COMPARATIVE STUDY OF INTRAVENOUS TRANEXAMIC ACID AND OXYTOCIN VERSUS OXYTOCIN ALONE IN REDUCING BLOOD LOSS DURING AND AFTER LSCS UNDER SPINAL ANAESTHESIA

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ABSTRACT

BACKGROUND

Cesarean section (CS) rates have been increased to as high as 25 to 30% in many areas of the world. Risk of postpartum haemorrhage increases in cases of cesarean section & PPH is a major cause of maternal morbidity & mortality. Routinely uterotonic drugs are used for active management of third stage of labour. Tranexamic acid by its antifibrinolytic action further reduces blood loss. This study will evaluate the efficacy and safety of tranexamic acid in combination with uterotonic drugs in reducing the blood loss after placental delivery following lower segment caesarean section (LSCS).

METHODS

A randomized, case controlled, prospective study was conducted on 100 women undergoing lower segment caesarean section (LSCS) at term between 37 and 41 wks. and have been studied prospectively. They are divided in two groups, 50 control & 50 cases. Cases (50) were given tranexamic acid immediately before LSCS along with 10 units of oxytocin whereas control group were given 10 units of oxytocin alone after delivery of foetus. Blood loss was collected and measured during two periods.

RESULTS

The patient characteristics, namely age, height, weight, gestational age and gravidity in two groups were similar which was statistically insignificant. There was no episode of thrombosis in the study. Tranexamic acid significantly reduced the quantity of the blood loss from time of placental delivery to 2 hours postpartum (p<0.001) and from end of LSCS to 2 hours postpartum (p<0.001). However there was no statistical difference in quantity of blood loss from time of placental delivery to end of LSCS in both groups.

CONCLUSIONS

A safe dose of Tranexamic acid has an effective role in reducing blood loss during LSCS without causing adverse reaction. Thus the drug can be used effectively in reducing maternal morbidity and mortality during LSCS.

KEYWORDS

Cesarean section, Tranexamic acid, Blood loss

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BACKGROUND

Reducing blood loss and the need for blood transfusions in LSCS remains a major concern. Many interventions have been developed over the past decade to achieve this goal. Many interventions have been developed over the past decade to achieve this goal. Despite significant progress in obstetric care, 125,000 women die from obstetric haemorrhage annually in the world.¹ The lower segment cesarean section (LSCS) is an established procedure. It involves a transverse incision on the lower uterine segment which is easier to repair and heal well. It is important to take proper steps to reduce the amount of bleeding during and after LSCS.² Cesarean section rates have increased to as high as 25% to 30% in many areas of the world.² In spite of the various measures to prevent blood loss during and after cesarean section, postpartum haemorrhage(PPH) to be continues to be the most common complication seen in almost 20% of the cases, leading to increased maternal morbidity and mortality.³ Postpartum haemorrhage (20%) is a leading cause of morbidity &mortality in developing countries like India due to almost universal presence of anemia in pregnant women, even small amount of blood loss can be detrimental. 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 and plasmin. It effectively blocks the conversation of plasminogen to plasmin, thus fibrinolysis thus retarded.⁴ Tranexamic acid may be of value in thrombocytopenia (Idiopathic or following cytotoxic chemotherapy).
The natural fibrinolytic destabilization of small platelet plugs is inhibited, reducing the risk of haemorrhage and requirement for platelet transfusion. More recently, the clinical Randomization of an antifibrinolytic in Significant Hemorrhage (CRASH-2) TRIAL has shown that early administration of tranexamic significantly reduces mortality in bleeding trauma patients. Adverse effects are rare but include nausea, diarrhea and sometimes orthostatic hypotension. Tranexamic acid is contraindicated for patients with hematuria because clot lysis in the urinary tract is prevented and clot colic results. Antifibrinolytics such as tranexamic acid is commonly used to modulate CPB-mediated effects on coagulation and thereby reduce the amount of transfused blood given.

