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EFFICACY AND SAFETY OF TRANEXAMIC ACID IN REDUCING BLOOD LOSS DURING AND AFTER CAESAREAN SECTION.

Gynaecology

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ABSTRACT

BACKROUND: Caesarean section rates have increased to as high as 25 to 30% in many areas of the world. Delivery by caesarean section can cause more complications than normal vaginal delivery and one of the most common complications is primary and secondary post partum haemorrhage. Tranexamic acid is a synthetic derivative of the amino acid lysine, it exerts antifibrinolytic effect through the reversible blockade of the lysine binding residues on plasminogen molecules. Tranexamic acid has been shown to be very useful in reducing blood loss and incidence of blood transfusion in many surgeries, and it is also cost effective.

OBJECTIVE(S): To study the efficacy and safety of preoperative intravenous tranexamic acid in reducing blood loss during and after caesarean section.

METHOD(S): A randomized case controlled prospective study was conducted on 300 women undergoing lower segment caesarean section(LSCS).One fifty of them were given intravenous tranexamic acid 20 minutes prior to LSCS compared with 150 others to whom tranexamic acid was not given. Blood loss was collected and measured during two periods. The first period was from placental delivery to end of LSCS and 2nd from end of LSCS to2hours postpartum. Vital signs at the time of delivery, at the time of placental delivery, 1hr,&2hrs postpartum and apgar score were studied in both the groups.

Post operatively haemoglobin, and haematocrit were tested in both the groups.

RESULTS: Tranexamic acid significantly reduced the amount of blood loss from end of LSCS to 2hrs postpartum 74.28ml in the study group compared to114.48ml in the control group(P=0.001). It also significantly reduced the amount of blood loss from the time of placental delivery to end of LSCS379.66ml in the study group versus 485.45ml in the control group (P=0.001).The fall of postoperative haemoglobin and haematocrit was significantly reduced in study group(1gm/dl) versus (1.551gm/dl) in control group. No side effects or no adverse perinatal outcome was noted in either group.

CONCLUSION(S): Tranexamic acid significantly reduced the amount of blood loss during and after caesarean section and its use was not associated with any side effects or complications like thrombosis. Further studies are necessary to evaluate its efficacy in pregnancies at high risk for PPH.

KEYWORDS:

Caesarean section, Blood loss, Tranexamic acid.

INTRODUCTION

Caesarean section was introduced in clinical practice as a lifesaving procedure both for the mother and the baby. Caesarean section rates have increased to as high as 25 – 30% in many areas of the world[1].Delivery by caesarean section causes more complications than normal vaginal delivery. One of the most common complications is primary and secondary postpartum hemorrhage[2]. Obstetric haemorrhage can be life threatening. Major haemorrhage continues to be one of the most common causes(25%) of direct maternal death[3]. Confidential enquiry in to maternal death 2000-2002 in UK reveals that 17% deaths were due to haemorrhage. In order to reduce mortality and morbidity due to obstetric haemorrhage we need to reduce the amount of bleeding at caesarean section[1].

Blood loss in caesarean section frequently leads to transfusion of allogenic blood products. (Alexander et al 2009) reported that 2.3% were given blood transfusions for hypovolemia in caesarean section and this is related to increased maternal morbidity and mortality [4]. Each unit of transfusion of blood or blood products exposes the patient potentially to the risk of transfusion related adverse effects such as febrile non haemolytic reactions, blood borne infections and errors in transfusion.

Blood is a scare resource, even when it is available the safety of blood transfusion and shortages of blood products, and rising costs of blood bank operations have generated interest in reduction of blood transfusion during and after surgery. A popular approach is to reduce perioperative blood loss through the prophylactic use of anti fibrinolytic agents. Aprotinin, tranexamic acid and epsilon amino caproic acid are the three anti fibrinolytics[5].

Tranexamic acid is a synthetic derivative of lysine. The anti fibrinolytic activity of tranexamic acid is a result of interference with plasminogen binding to fibrin. It reversibly blocks the lysine binding sites on plasminogen molecules[6]. Intravenous administration of tranexamic acid had been used for many years for reducing blood loss in surgeries like cardio pulmonary bypass, orthoptic liver transplantation, transurethral prostatic surgery, total hip or knee arthroplasty, urinary tract surgery. Tranexamic acid has been shown to be very useful in decreasing blood loss and the incidence of blood transfusion in these surgeries.

