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To Study the Effect of Intravenous Tranexamic Acid on Blood Loss During and After Caesarean Section

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Abstract

Introduction: Incidence of postpartum haemorrhage is 6.4% in caesarean section. WHO guidelines for prevention of PPH include oxytocin as first line drug. Intravenous tranexamic acid has been used to reduce hemorrhage during surgical procedures. In this study use of tranexamic acid on blood loss during and after Lower Segment Caesarean Section (LSCS) was evaluated. **Aims and Objectives:** 1. To study the efficacy of tranexamic acid in reducing blood loss during and after lower segment caesarean section, and 2. To study any side effect on neonate. **Materials and Methods:** A randomized prospective observational study of 100 patients were conducted. Patients were divided into: Group (A group) had received 1 gm tranexamic acid intravenous 20 minutes before skin incision + 20 units oxytocin drip in 500ml Ringer Lactate after delivery of baby. Group (B group) received only 20 units oxytocin drip in 500ml Ringer Lactate after delivery of baby. Patient's blood loss was measured (intra operative, post placental and post-operative period) by weighing dry and soaked mops and separate suction bottle for blood. **Results:** Statistically significant difference ($P < 0.001$) in the quantity of blood loss was observed. In group A total blood loss during LSCS was 476.49 ml while in group B it was 576.06 ml. Intra operative blood loss in group A was 455.63 ml while in group B it was 536.53 ml. Post placental blood loss in group A was 411.59 ml while in group B was 485.08 ml. Not a single neonate had poor APGAR score and no NICU admission was required. **Conclusion:** Use of tranexamic acid with oxytocin significantly decreased blood loss during and after caesarean section without any side effect on neonate.

Keywords: Lower Segment Caesarean Section (LSCS), Oxytocin, Post-Partum Haemorrhage, Tranexamic Acid

1. Introduction

Post Partum Haemorrhage (PPH) is one of the most common complications associated with childbirth. Incidence of postpartum haemorrhage is 3.9% in vaginal deliveries and 6.4% in caesarean section and it is the leading cause of maternal mortality and morbidity especially in developing countries[1]. Nowadays caesarean section rates have increased as high as 25 to 30%[2]. Therefore, reducing amount of blood loss during Lower Segment Caesarean Section (LSCS) is of utmost importance.

There are several drugs used to prevent and treat postpartum haemorrhage like Oxytocin, Ergometrine, and Prostaglandins. If PPH is not controlled with medical management surgical stepwise devascularisation, uterine artery embolisation and most radical approach obstetric hysterectomy is available[3].

In this research, to further reduce the blood loss we decided to study tranexamic acid to decrease blood loss during and after LSCS and to study side effect of tranexamic acid on neonate.

Tranexamic acid is an analogue of lysine that inhibits fibrinolysis by competitively binding to plasminogen. It prevents the lysis of formed clot by inhibiting activation of plasminogen to plasmin. It is ten times more potent than Amino-caproic acid[4,5].

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Haemostatic drugs are not used as first-line treatment in Post-Partum Haemorrhage (PPH)[6]. Extensive tissue injury can direct the haemostatic equilibrium toward increased fibrinolysis, leading to coagulopathy and bleeding[7]. Antifibrinolytic drugs, namely Trane-Xamic Acid (TXA) have been recognized to decrease blood loss and transfusion needs in various elective surgeries[8]. Furthermore, the Clinical Randomization of an Anti-fibrinolytic in Significant Haemorrhage (CRASH-2) study concluded that tranexamic acid decreases morbidity and mortality by reducing surgical blood loss in trauma patients[9].

2. Material and Methods

A randomised case controlled prospective study of 100 cases from August 2015 to August 2017 was carried out in department of Obstetrics and Gynaecology of medical college and tertiary health care centre. Cases were included in the study after satisfying inclusion and exclusion criteria after written informed consent.

