delivery pulse rate, blood pressure, Hb gm% and PCV% were noted. Labour was monitored carefully using a partogram, and augmentation was done whenever required. Thirty-four patients were excluded from the study as they required caesarean delivery.

AMTSL is standardly followed in all patients in our institute. In the study group, first, ten units Inj. Oxytocin was given to the mother IM within 1 min of delivery of the baby, followed by Inj. Tranexamic acid slow IV. In the control group, ten units Inj. Oxytocin IM was given within 1 min of delivery of the baby followed by placebo injection of normal saline (5 ml) slow IV.

Immediately after delivery of the baby, when all the liquor was drained, the patient was placed over a blood drape—a disposable conical, graduated plastic collection bag. The amount of blood collected in the blood drape was measured. Then the patient was given pre-weighed pads, which were weighed 2 h post-partum. The blood loss was measured by measuring the blood collected in the drape and by weighing the swabs before and after delivery. Blood loss from delivery of the baby to 2 h post-partum was calculated.

$$\text{Total blood loss (ml)} = \text{Blood in the drape (ml)} + \text{Pad weight after 2 hours (gms)} - \text{Pad weight prior to use (gms)}$$

The side effects of the drug, if any, were noted. The patient was shifted to the post-natal ward after she passed urine.

The patient's post-delivery pulse rate, blood pressure, Hb gm% and PCV% were also noted. Special attention was given to any significant drop in Hb gm% and PCV% resulting in blood transfusions or parenteral iron infusions in the mother. After collecting all the data, the data were tabulated in a master chart and analysed.

Statistical Methods

Statistical analysis was carried out using commercial software SPSS (Statistical Package for Social Sciences) version 16. The descriptive measures such as mean, median and standard deviation for continuous variables were obtained. Frequencies and percentages were calculated for all categorical variables.

Results

The total number of patients studied was 100—equally distributed in both the groups. Thirty-four patients who were randomized into the study, but required caesarean delivery were excluded from the study. Eighteen patients were from the study group, whereas 16 patients were from the control group. The majority of patients in both the groups were aged between 21–24 years and had their BMI between 23 and 24 kg/m^2. Ten patients in study group and 15 patients in control group were primigravida. Forty patients in study group and 35 patients in control group were second gravida. The parity index was comparable in both the groups. Majority of the patients (55 %) had spontaneous onset of labour in both the groups.

The mean increase in pulse rate was 1.40 bpm in study group and 5.60 bpm in control group. The mean fall in systolic BP was 1.40 mmHg in study group and 3.30 mmHg in control group. Mean fall in diastolic BP was 0.50 mmHg in study group and 3.20 mmHg in control group. There was a statistically significant increase in the

Table 1 Variation in vital parameters

Parameters	Study group (mean)	Control group (mean)	*p*
Pulse rate (bpm)			
Pre-delivery	82.46	82.86	
Post-delivery	83.86	88.46	<0.0001
Difference	+1.40	+5.60	
Systolic BP (mmHg)			
Pre-delivery	117.80	108.18	
Post-delivery	116.40	104.88	<0.0001
Difference	−1.40	−3.30	
Diastolic BP (mmHg)			
Pre-delivery	76.90	76.84	
Post-delivery	76.40	73.64	<0.0001
Difference	−0.50	−3.20	

Table 2 Variation in blood indices

Parameters	Study group (mean)	Control group (mean)	*p*
Haemoglobin (gm%)			
Pre-delivery	10.86	10.26	
Post-delivery	10.66	9.56	<0.0001
Difference	−0.20	−0.70	
PCV (%)			
Pre-delivery	33.04	32.60	
Post-delivery	32.64	31.40	<0.0001
Difference	−0.40	−1.20	

pulse rate and decrease in blood pressure in the control group as compared with the study group (Table 1).

The mean fall in haemoglobin was 0.20 gm% in study group and 0.70 gm% in control group. Mean fall in haematocrit was 0.40 % in study group and 1.20 % in control group. The post-delivery haemoglobin and haematocrit were significantly reduced in the control group as compared to the study group. The mean blood loss at the end of 2 h was 105 ml in the study group and 252 ml in the control group. The blood loss was significantly low in the study group compared to the control group (Table 2).