The changes in the fibrinolytic components during and immediately after placental delivery are consistent with increased fibrinolysis and the plasma fibrinogen level decreases during 3rd stage of labour and after placental delivery[19]. Hence anti fibrinolytics will be useful and effective in reducing blood loss by interfering with the fibrinolytic mechanism. In this study the efficacy and safety of tranexamic acid in reducing blood loss during and after LSCS was investigated.

AIM OF THE STUDY

1)To evaluate the efficacy and safety of preoperative intravenous tranexamic acid in reducing blood loss during and after caesarean section.

2)To compare it with the amount of blood loss in patients who did not

receive tranexamic acid preoperatively.

MATERIAL AND METHODS

It is a prospective randomized case controlled study commencing from December2015 to November 2016 (1year). 300 pregnant women undergoing LSCS in Government Dharmapuri Medical college Hospital, Dharmapuri were included in this study.

In all the patients detailed medical and obstetric history was taken. Vital parameters like heart rate, respiratory rate and blood pressure were checked. Preoperative basic investigations were done.

General and obstetric examination was done for all patients. Gestational age was confirmed by USG. All 300 patients were allocated into two groups 150 patients in the study group and 150 patients in the control group. All patients were counselled and informed consent obtained.

Study Group:-

One gram tranexamic acid (10ml) in 100ml NS over 10 minutes 20 minutes before the skin incision.

Inj. Oxytocin 10 U intramuscularly after the delivery of baby and 10Uadded into intravenous infusion.

Control Group:-

Placebo injection of 100ml normal saline over 10minutes 20 minutes prior to skin incision.

Inj.oxytocin 10U intramuscularly after the delivery of baby and 10U added to intravenous infusion.

Inclusion Criteria

Primi and 2nd gravida with term live singleton pregnancy being delivered by LSCS.

Exclusion Criteria

Multiple pregnancy
Pre eclampsia
Macrosomia
Prev. H/o caesarean delivery
Polyhydramnios
Those requiring blood transfusion due to anaemia
Fibroid complicating pregnancy
Placental abnormalities like
Placenta previa
Abruptio placenta
Placenta accreta, increta, percreta,
H/o bleeding disorders
Persons allergic to tranexaneic acid
Associated systemic complication involving Heart, Liver and Kidney
Prev. H/o PPH Prolonged and obstructed labour Gravidity more than 3.

Methods:-

Study and control group patients received the injection as mentioned above. All the LSCS were done under spinal anaesthesia. The following parameters were monitored in all the cases.

Preoperative pulse rate, blood pressure, respiratory rate was monitored. Haemoglobin and haematocrit was done.

Vital Signe: pulse rate, respiratory rate, blood pressure were checked immediately after placental delivery and 1hour and 2hours after surgery.

Blood was collected and estimated for two periods following placental delivery to end of surgery and from end of surgery to 2hrd postpartum. Uterine contractility. Neonatal manifestation.

Need for Maternal blood transfusion were noted.

After collecting all the data the data were tabulated in a master chart and analysed. The data were analysed by using the statistical package for social science (SPSS) version 11.5. Normality of distribution was checked as needed. The results were expressed as frequency, mean plus or minus standard deviation and median. Statistical comparison was carried out using chi square test(x2) test, independent t test, or mann-whitney test, and paired t test where appropriate. Equal variance assumption was assessed by the levene test. Two tailed P<0.05 was considered significant.

RESULTS AND ANALYSIS

TABLE -1 DISTRIBUTION OF CASES ACCORDING TO AGE GROUP

Age in years	Number of cases			
	Study Group		Control Group	
	Number	%	Number	%
< C20	9	6%	9	6%
20 – 24	71	47.3%	82	54.7%
25 – 29	62	41.7%	50	33.3%
>30	8	6%	9	6%

Table – 1 Shows distribution of cases according to age group. Majority of the patients (50%) in both groups were 20 – 24 years and 6% of the patients belong to < 20 and > 30 yrs.

TABLE – 2 EFFECT OF TRANEXAMIC ACID COMPARISON OF BLOOD LOSS FROM THE TIME OF PLACENTAL DELIVERY TO END OF SURGERY

	Study		Control		P Value
	Mean	S.D	Mean	S.D	
Mean Blood Loss	305.38	56.2	371.30	104.5	0.001 ** Highly significant

Table – 2 Shows blood loss from placental delivery to end of LSCS. The blood loss was about 305.38 ml in study group and 371.30 ml in control group (P = 0.001) suggesting there was statistically highly significant difference in blood loss between both groups. Those who received Tranexamic acid had 65.92 ml less blood loss than who did not receive the drug.

