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Original Research Article

Prophylactic Administration of Tranexemic Acid in Reducing the Incidence of Postpartum Haemorrhage in A Tertiary Care Center – A Cross Sectional Study

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Abstract:

Background: Caesarean section is the commonest operative procedure done in the world. Incidence of caesarean section is increasing throughout the world because of social factors like advanced maternal age, improved surgical techniques and increasing litigation problems. Tranexamic acid is an effective agent for the reduction of blood loss, which has been widely used in various areas of medicine. It is an inhibitor of fibrinolysis that blocks the lysine-binding site of plasminogen to fibrin. It has been used to decrease blood loss for many years in cases of hemorrhage, and is reported to reduce intraoperative and postoperative blood loss. The present study observes the blood loss reduced by Tranexamic acid an antifibrinolytic agent during and after caesarean section and normal delivery.

Aims: 1) To study the efficacy of tranexamic acid in reducing blood loss during and after lower segment cesarean section and normal delivery. 2) Our objective is to determine the reduction in amount of blood loss after administration of tranexamic acid during and after cesarean section and normal delivery.

Settings and Design: This study was carried out in the dept. of Obstetrics and Gynecology of Govt. Karur Medical College Hospital in Karur district of Tamilnadu, India, from Jan 2023 to June 2023 as a case-control study.

Materials and Methods: In all patients detailed history – medical history, obstetric history were taken. Vital parameters checked and basic investigations done. Weight of the patient checked. Detailed general examination and obstetric examination done. Gestational age confirmed by USG. 100 patients were placed in group A ie. Control, Normal delivery (50)+ LSCS(50), and 100 patients were placed in group B ie, Cases, Normal delivery (50) + LSCS (50) patients. All patients were counselled and informed consent obtained. Control group –Inj. Oxytocin 10 U IM was administered and Inj. Tranexamic acid 1gm IV was not given. Study group- Both Inj. Tranexamic acid 1gm iv and Inj. Oxytocin 10 U IM was given. Then the results were analysed in terms of vitals monitoring till 2 hours postpartum, uterine contractility, blood loss, etc., and the observations were tabulated and analysed.

Results and Conclusion: Tranexamic acid significantly ($p<0.001$) reduced the blood loss from placental delivery to 2 hour post-partum. Tranexamic acid significantly reduced the amount of blood loss during & after the lower segment cesarean section and normal delivery. 2) Its use was not associated with any adverse drug reaction like diarrhea or thrombosis. Fetal outcome as evaluated by APGAR score was not adversely affected by use of tranexamic acid. 3) Tranexamic acid can be used safely in subjects with lower cesarean section and normal delivery.

Keywords: Cesarean section, Bleeding, Antifibrinolytics.

Introduction

Postpartum Hemorrhage contributes to 25% of global maternal deaths and hence it has to be prevented and/or treated within the golden hour so as to prevent maternal mortality and morbidity as well. Cesarean section (CS) rates have increased to as high as 25 to 30 % in many areas of the world. Delivery by CS can cause more complications than normal vaginal delivery and one of the most common complications is postpartum hemorrhage (20%). It leads to increased maternal mortality and morbidity. In order to reduce maternal mortality and morbidity caused by bleeding, it is important to reduce the amount of bleeding during and after lower segment cesarean section (LSCS) and normal delivery [1]. Tranexamic acid potentiates the

blood clotting system and is used to treat and prevent bleeding. The mechanism of action of tranexamic acid is related to its antifibrinolytic effect, which makes this drug potentially very effective in the third stage of labour. During placental delivery, rapid degradation of fibrinogen and fibrin occurs, as well as an increase in the activation of plasminogen activators and fibrin degradation products due to activation of the fibrinolytic system.

This activation can last up to six to 10 hours postpartum, which may cause more haemorrhage [1],[2]. The antifibrinolytic effect of tranexamic acid in the third stage of labour could make it a safe and effective alternative or adjunct to other regimens currently used in the third stage of labour for prevention of PPH. Tranexamic acid could reduce blood loss associated with complications such as placenta praevia and lower genital tract trauma, as well as bleeding from the upper segment placental site.

Use of tranexamic acid could potentially have prevented some PPH cases if it was given to women with the risk factors for PPH, as reported in WHO in treatment of PPH. Therefore, it may be particularly useful in preventing cases of PPH due to factors other than uterine atony, where uterotonics will not be effective[3],[4].