2.1 Inclusion Criteria

1. Full term gestation.
2. Singleton pregnancy.
3. Primigravida or Multigravida.

2.2 Exclusion Criteria

1. Medical disorders like hypertension, diabetes, renal failure, moderate to severe anemia.
2. Any bleeding disorders.
3. History of thromboembolic episodes in past.
4. Multiple pregnancy, macrosomia, polyhydramnios.
5. Previous scar on uterus.

A detailed history regarding the parity, high risk factors, investigations and drug history of women was noted. The findings were recorded in a pre-described proforma.

3. Protocol

- Cases group (A group) had received 1 gm tranexamic acid intravenous 20 minutes before skin incision + 20 units oxytocin drip in 500ml Ringer Lactate after delivery of baby during LSCS.
- Control group (B group) had not received tranexamic acid and received only 20 units oxytocin drip in 500ml Ringer Lactate after delivery of baby.

Heart rate, respiratory rate, blood pressure monitored throughout conductance of surgery and till 2 hrs after LSCS. All the LSCS were done under spinal anaesthesia.

4. Blood Loss Measurement

Mops (dry and weight) kept and weighed separately before and after LSCS. Two separate suction bottles were used, one for amniotic fluid and second for blood loss after placental delivery till closure of skin incision.

1. Preplacental (Blood loss from mops before placental separation).
2. Intraoperative post placental:
   a) Blood loss from mops after placental separation.
   b) Amount in second suction bottle.
3. Postpartum 2 hours (blood loss from vaginal pads):
   a) Intraoperative blood loss (1+2).
   b) Post placental delivery blood loss (2+3).
   c) Total blood loss (1+2+3).

Amniotic fluid collected in suction bottle 1 was not included.

Haemoglobin values were determined preoperatively and on the third day postpartum for all cases.

Perinatal outcome was assessed by following parameters:

- Apgar score at 0, 1, 5 minutes.
- NICU admission.

The data was analyzed using appropriate statistical software.

5. Observations and Results

A study to observe blood loss during and after caesarean section by using Tranexamic acid and oxytocin was conducted in the department of Obstetrics and Gynaecology of a medical college and tertiary health care centre. A total of 100 patients's blood loss, which had undergone LSCS from August 2015 to August 2017, was measured after fulfilling the eligibility criteria. But 2

Table 1. Comparison of intra – operative blood loss

Blood Loss	Groups	N	Mean blood loss in ml	Sd	Indepen-dent t-test	P
Intra-operative blood loss(1+2)	Tranexamic acid + Oxytocin (A)	49	455.63	+/- 81.88	4.837	<0.001
	Oxytocin (B)	49	536.53	+/- 83.67		

Table 2. Comparison of post placental blood loss till 2hrs post operatively

Blood Loss	Groups	N	Mean blood loss in ml	Sd	Inde-pendent t-test	P
Post placental blood loss (2+3)	Tranexamic acid + Oxytocin (A)	49	411.59	+/- 81.76	4.499	<0.001
	Oxytocin (B)	49	485.08	+/- 79.93		

Table 3. Comparison of total blood loss

Blood Loss	Groups	N	Mean blood loss in ml	Sd	Indepen-dent t-test	P
Total blood loss	Tranexamic acid + Oxytocin (A)	49	476.49	+/- 81.61	5.83	<0.001
	Oxytocin (B)	49	576.06	+/- 87.36		

patients were excluded from study because of emergency obstetric hysterectomy.

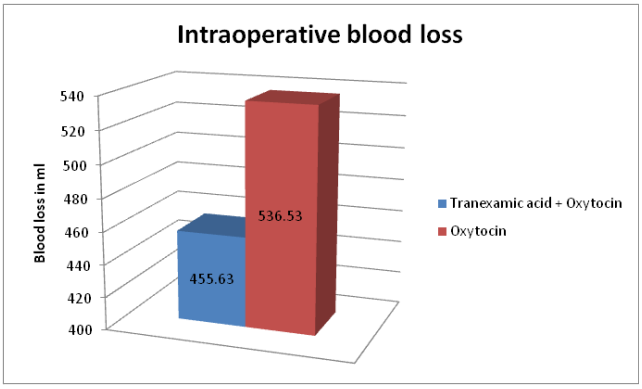

Figure 1. Comparison of intra –operative blood loss.

