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Evaluation of Effectiveness of Prophylactic Tranexemic acid for reducing Blood loss in Cesarean Section

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Abstract: ***Background: Obstetrics blood loss is the major cause of maternal mortality and cesarean section accounts for 25-30 % of all deliveries. Delivery by cesarean section is associated with primary and secondary hemorrhage. Tranexemic acid is a synthetic derivative of aminoacid lysine that exerts its anti fibrinolytic effects by its reversible blockade of lysine binding sites on plasminogen molecules. Objective: Main objective is to study the effectiveness of prophylactic parenteral Tranexemic acid(TXA) in reducing blood loss during and after elective lower segment cesarean section. Methodology: A Prospective randomized case control study conducted in the Dept of Obstetrics and Gynecology in Coimbatore Medical College on 150 women who underwent LSCS.75 of cases were given TXA before 20 minutes of skin incision. Other 75 were not given TXA. The amount of blood loss from the end of placental delivery to two hours post partum was measured along with vital parameters and adverse effects were compared among both the groups. Results: TXA significantly reduces the amount of blood loss from the end of placental delivery to two hours post partum in the present study it was observed that blood loss in TXA group is 340 ml compared to control group where blood loss is about 450 ml which is statistically significant. No complications or side effects are reported among both the groups. Conclusion: TXA significantly reduces the amount of blood loss in cesarean section and is not associated with any side effects.***

Keywords: Lower segment cesarean section, Tissue plasminogen activator, Tranexemic acid, Postpartum Hemorrhage

1. Introduction

Obstetric blood loss is a major cause of maternal mortality and is always underestimated and hence blood is inadequately replaced .Cesarean section rate has been increasing now a days accounting for 25 to 30 % of all deliveries. Cesarean section is specially associated with varying amounts of blood loss. Though active management of third stage of labour is practiced well and it can prevent sixty percent of postpartum hemorrhage but still PPH has a devastating impact on the society with increased maternal mortality and morbidity.

The importance of tranexemic acid is that it reduces blood loss as well as the need of blood transfusion .Blood is a precious product in which patients are associated with risk of transfusion related adverse effects such as febrile non hemolytic transfusion reactions and blood borne infections.

Tranexemic acid is a synthetic derivative of amino acid lysine that exerts its anti fibrinolytic effect through reversible blockade of lysine binding sites on plasminogen molecules. Intravenous administration of Tranexemic acid before skin incision routinely decreases the amount of blood loss during any surgery and also reduces the incidence of blood transfusion during surgery.

Tranexemic acid potentiates the blood clotting system as it is an anti fibrinolytic agent and is used to treat and prevent bleeding. During placental delivery rapid degradation of fibrinogen and fibrin occurs, as well as an increase in the activation of plasminogen activity and fibrin degradation products due to activation of the fibrinolytic system. This activation lasts for 6 to 10 hours postpartum which may cause more hemorrhage. The anti fibrinolytic effect of tranexemic acid in the third stage of labour could make it safe and effective alternative or can be used as an adjunct to other regimen in the third stage of labour for prevention of postpartum hemorrhage.

In this present study the effectiveness of prophylactic tranexemic acid in reducing the blood loss from the end of placental delivery to two hours postpartum in the third stage of labour during cesarean section has been investigated.

2. Materials and Methods

2.1 Participants and study design

Pregnant women undergoing LSCS in Coimbatore Medical College Hospital are the participants. It is a prospective randomized case control study commencing from August 2014 to August 2015.Ethical approval for the study was obtained from the hospital Ethics committee prior to the commencement of the study.150 women delivering in the hospital fulfilling the inclusion and exclusion criteria were included in this study after obtaining informed consent.

Sample size: 150
They are allocated in two groups
Study Group: Subject who receive Tranexemic acid
Control Group: Subject who did not receive Tranexemic acid.

2.2 Details of the Study

2.2.1 Inclusion Criteria
Full term primigravida or multigravida with singleton pregnancy delivered by LSCS.

2.2.2 Exclusion Criteria
1) Medical or surgical problem involving heart, liver, kidney, brain.
2) History of thromboembolic disorder
3) Pregnancy complications such as severe pre-eclampsia, abruptio placenta, placenta previa, fibroid complicating pregnancy.
4) Any blood dyscrasia
5) Allergy to Tranexemic acid
6) Multiple pregnancy, polyhydramnios.

2.3 Participants and Study Design

Pregnant women undergoing cesarean section in Coimbatore medical college. It is a prospective randomized case control study.