The present study analyses the blood loss reduced by Tranexamic acid, an antifibrinolytic agent, during and after caesarean section and normal delivery.

Aims and Objectives

- To study the efficacy of tranexamic acid in reducing blood loss during and after lower segment cesarean section and normal delivery.
- Our objective is to determine the reduction in amount of blood loss after administration of tranexamic acid during and after cesarean section and normal delivery.

Review of Literature:

- Tranexamic acid can be successfully used to treat women with history of recurrent abruption to get successful neonatal outcome.
- Tranexamic acid can be used safely and effectively to reduce bleeding resulting from caesarean section. (Tatsumoto K et al 2004).
- Tranexamic acid significantly reduces the amount of blood loss during and after caesarean section without any sideeffects or complications like thrombosis (Gobel Mayer et al 2007).
- Tranexemic acid effectively reduces the blood loss after caesarean section. (Sekhabat et al).
- Tranexamic acid and aprotinin reduce post-operative bleeding and transfusions during primary coronary revascularization. (Robert S. Brown et al).
- Orpen NM, Little C et.al (2006) studied effect of tranexamic acid on total knee arthroplasty by conducting a prospective, randomised, double blind, controlled trial. They concluded that one injection of 15 mg/kg of tranexamic given at the time of cementing the prosthesis in total knee arthroplasty, before deflation of the tourniquet, significantly decreases the amount of blood loss in the early post-operative period. The treatment was not associated with an increase in thromboembolic complications.

Materials and Methods

This study was carried out in the dept of Obstetrics and Gynecology of Govt. Karur Medical College Hospital in Karur district of Tamilnadu, India, from Jan 2023 to June 2023 as a case-control study.

In all patients detailed history – medical history, obstetric history were taken. Vital parameters checked and basic investigations done. Weight of the patient checked. Detailed general examination and obstetric examination done. Gestational age confirmed by USG. 100 patients were placed in group A ie. Control, Normal delivery (50)+ LSCS(50), and 100 patients were placed in group B ie, Cases, Normal delivery (50) + LSCS (50) patients. All patients were counselled and informed consent obtained. Control group –Inj. Oxytocin 10 U IM was administered and Inj. Tranexamic acid 1gm IV was not given. Study group- Both Inj. Tranexamic acid 1gm IV and Inj. Oxytocin 10 U IM were given.

Inclusion Criteria:

- 100 Term Primi delivered by CS and normal Delivery
- Patients giving informed consent
- Singleton pregnancies
- Regular antenatal care

Exclusion Criteria:

- Patient not giving informed consent
- History of thromboembolic disorders
- Allergy to tranexamic acid
- Medical and surgical disorders
- Multiple Pregnancies
- Pregnancy complications such as severe preeclampsia, polyhydramnios.

Intraoperative and Post-operative assessment:

- Vital Signs: Heart Rate, Blood Pressure, Respiratory Rate were checked immediately after placental delivery and 2 hours after birth respectively
- Amount of blood loss

- Uteirne contractility and placental separation
- Side effects caused by tranexamic acid
- Neonatal manifestation
- After collecting all the data, the data were tabulated in a master chart and analysed. Data analysis was done with the help of computer using SPSS 16 software.
- Using these software frequencies, percentage, mean, Standard Deviation, chi square and 'p' values were calculated. Chi square test was used to test the significance of difference between quantitative variables and Student't' test for qualitative variables. A 'p' value less than 0.05 is taken to denote significant relationship.

Statistical Analysis

Table 1: Age Distribution

Age	Control		Case	
	Normal	LSCS	Normal	LSCS
<25	42	39	42	41
>25	8	11	8	9
Total	50	50	50	50
Mean	21.96	22.48	22.92	23.2
SD	2.587	2.557	2.302	2.711
P'value	0.082 Not significant			

The Mean age of the cases in both the group doesn't differ significantly. Mean age of the patients 22.48 belong to the age group of 20-24 years and mean age of the patients 23.2 belong to the age group of 25-29 years.

Table 2: Antenatal care

Antenatal care	No of Cases in			
	Control		Case	
	Normal	LSCS	Normal	LSCS
Booked	50	50	50	50
Unbooked	0	0	0	0
Total	50	50	50	50
P	1.0 Not significant			

Antenatal booking does not differ in both groups significantly. All cases were booked.