The observations and results of various groups in relation to subjective characteristics like age of patient, parity, indication of LSCS were comparable. Blood loss (Intra operative, Post placental delivery and total), haemoglobin levels are given in following paragraph and data collected has given in table form with statistical analysis wherever applicable.

In this study we calculated amount of blood loss in ml separately in each group. When we compared blood loss between (A) group and (B) group, we found that in (A) group Intra–operative blood loss was 455.63 ml, post placental separation till post-operative two hours blood loss 411.59 ml, and total blood loss 476.49 ml while in (B) group Intra–operative blood loss was 536.53 ml, post placental separation till post-operative two hours blood loss 485.08 ml, and total blood loss 576.06 ml.

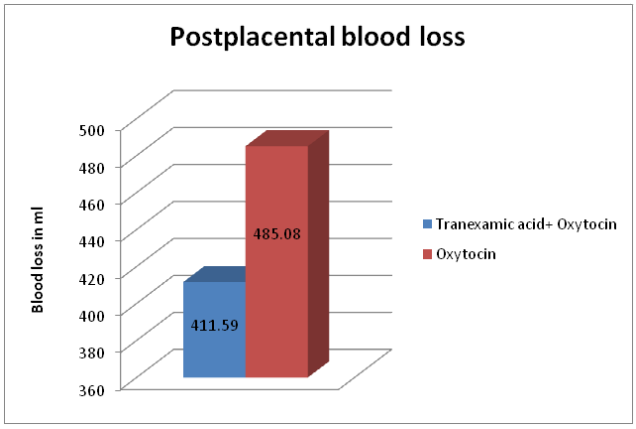

Figure 2. Comparison of post placental blood loss till 2hrs post operatively.

It has been seen that there was statistically significant difference in (A) and (B) group in Intra-operative blood loss (p value<0.001) (Table 1 and Figure 1).

Table 4. Comparison of mean difference in preoperative Hb and postoperative Hb in both groups

Comparison of Mean Difference Pre – Post Hb					
Groups	**N**	**Mean Hb in gm%**	**Sd**	**Indepen-dent t-test**	**P value**
Tranexamic acid + Oxytocin (A)	49	0.89	+/- 0.42	7.655	<0.000 HS
Oxytocin (B)	49	01.68	+/- 0.59		

It has been seen that there was statistically significant difference in (A) and (B) group in post placental till postpartum 2 hours blood loss (p value<0.001) (Table 2 and Figure 2).

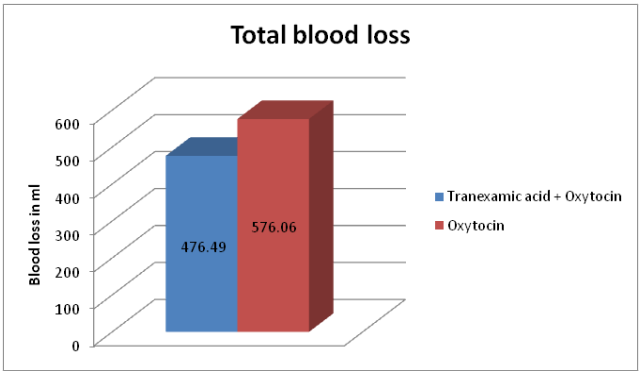

Figure 3. Comparison of total blood loss.

It has been seen that there was statistically significant difference in (A) and (B) group in total blood loss (p value<0.001) (Table 3 and Figure 3).

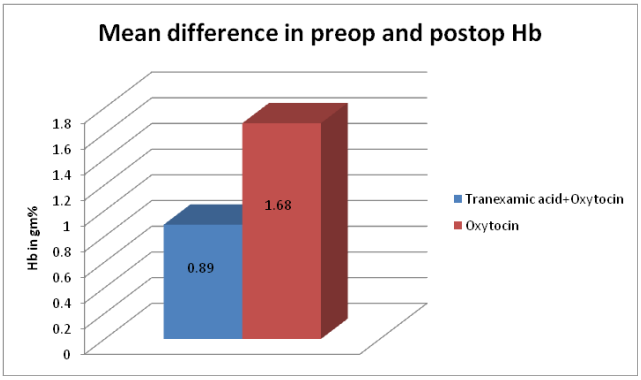

Figure 4. Comparison of mean difference in preoperative Hb and postoperative Hb in both groups.