2.4 Administration Study Group

Tranexemic acid is administered 15 to 20 minutes before incision in a dosage of one gram intravenously slowly infused over 5 minutes. After delivery of the neonate 10 units of Oxytocin is administered in intravenous drip.

Control Group
Tranexemic acid is not administered .Oxytocin 10 units is administered in intravenous drip after the delivery of the neonate.

2.5 Observations

2.5.1clinical Observation
1) Vital Signs: Heart rate, respiratory rate, blood pressure were checked immediately after placental delivery as well as one hour and two hours after birth of the neonate.
2) Blood Loss: The blood loss was measured from the period of placental delivery to the end of surgery and then again from the end of operation to two hours post operatively. The weight and volume of blood loss was estimated.
3) Assess the contraction of uterus and placental separation.
4) Neonatal outcome by Apgar scoring
5) Any obvious side effects caused by administration of Tranexemic acid.

2.5.2 Laboratory Examination
1) Complete blood count with platelet count done before delivery and 24 hours after delivery.
2) Renal function test and Liver function test is done before delivery and second day post operatively.
3) Coagulation profile is performed before and after delivery.

2.6 Quantification of Blood Loss

Blood was collected into the suction container after the placental separation, thus excluding the collection of amniotic fluid into the suction container, so that the collected blood is only from that has occurred after placental delivery. All the soaked guage pads and operation table sheets are weighed. The measurement in two different period one from the time of placental separation to the end of surgery. Next one from the end of surgery to that of two hours postpartum.

Quantity of Blood Loss =(weight of used material +weight of unused material) –(weight of all material prior to surgery) + volume collected in the suction container after placental delivery.

Evaluation of effectiveness of tranexemic acid is given by
1) Efficacy of the drug
2) Safety of the drug

2.7 Efficacy of the Drug

Efficacy is given by
1) Amount of blood loss
2) The Incidence of PPH

2.8 Safety of the Drug

Safety profile is given by
1) Monitoring vital signs
2) General side effects with administration of drug
3) Laboratory findings

3. Results

The prospective randomized case control study conducted among 150 pregnant women undergoing cesarean section were included in the study. In this study group 75 received tranexemic acid and 75 did not receive tranexemic acid

Table 1: Distribution Based on Patient Characteristics

	Study Group (mean +/-SD)	*Control Group* (mean+/-SD)	*P value*
Age	26.33+/-4.14	25.56+/-3.85	0.238

Table 1. shows that the confounding variable age which is matched effectively in both groups of study and control. The difference in age of subject of both group is not statistically significant.

Table 2: Comparison of Blood Loss from Time of Placental Delivery to Completion of Skin Closure

Blood loss(ml)	Cases (median)	Control (median)	P value
Placental delivery to end of surgery	300 ml	380 ml	<0.001

Thus table 2 shows that the mean blood loss in patients who received tranexemic acid is nearly 80 ml less than those of patients who did not receive tranexemic acid.

Table 3: Comparison of Blood Loss from the End of Surgery to Two Hours Postpartum

Blood loss(ml)	Cases (median)	Control (median)	mean	P value
End of surgery to 2 hrs postop	40	70	30	<0.001

Thus table 3 reveals to us that the patients on tranexemic acid had 30 ml blood loss less than that of control group who did not receive TXA in the post operative period two hours after the surgery.

Table 4: Comparison of Total Blood Loss from the End of Placental Delivery to Two Hours Postpartum

Blood loss(ml)	Cases (median)	Control (median)	Mean difference	P value
Total blood loss	340	450	110	<0.001

Thus the blood loss right from the delivery of placental till two hours postpartum totally accounts for 340 ml in the cases and 450 ml among the control group with a statistically significant p value. Thus patients who receive tranexemic acid before surgery has 110 ml less blood loss compared to the patients who did not receive tranexemic acid.

Table 5: Comparison of Blood Loss More than 500ml among Both the Groups

Blood loss>500ml	cases	control	P value
present	0	7	0.013
absent	75	68	

Table 5 confirms that the incidence of PPH is present in the control group but among the study group who received tranexemic acid pre -operatively there is no occurrence of PPH.

Table 6: Comparison of the Difference in Hemoglobin% Postoperatively among both the Groups

Hb	Cases (median)	Control (median)	Mean difference	P value
After surgery	0.60	0.80	0.20	<0.001

The mean difference in hemoglobin percentage among both the groups is 0.20 with p value <0.001 which is statistically significant.

Table 7: Comparison of Vital Signs among both Groups Post Operatively

Vital signs	cases		control		P value
	mean	SD	mean	SD	
HR	90.02	4.23	91.41	3.86	0.038
RR	14.5	1.45	15.16	1.62	0.014

Table 7 shows that heart rate (HR)and respiratory rate(RR) in both the groups does not show any statistically significant difference.