TABLE – 3 EFFECT OF TRANEXAMIC ACID COMPARISON OF BLOOD LOSS FROM END OF SURGERY TO 2 HRS POSTPARTUM

	Study		Control		P Value
	Mean	S.D	Mean	S.D	
Mean Blood Loss	74.28	14.90	114.48	13.9	0.001 ** (HS)

Table – 3 Shows mean blood loss from end of surgery to 2 hours post partum was 74.28 in study group and it was 114.48 ml in control group (P = 0.001) suggesting there was statistically highly significant difference in blood loss in both the groups. Patient who received tranexamic acid had 40.2 ml less blood loss than who did not receive the drug.

TABLE – 4 EFFECT OF TRANEXAMIC ACID: COMPARISON OF BLOOD LOSS FROM THE TIME OF PLACENTAL DELIVERY TO 2 HOURS POSTPARTUM.

	Study		Control		P
	Mean	S.D	Mean	S.D	
Mean Blood Loss (ml)	379.66	70.73	485.45	116.16	0.001** (HS)

Table -4 shows mean blood loss from placental delivery to 2 hours postpartum was 379.66ml in the study group and 485.45 ml in the control group(P =0.001) suggesting there was statistically highly significant difference in blood loss in both the groups. Patient who received the drug had 106.12 ml less blood loss than who did not receive the drug.

TABLE – 5 EFFECT OF TRANEXAMIC ACID COMPARISON OF INCIDENCE OF BLOOD LOSS >500 ML

	Study		Control		P Value
	No of cases	%	No of cases	%	
Mean BL > 500ml	14	9%	29	19%	0.013
Mean BL < 500 ml	136	91%	121	81%	

Table-5 shows the incidence of blood loss more than 500ml in both the groups. 14women (9%) in the study group had blood loss more than 500ml compared to 29 women (19%) in the control had more than 500ml blood loss P =0.013(S) suggesting statistically significant difference in blood loss in both the groups. Blood loss >500 ml was significantly reduced in tranexamic acid group than who did not received the drug.

TABLE –6 COMPARISON OF DURATION OF SURGERY BETWEEN THE TWO GROUPS

	Study		Control		P Value
	Mean	S.D	Mean	S.D	
Duration of LSCS (min)	41.69	1.165	41.90	1.257	0.128 (NS)

Table – 6 Shows mean duration of surgery which was about 41.69 minutes in the study group and 41.90 in the control group(P=0.128). Duration of surgery may influence the intra operative blood loss. There was no statistically significant difference in the duration of surgery between the groups.

TABLE-7 CHANGE IN BLOOD INDICES

Blood Indices	Study		Control		P Value
	Mean	S.D	Mean	S.D	
Hb in gms Pre op HB	9.767	0.2089	9.788	0.1886	0.001**
Post op HB %	8.762	0.2195	8.237	0.215	(HS)
Change	- 1.00		- 1.551		
PCV(%) Pre op PCV	28.83	0.999	28.91	0.948	0.001**
Post op PCV	27.85	1.006	26.62	1.235	(HS
change	-0.98		-2.29		

Table – 7 Shows comparison of mean fall of haemoglobin and haematocrit in both the groups. Mean fall of haemoglobin was 1.00 in the study group and 1.55 in the control group. Mean fall of haematocrit was 0.98 in study group and 2.29 in control group.

Mean fall of postoperative haemoglobin and haematocrit was significantly reduced in study group than control group.(P=0.001) There was statistically highly significant difference in both the groups.

TABLE – 8 MATERNAL BLOOD TRANSFUSION

Blood Transfusion	Study		Control	
	Number	%	Number	%
Yes	2	1%	9	6%
No	148	99%	141	94%

Chi – Square cost = 4.624
P Value = 0.032 (S)

Table-8 shows number of patients those who needed blood transfusion in both groups.9 Patients (6%) in the control group needed blood transfusion compared to only 2 patients (1%) needed blood transfusion.

There was statistically significant difference(P = 0.03) in both the groups.

DISCUSSION

Caesarean section is one of the most frequently performed obstetric surgery all over the world[8](Ramadani et al). Maternal mortality and morbidity is increased due to increased blood loss during caesarean section.

During placental delivery the fibrinolytic system gets activated and fibrinogen and fibrin are rapidly degraded. These effects can last up to 6-10 hrs postpartum causing more bleeding.