It has been seen that there was statistically significant difference in (A) and (B) group in Pre - Post Hb (p value<0.000) (Table 4 and Figure 4).

6. Discussion

During placental delivery, fibrinogen and fibrin are rapidly degraded, whereas plasminogen activators and Fibrin Degradation Products (FDP) increase due to activation of the fibrinolytic system. This activation can last up to 6 to 10 hours postpartum, causing more bleeding[7].

Our present study evaluated efficacy and safety of tranexamic acid in reducing blood loss during and after LSCS. A total of 98 were divided in two groups, 49 cases received tranexamic acid with oxytocin and 49 cases received only oxytocin. The effect of this these drugs oxytocin and tranexamic acid on blood loss during and after LSCS is summarized below:

1. When tranexamic acid used in combination with oxytocin it significantly reduces intra operative, post placental and total blood loss. (Table 1-3).
2. There is significant reduction in haemoglobin post operatively (mean difference pre-post Hb) in oxytocin group is 01.68 gm% compared to Tranexamic acid + Oxytocin group, 0.89 gm% (Table 4).
3. Not a single neonate had poor 5 minutes APGAR score, average APGAR score was >6 and no neonate required NICU admission.
4. There was no serious side effect noticed in this study like thrombosis, deranged kidney or liver function test.

We can clearly make out from above summary of the study that tranexamic acid can be safely used during LSCS with oxytocin. And this combination significantly reduces blood loss during and after LSCS.

There are various studies related to tranexamic acid use in LSCS which has similar results with our study.

1. Similar study related to tranexamic acid carried out[10] in 2004 in China including one hundred and eighty

Table 5. Showing comparison of present study with Ming-Ying Gai *et al.*, study

Study	Intra operative blood loss	Post operative Blood loss	Total blood loss	P value
Ming-Ying Gai et al	308.82 ml	42.75 +/-40.45 ml	351.57 +/- 148.20 ml	0.002
Present study (A) VS (B)	455.63 ml	20.86 +/- 07.28 ml	476.49+/- 81.61 ml	0.001

primiparas were randomized into two groups also showed that Tranexamic acid significantly reduced the quantity of blood from the end of LSCS to 2 hours postpartum: 42.75 +/- 40.45 ml in the study group versus 73.98 +/- 77.09 ml in the control group (P=0.001). In our study Blood loss (3) was similar to above study which was 20.86 +/- 07.28 ml in the study (A) group versus 39.53 +/- 12.49 ml in oxytocin (B) group which is also significantly reduced by 21.89 ml (P Value < 0.001). It also significantly reduced the quantity of total blood from placental delivery to 2 hours postpartum: 351.57 +/- 148.20 ml in the study group, 439.36 +/- 191.48 ml in the control group (P=0.002). In our study Blood loss (b+c) was similar to above study and was also significantly reduced the quantity of total blood from placental delivery to 2 hours postpartum: 411.59ml in the study (A) group, 485.08ml in the oxytocin (B) group. The study also shows significant decrease in the incidence of > 500ml blood loss in the study group as compared to control group (P value 0.029) while our study shows significant difference of 99.57 ml in total blood loss (T) in both groups where we found (A) group is better than (B) group in reducing intra as well as post-operative blood loss. No complications or side effects were reported in either study.

Table 5 we can see that result of above study are comparable with our study.

2. Another study[11] in 2007 at Baroda, Gujarat with 100 patients out of which 50 were cases and 50 were control also showed that the Tranexamic acid significantly reduced the quantity of blood loss from the end of LSCS to 2 hours postpartum: 75.71 ml in the study group versus 133.03 ml in the control group (p=0.001). It also significantly reduced the quantity of blood loss from placental delivery to 2 hours post-partum: 372.71 ml in the study group, versus 469.70 ml in the control group. (P=0.003). No complications or side effects were reported in either group.