Table 3: Indications for caesarean

Indications for caesarean	LSCS	
	Control	Case
Breech	1	2
CPD	5	6
Deep transverse arrest	1	0
Fetal distress	22	18
Failed induction	11	21
Obstructed labour	3	1
Severe oligohydramnios	7	2
TOTAL	50	50
p value	0.190	Not sig

Table 3 shows distribution according to indication of LSCS in both the groups. There was no statistical significance in indication of LSCS between the two groups. Indications of LSCS can have an amount of intraoperative blood loss. The fact that these were matched adequately in the study group removes the effect of these confounding variables.

Table 4: Blood Loss - Placental delivery to end of CS

Placental delivery to end of CS	Blood Loss	
	Control	Case
<350	11	47
351 – 550	35	2
>550	4	1
TOTAL	50	50
Mean	403.8	320.2
SD	113.333	74.217
P VALUE	< 0.001 Significant	

Table 4 shows mean blood loss from time of placental delivery to to end of cesarean section was 403ml in control group and it was 320 ml in the study group, suggesting that there was statistically significant difference

in blood loss in both the groups. Patients who received tranexamic acid had less blood loss in both the groups. The blood loss from placental delivery to end of cesarean section is reduced in cases than control and the P value <0.0001 is significant.

Table 5: End of CS to 2 hrs postpartum

End of CS to 2 hrs postpartum	Blood Loss	
	Control	Case
<50	0	46
51 – 100	49	4
>100	1	0
Total	50	50
Mean	79.8	45
SD	10.784	7.89
P Value	< 0.001 Significant	

Table 5 reveals mean blood loss from time of completion of skin closure to 2 hours postpartum was 45ml in study group and it was 79.8 ml in control group. The blood loss from end of cesarean to 2 hrs postpartum is reduced in cases than controls and the P value is <0.001 is significant.

Table 6: Total Blood Loss

Total Blood loss (ml)				
Total	Control		Case	
	Normal	LSCS	Normal	LSCS
<500	49	46	49	46
>500	1	4	1	4
TOTAL	50	50	50	50
Mean	367.4	483.6	311.8	365.2
SD	38.641	118.145	49.433	78.928
P'value	<0.001 Significant			

Table 6 shows the total blood loss which shows that after the use of tranexamic acid there was a significant reduction in amount of blood loss and the p value was significant.

Table 7: Hb levels

HB% (gm/dl)				
Before Delivery	Control		Case	
	Normal	LSCS	Normal	LSCS
<10	15	12	18	18
10.1 - 12.0	33	35	30	29
>12	2	3	2	3
TOTAL	50	50	50	50
Mean	10.904	11.016	10.516	10.54
SD	0.859	0.87	0.726	0.81
P'value	0.003 Significant			

Table 7 shows fall in Hb % is more in patients – not given tranexamic acid and the P value 0.003 is statistically significant

Table 8: Fall in Hb

HB% (gm/dl)				
Fall in Hb% (gm/dl)	Control		Case	
	Normal	LSCS	Normal	LSCS
<1	0	0	15	13
1.0-2.0	33	36	34	37
>2	17	14	1	0
TOTAL	50	50	50	50
Mean	1.764	1.782	1.122	1.138
SD	0.365	0.371	0.367	0.32
P'value	<0.001 Significant			

There is a significant fall in Hemoglobin between the two groups.

Table 9: Heart rate

Heart rate	Control		Case	
	Normal	LSCS	Normal	LSCS
<80	22	24	26	26
>80	28	26	24	24
TOTAL	50	50	50	50
Mean	82.2	82	82.08	81.48
SD	2.836	2.74	3.702	2.013
P'value	0.612 Not significant			

There is no significant difference between heart rate between the two groups.

Table 10: Respiratory rate

Respiratory rate	Control		Case	
	Normal	LSCS	Normal	LSCS
<17	30	28	31	27
>17	20	22	19	23
TOTAL	50	50	50	50
Mean	17	17.14	17.1	17.26
SD	0.904	0.99	1.055	1.026
P' value	0.626 Not significant			

There is no significant change in respiratory rate between the two groups.