Tranexamic acid is an anti fibrinolytic and its use appears to reduce blood loss during caesarean section. Reducing operative blood loss would reduce the need for blood transfusions and also reduces the post partum anaemia which is a major cause of maternal morbidity and makes the women more vulnerable to major PPH in future pregnancies. Hence, we decided to use tranexamic acid prophylactically, a cost effective drug in our study and observe its efficacy and safety in reducing blood loss during and after caesarean section.

MATERNAL AGE:-

In our study the age groups were distributed from 18 to 35 years of age. Maximum percentage of patients belongs to 20-24yrs of age of which 47% in the study group and 55% in the control group. In a study conducted at Lyari general hospital Karachi from March 2009 to April 2011 the mean age was 24yrs.

BLOOD LOSS:-

Our study showed mean blood loss from placental delivery to end of surgery was 305.38ml in the study group and 371.30ml in the control group. The mean blood loss from end of surgery to 2hrs postpartumwas74.28ml in the study group and 114.48 in the control group. The mean total blood loss from placental delivery to 2hrs postpartum was 379.66 in the study group, 485.45ml in the control group.

In a similar study by Gohel Mayar, Patel purvi, at Baroda medical college hospital Gujarat 2007 showed that blood loss from placental delivery to end of surgery was 339.76ml in the control group and 299.21ml in the study group. Blood loss from end of LSCS to 2hrs postpartum was 75.7ml in the study group and 133.03ml in the control group. Total blood loss from placental delivery to 2hrs postpartum was 374.9ml in the study group and 472.79ml in control group.

AfshanShahid et al – Lyari general hospital Karachi 2011

Blood loss from placental delivery to end of LSCS was 356.44 in study group 710.22ml in the control group. Blood loss from end of LSCS to 2hrs postpartum was 35.68ml in the study group and 43.63ml in the control group.

Ali Movofegh et al – Shariati hospital Tehran 2011.

Blood loss from placental delivery to end of LSCS was 262ml in the study group and404ml in the control group. Blood loss from end of LSCS to 2hrs postpartum was 67.1ml in the study and 141ml in the control group. These results were comparable with our study.

INCIDENCE OF BLOOD LOSS >500ML

Our study showed, fourteen members 9% in the study group had blood loss >500ml compared to 29 members 19% in the control group.

Similarly GoelMayur et al at SSG medical college hospital, Baroda blood loss >500ml was 10% in the study group and 28% in the control group. Zheng et al, Teaching hospital of Beijing 2011, Blood loss more than 400ml was significantly reduced by tranexamic acid during normal vaginal delivery.

Gai, Wu et al, Peking union medical college hospital, Beijing Blood loss more than 500ml was significantly reduced by tranexamic acid

during and after caesarean section.

Bresnoc K et al, observed that tranexamic acid significantly reduces the blood loss and the incidence of postpartum haemorrhage in vaginal delivery.

CHANGES IN BLOOD INDICES.

Our study showed mean postoperative fall of haemoglobin was about 1gm% in the study group and 1.551gm% in the control group.

Afshanshahid et al, Lyari hospital Karachi 2011.

Mean fall of haemoglobin was 1.09 in the tranexamic acid group, and 1.88gm% in the control group. Mean fall of post operative haematocrit was 1.89 in the tranexamic acid group, and 4.30 in the control group.

Ali Movafegh et al 2011. Iran

Mean fall of postoperative haemoglobin was 1.0gm% in tranexamic acid group and 1.8gm% in the control group.

SanjanaHalder et al 2013. India

Mean fall of haemoglobin value was1.214gm% in the tranexamic acid group and 1.7256gm% in the control group.

These results were comparable with our study.

MATERNAL BLOOD TRANSFUSION:-

In our study, maternal blood transfusion was 1% in the tranexamic acid group and 6% in the control group. The results were same in a similar study conducted by the division of obstetrics and Gynecology, University of Oslo, Norway in 2000.

DURATION OF SURGERY:-

Our study showed, mean duration was 41.69 minutes in the tranexamic acid group and 41.90 minutes in the control group.

Shahid et al Dow University of Health Sciences, mean duration of surgery was 45 to 50 minutes in all patients and Ali movafegh et al,mean duration of surgery was 40.2 in all the patients.

CONCLUSION

Intravenous tranexamic acid when given prophylactically 20 minutes before skin incision appears to reduce the amount of blood loss during and after caesarean section. Hence it can be recommended for reducing blood loss in caesarean section. Tranexamic acid was not associated with any adverse perinatal outcome.

It did not have much maternal side effects. Some studies observed that tranexamic acid minimally increases the risk of thromboembolism which was not observed in our study. Further studies are necessary to evaluate the efficacy in pregnancies at high risk for PPH.

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