Table 6. Showing comparison of present study with Gohel Mayur et al. study

Study	Post operative blood loss	Post placental blood loss	P value
Gohel Mayur et al.	75.71ml	372.71ml	0.003
Present study (A) VS (B)	20.86 ml	411.59ml	0.001

Table 6 we can see that result of above study are comparable with our study.

3. Another study done in 2009[12] of Shahid Sedughi Hospital, Shahid Sedughi University of Medical Sciences and Health Services, Yazd, Iran with inclusion of 90 primipara patients undergoing LSCS also showed that Tranexamic acid significantly reduced the blood loss from the end of LSCS to 2 hours postpartum 28.02 +/- 5.53 ml in the Tranexamic group versus 37.12 +/- 8.97 ml in the control group (p = 0.000). Haemoglobin 24 hours after LSCS was significantly greater in Tranexamic group than control group (12.57 +/- 1.33 in the Tranexamic group and 11.74 +/- 1.14 in the control group, p = 0.002). No complications or side effects were reported in either group.

Table 7 we can see that result of above study are comparable with our study. In the above study only primipara patient undergoing LSCS included. Haemoglobin level 24 hour after LSCS measured in the above study. In that they found Haemoglobin 24 hours after LSCS was significantly greater in Tranexamic group than control group (12.57 +/- 1.33 in the Tranexamic

Table 7. Showing comparison of present study with Shekhavat *et al.,* study

Study	Post operative blood loss	P value	Haemoglobin (gm%) 24 hours after LSCS	P value
Shekhavat et al.	28.02 +/-5.53 ml	0.000	12.57 +/- 1.33	0.002
Present study (A) VS (B)	20.86 +/- 07.28 ml	0.000	08.09+/- 0.98	<0.025

group and 11.74 +/- 1.14 in the control group, P 0.002). In present study we also found statistically significant difference in mean pre and post Hb (P value 0.025) as shown in Table 4.

In the present study there was no abnormality in liver and renal function and urine analysis. The incidence of thrombosis during pregnancy and puerperium is five to six times higher than that of general population. When the antifibrinolytic drug Tranexamic acid is administered, the increased risk of postpartum thrombosis after LSCS should be considered. In the present study not, a single patient developed thrombosis and incidence of side effects like nausea vomiting and diarrhoea were not statistically significant by difference in the four groups. This has been collaborated by other studies.

Not a single neonate had poor 5 minutes APGAR score, average APGAR score was >6 and no neonate required NICU admission.

It is recommended that this study of ours is quite encouraging and can be continued for large group of cases and can also be taken up at other centres.

7. Summary

Our present study evaluated efficacy and safety of tranexamic acid in reducing blood loss during and after LSCS. A total of 98 patients were divided in two groups, 49 cases who had received tranexamic acid with oxytocin and 49 cases who had received only Oxytocin. The effect of these drugs oxytocin and Tranexamic acid on blood loss during and after LSCS are summarized below:

1. When tranexamic acid used in combination with Oxytocin it significantly reduces intra operative, post placental and total blood loss (Table 6).
2. There is significant reduction in haemoglobin post operatively (mean difference pre-post Hb) in oxytocin group is 01.68 gm% compared to Tranexamic acid + Oxytocin group, 0.89 gm%. So Tranexamic acid with oxytocin is more effective in reducing blood loss during and after LSCS than oxytocin alone.
3. Not a single neonate had poor 5 minutes APGAR score, average APGAR score was >6 and no neonate required NICU admission
4. There was no serious side effect noticed in this study like thrombosis, deranged kidney or liver function test.

We can clearly make out from above summary of the study that tranexamic acid can be safely used during LSCS with oxytocin and significantly reduces blood loss during and after LSCS.

8. Conclusion

In conclusion from our study we can say that administration of Tranexamic acid during LSCS with uterotonic agent after excluding risk factors significantly decreases blood loss during and after LSCS. And it significantly decreases morbidity and mortality with blood loss.

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