Intravenous administration of tranexamic acid has been routinely used for many years to reduce haemorrhage during and after surgical procedures like coronary artery bypass, oral surgery, prostatic surgery, tonsillectomy, orthotopic liver transplantation, total hip and knee arthroplasty and urinary tract surgery. Tranexamic acid has been shown to be useful in reducing blood loss and incidence of blood transfusion in these surgeries. Synthetic oxytocin (Syntocinon) is pure and not contaminated with vasopressin as is the natural product, which is obsolete. Oxytocin is used intravenously in the induction of labor and sometimes for uterine inertia, haemorrhage or during abortion. It has a t/2 of 6 minutes and given by intravenous infusion using a pump. Overdose of oxytocin can cause uterine tetany and even rapture. Oxytocin has been supplanted by the ergot alkaloid, ergometrine, as prime treatment of postpartum haemorrhage. Although uterotonic drugs plays important role in preventing and controlling PPH. sometimes there is oozing from the cesarean incision site and for this administration of tranexamic acid was chosen as a drug for prevention of PPH in addition to uterotonic drugs and results were recorded and analyzed.

In this study, the efficacy and safety of tranexamic acid in reducing blood loss during and after LSCS was investigated.

**METHODS**
This study was at Murshidabad Medical College & Hospital and Calcutta National Medical College & Hospital, on & from 1st January 2017 to 31st December 2018. This is a prospective randomized case controlled study. Randomization was done by the rule of odds and even. In 50 subjects tranexamic acid was given immediately before LSCS and the blood loss was compared with that in 50 subjects in whom tranexamic acid was not given. Full term primiparas/multiparas with singleton pregnancy being delivered by LSCS were included in the study while subjects having medical and problems having the heart, liver, kidney, and brain and having blood disorders were excluded from the study.

Subjects having allergy to tranexamic acid, history of thromboembolic disorders, abnormal presentation, severe pre-eclampsia, multiple pregnancy, macrosomia, polyhydromnios and those requiring blood transfusion due to anemia were excluded from the study. This study was not supported by any pharmacological company. In the study group, 20 minutes before taking the skin incision, 1gm tranexamic acid was given slowly intravenously over 5 minutes. After delivery of the neonate, 10 units of oxytocin in a pint of dextrose normal saline was given by intravenous drip over 30 minutes while 0.4 mg methyl ergometrine was given intravenously. Tranexamic acid injection was prepared by diluting 1g (10 ml) tranexamic acid with 20 ml of 5% glucose. Tranexamic acid was not given in the control group. But after delivery of the neonate, oxytocin and methyl ergometrine were given as in the study group. Heart rate, respiratory rate and blood pressure were checked and noted before the surgery, immediately after placental delivery and 1 and 2 hours after birth respectively. The blood loss was measured following placental delivery to the end of surgery and from the end of operation to 2 hours after birth. Uterine contractility, placental separation, neonatal manifestation and side-effects caused by tranexamic acid were noted.

**Measuring Blood Loss**
The quantity of blood loss (ml)= (Weight of the used materials in both the periods - Weight of the materials prior to the surgery)+ the volume sucked in the suction bottle after placental delivery in ml. In addition, the pads used after completion of LSCS to 2 hours postpartum were separately weighted. Amniotic fluid and the amount of blood loss before placental delivery was thus not included in the measuring blood loss in the study. Hemoglobin, Urine analysis, Liver and renal function were noted before and on the 3rd day after operation. The data so obtained was statistically evaluated using Epi Info software, Vol. 3.2; February 2004: //www.cdc.gov/Epi info.

**RESULTS**
The subject characteristics in the two groups were similar with no statistically significant difference between age, weight and gestational age (Table-1). There was no significant difference in regard to obstetrical complications and indications of LSCS. All LSCS were done under spinal anesthesia, the duration of surgery being 40.75 minutes in the study group and 41.65 minutes in the control group, the difference being no significant statistically. There was no significant difference in uterine contractions after placental delivery between two groups, indicating the bleeding caused by uterine inertia was similar in both the groups. There was no significant difference in the heart rates, respiratory rates and blood pressures in the two groups. (Table-2).