Table 8: Comparison of Blood Pressure Measurement among both the Groups

BP(mm/hg)		cases		control		P value
		N	%	N	%	
SBP	100	15	20	15	20	0.858
	110	33	44	36	48	
	120	27	36	24	32	
DBP	60	0	0	6	8	0.040
	70	33	44	28	37.33	
	80	42	56	41	54.67	

Thus the systolic blood pressure (SBP) and diastolic blood pressure(DBP) does not show any significant difference between both the groups.

Table 9: Comparison of Apgar Score among both the Groups

Apgar score	cases		control		P value
	N	%	N	%	
7/10	1	1.33	7	9.33	0.29
8/10	74	98.67	68	90.67	

The Apgar score at one minute in the newborn in both the groups is not statistically significant**.**

Table10: Comparison of Adverse Drug Reaction in both the Groups

Adverse reaction	cases		control	
	N	%	N	%
nausea	15	54.55	9	52.94
vomiting	12	45.45	8	47.06
others	nil	-	nil	-
thrombosis	nil	-	nil	-
ARF	nil	-	nil	-

Thus it can be concluded that the incidence of side effects profile is not increased among the TXA group compared to the control group where TXA is not given. As there is no incidence of thrombosis and acute renal failure (ARF) among both the groups, the fear of main side effect of tranexemic acid as thrombosis can be left apart according to this present study

4. Discussion

Tranexemic acid is an anti fibrinolytic agent. Tranexemic acid literally dismiss the dissolution of hemostatic fibrin by plasmin due to its anti fibrinolytic effect. More over during the placental delivery the fibrinogen and fibrin gets degraded rapidly and simultaneously plasminogen activator as well as fibrin degradation products increases as tranexemic acid which is an anti fibrinolytic agent for our study. Tranexemic acid actively binds at the lysine receptor binding site of fibrin and hence it stabilizes fibrin and prevents it undergoing fibrinolysis. Tranexemic acid also inhibits plasminogen conversion into plasmin by inhibiting plasminogen activator. Thus tranexemic acid is used in treatment of reducing blood loss for many years.[1]

From our study it has been evident that tranexemic acid significantly reduces the blood loss from the time of placental delivery to that of two hours postpartum. The value

that are being obtained in the study group is 340 ml and in the control group is 450 ml with a median blood loss of 110 ml which gives the p value of <0.001 which is highly statistically significant difference. Thus, the blood loss is nearly 35%less than in the control group which is significant. The blood loss from the time of placental delivery to end of caesarean section is 350 ml in study group and 380 ml in control group giving p value <0.001 which is statistically significant.

The blood loss from the end of cesarean section to two hours postpartum as given in the study group is 40 ml and in the control group is 70 ml with a p value of <0.001 which is once again statistically significant.[2]

Thus, tranexemic acid administration reduces the blood loss right from the end of placental delivery to two hours postpartum .In case of calculating blood loss >500 ml in both the groups gives us the value as follows. There is no evidence of blood loss >500 ml in the study group where as the incidence of blood loss more than 500ml in control group is 7 giving us the impression that blood loss is more in the group who are not administered tranexemic acid prior to surgery and the p value that is obtained is 0.013 which is significant statistically[4].The list extends that the group has been administered tranexemic acid showed the post operative hemoglobin difference less compared to the group not administered with tranexemic acid with p value of <0.001. Hence the efficacy of using tranexemic acid is proven as it not only reduces blood loss and decreases incidence of post partum hemorrhage as well as improves the hemoglobin difference.

Coming to the vital parameters both the study and control group does not show any statistical difference in heart rate, respiratory rate, blood pressure. Hence tranexemic acid can be safely given without any significant changes in the vital parameters.

In view of apgar score, administration of tranexemic acid has no effects on the outcome difference in the apgar among both the groups.

In view of adverse effects among the tranexemic acid administered group does not show any significant difference with that of control group. There is no evidence of increased risk of thrombosis in the present study.[3]

5. Conclusion

1) Tranexemic acid is highly effective in significantly reducing the blood loss during as well as after the lower segment caesarean section.[5]
2) Tranexemic acid usage has not resulted in excess blood loss exceeding more than 500 ml and hence the incidence of postpartum hemorrhage among the Tranexemic acid group is minimal.
3) Tranexemic acid administration is not associated with any adverse drug reaction.
4) There is no risk of thrombosis among the users of Tranexemic acid.
5) Fetal outcome as given by Apgar score is not affected by the usage of Tranexmic acid.

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