Table 11: Use of additional oxytocin

Use of additional Oxytocin	Control		Case	
	Normal	LSCS	Normal	LSCS
Positive	2	4	0	1
Negative	48	46	50	49
TOTAL	50	50	50	50
P'value	0.159 Not Significant			

There is no significant change in oxytocin additional use between the two groups,

Table 12: Incidence of PPH

Complications	Control		Case	
	Normal	LSCS	Normal	LSCS
PPH	2	4	0	1
Nil	48	46	50	49
TOTAL	50	50	50	50
P'value	0.159 Not Significant			

The incidence of PPH was not statistically different in the control group than study group, it was effectively managed with medical methods and blood transfusion.

Table 13: Side effects of Tranexemic acid

Side Effects	Control		Case	
	Normal	LSCS	Normal	LSCS
Nausea	0	0	1	1
Vomiting	0	0	1	2
Nill	50	50	48	47
TOTAL	50	50	50	50
P'value	0.056 Not significant			

No significant side effects were observed in the study group.

Discussion

As obstetric blood loss contributes to one fourth of global maternal death its incidence has to be reduced. As the fibrinolytic system gets activated after placental delivery antifibrinolytic agents can be used to reduce obstetric blood loss.

WHO recommends early use of inj. tranexamic acid within 3 hours of birth in addition to oxytocin reduce the incidence of postpartum hemorrhage (WHO Maternal Antifibrinolytic Trial 2017)[1]

Tranexamic acid exerts its antifibrinolytic effect by blocking the lysine binding locus of the plasminogen & plasmin molecules, thereby preventing the binding of plasminogen & plasmin to the fibrin substrate. Tranexamic acid also inhibits conversion of plasminogen to plasmin by plasminogen activators. It has been

used in the treatment of bleeding for many years [5],[6].

During placental delivery, fibrinogen & fibrin are rapidly degraded, whereas plasminogen activators & fibrin degradation products (FDP) increase due to activation of fibrinolytic system [6],[7]. This activation can last up to 6-10 hrs postpartum, causing more bleeding. It was because of this activation of fibrinolytic system that we decided to use tranexamic acid in this trial [5],[6]. As prevention is always better than cure regarding PPH- an antifibrinolytic agent tranexamic acid was used prophylactically in our study to observe its efficacy in reducing blood loss during and after caesarean section and normal delivery.

In our study, the age group of patients included varied from 18 to 35 years. Maximum percentage of patients belongs to the age group of 20-24 years. 81% of group A and 83% group B were between 20-24 years. The mean age was 23 + 2.5 years.

Tranexamic acid also reduced the incidence of postpartum hemorrhage (patients with blood loss more than 500 ml)in study group as compared to control group.

In this study, statistically significant fall in Hb% occurred after surgery in the group B than with group A. mean fall of Hb% in group A was 1.78 and in group B was 1.14. In contrast in a similar study conducted by Beijing Obst and Gyn hospital, Beijing, China there was also post-operative fall in Hb% in both groups.

In our study, mean decrease in PR was 0.2 in group A and 0.5 in group B post operatively. Mean fall in SBP was 0.3 in group A and 0.5 in group B. There was no significant fall in SBP and in PR without any significant change in RR post operatively. In this study conducted by International Medical Communication department, Daiichi Pharmaceutical Co. Ltd, Tokyo, Japan also there was no statistical significant change in vital parameters.

The incidence of thrombosis during pregnancy and puerperium is 5-6 times higher than general population. when the anti-fibrinolytic drug is administered the increased risk of thrombosis should be considered. But none of the patients in both groups had thromboembolic complications postoperatively.

In this study, neonatal outcome were comparable in both groups. Neonatal outcome was good in both groups. The inference was that tranexamic acid use was not associated with any impact on neonatal outcome in our study. In a similar study conducted by Department of Obs & Gyn King's College hospital, London, there was no significant difference in the neonatal outcome between study and control group. All data demonstrated that tranexamic acid can be used safely without increasing the occurrence of thrombosis.

Conclusion

Tranexamic acid injection, an antifibrinolytic agent when given prophylactically 20 minutes before skin incision by intravenous route appears to reduce the blood loss during and after caesarean section and normal delivery effectively without significant complications.

1. Tranexamic acid significantly reduced the amount of blood loss during & after the lower segment cesarean section and normal delivery
2. Its use was not associated with any adverse drug reaction like diarrhea or thrombosis. Fetal outcome as evaluated by apgar score was not adversely affected by use of tranexamic acid.
3. Tranexamic acid can be used safely in subjects with lower cesarean section and normal delivery.

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