The mean duration of third stage of labour was 4.6 min in the study group and 4.48 min in the control group. There was no influence of the drug in the duration of third stage; 22 % of the patients in the control group needed additional uterotonics compared to only 2 % in the study group. There was a significant difference in the requirement of uterotonics between the two groups. One patient in the study group needed additional uterotonics (carboprost and methergine) and also needed blood transfusion. Eleven patients in the control group needed additional uterotonics, of which five had PPH and other six had mild atonicity. All the 11 patients were given 250 μg Inj. Carboprost IM. Four patients responded to Inj. Carboprost. Seven patients also needed Inj. Methergine 0.2 mg IV. Five patients required per rectal misoprostol 600 μg and blood transfusion; 10 % of the patients in the control group needed blood transfusion compared to 2 % in the study group. There was a significant difference in the need for blood transfusion between the two groups. The patients in both the groups, who had PPH, lost almost 450–600 ml of blood (Table 3).

Table 3 Usage of additional uterotonics

Additional uterotonics	Study group		Control group	
	No.	%	No.	%
Yes	1	2	11	22
No	49	98	39	78
p	<0.001			

Table 4 Requirement for maternal blood transfusions

Blood transfusions	Study group		Control group	
	No.	%	No.	%
Yes	1	2	5	10
No	49	98	45	90
p	<0.01			

Twelve percentage of the patients in the control group had to stay for more than 3 days compared to 2 % in the study group. There was no significant difference in maternal complications such as vomiting, diarrhoea or fever between the two groups (Table 4).

Discussion

Prevention is always better than cure, and hence regarding PPH—an anti-fibrinolytic agent, tranexamic acid was used prophylactically in our study to observe its efficacy in reducing blood loss after vaginal birth.

In our study, mean post-delivery increase in pulse rate was 1.40/min in study group and 5.60/min in control group. The mean fall in systolic BP was 1.40 mmHg in study group and 3.30 mmHg in control group. Mean fall in diastolic BP was 0.50 mmHg in study group and 3.20 mmHg in control group. There was a significant fall BP and rise in pulse rate. In a similar study conducted by Novikova et al. [10], there was a statistically significant change in vital parameters.

Our study noted a statistically significant fall in Hb % in the control group as compared to the study group in

Table 5 Duration of hospital stay

Hospital stay	Study group		Control group	
	No.	%	No.	%
>3 days	1	2	6	12
<3 days	49	98	44	88
p	<0.03			

concordance with a similar study [11]. Additionally, there was a statistically significant reduction in blood loss in the post-partum period. Mean blood loss from the time of delivery to 2 h was 105 ml in study group and 252 ml in control group again in concordance with a similar study conducted elsewhere in 2010 [12].

Our study demonstrated that 22 % of the patients in the control group needed additional uterotonics compared to only 2 % in the study group, which was statistically significant ($p < 0.001$). Thus, significant decrease in the need for additional uterotonics has been reiterated, as also noted in previous trials [13]. Only one patient (2 %) in the study group compared to five patients (10 %) in the control group needed blood transfusion which has also been observed in erstwhile trails [14, 15]. One patient in the study group had to stay for more than 3 days as she was anaemic and needed blood transfusion and parenteral iron therapy. Five patients in the control group were anaemic and were transfused blood and given parenteral iron therapy. One more patient in the control group was not discharged as she developed fever secondary to breast engorgement as the baby was in NICU (Table 5).

Conclusion

Tranexamic acid injection, an antifibrinolytic agent when given prophylactically after the delivery of the baby, by intravenous route appears to reduce the blood loss during normal labour effectively [16], and we would advocate its use as a safe adjunct to oxytocin for regular management of third stage of labour. Some prior studies have demonstrated that tranexamic acid minimally increased the risk of thromboembolism [17] which, however, did not reach statistical significance and was not enumerated either in our experience.

Compliance with Ethical Standards

Conflict of interest There is no conflict of interest involved within the authors of the study.

Ethical Statement Ethical clearance was obtained from the ethical committee. This study was self-funded and no grants were received in the form of sponsorship.

Informed Consent Written informed consent has been obtained from all the patients before they were enrolled into the study.

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