<table>
<thead>
<tr>
<th>Group</th>
<th>Age (years) (Mean±SD)</th>
<th>Height (cm) (Mean±SD)</th>
<th>Weight (kg) (Mean±SD)</th>
<th>Gestational Age (wks) (Mean±SD)</th>
<th>Gravidity (Mean±SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study</td>
<td>24.29±3.64</td>
<td>152.58±4.27</td>
<td>49.72±3.66</td>
<td>38.86±1.28</td>
<td>2.11±0.96</td>
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<tr>
<td>(n=50)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>24.88±3.98</td>
<td>152.1±4.23</td>
<td>49.65±4.81</td>
<td>38.65±1.25</td>
<td>2.09±0.87</td>
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<tr>
<td>(n=50)</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>p value</td>
<td>0.99</td>
<td>0.992</td>
<td>0.841</td>
<td>0.790</td>
<td>0.233</td>
</tr>
</tbody>
</table>

**Table 1. Distribution Based on Subject Characteristics in the Two Groups**
There was statistically significant difference in the quantity of the blood loss from the time of placental delivery to 2 hours postpartum (P=0.003). There was also statistically significant difference in the quantity of the blood loss from the end of LSCS to 2 hours postpartum (P=0.001). There was no statistical difference from the time of placental delivery to the end of LSCS in both the groups (P=0.056). (Table 3).

Table 3. Comparison of the Extent of Postoperative Haemorrhage in the Study Group and the Control Groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Placental Delivery to the End of LSCS (mL)</th>
<th>The End of LSCS to 2 Hours Postpartum (mL)</th>
<th>Placental Delivery to 2 Hours Postpartum (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study</td>
<td>259.2±11.45</td>
<td>75.7±20.01</td>
<td>472.8±43.52</td>
</tr>
<tr>
<td>Control</td>
<td>336.7±12.87</td>
<td>131.0±14.69</td>
<td>472.8±43.52</td>
</tr>
<tr>
<td>P-value</td>
<td>0.056</td>
<td>0.001</td>
<td>0.003</td>
</tr>
</tbody>
</table>

There was no difference in the mean birth weight between the two groups. Tranexamic acid had no significant effect on the 1 and 5 minutes Apgar score between the two groups (P=0.5). After birth in both the groups, hemoglobin decreased slightly but there was no significant difference between the groups. There was no significant difference in urine analysis, liver and renal function tests in the two groups.

DISCUSSION

PPH is commonly defined as blood loss of ≥500ml after vaginal delivery of a baby or ≥1000ml after cesarean section. However, these thresholds do not take into account pre-existing health status, and blood loss of as little as 200-300 ml can be life threatening for a woman with severe anaemia or cardiac disease. During placental delivery, fibrinogen and fibrin are rapidly degraded, whereas plasminogen activators and fibrin degradation products (FDP) increase due to activation of the fibrinolysis system. This activation can last up to 6-10 hours postpartum, causing more bleeding. It was happened because of this activation of the fibrinolysis system that we decided to use tranexamic acid in this trial. This study showed that tranexamic acid significantly reduces bleeding from time of placental delivery to 2 hours postpartum in LSCS (P=0.001). This study shows significant decrease in the incidence of >500ml blood loss in the study group as compared to control group (P=0.049). Similar study carried out by Ming-Ying Gai et al in China showed that tranexamic acid significantly reduces bleeding from the time of placental delivery to 2 hours postpartum. The study showed significant decrease in the incidence of >500ml blood loss in the study group as compared to control group (P=0.029) Zheng et al, showed similar results after vaginal delivery.

Following tranexamic acid administration, there was no significant alteration in the vital signs of the subjects. There were no abnormalities in haemoglobin, liver and renal function and urine analysis. The incidence of thrombosis during pregnancy and puerperium is 6-10 times higher than that in the general population. The increased risk of postpartum thrombosis should be considered when the antifibbinolytic drug tranexamic acid is administered. In this study, not a single patient developed thrombosis and incidences of side-effects like nausea, vomiting and diarrhea were not statistically significant by difference in the two groups. These have been corroborated by other studies.

REFERENCES

[6] Brown RS, Thwaites BK, Morgan PD. Tranexamic acid is effective in decreasing postoperative bleeding and transfusions in primary coronary artery bypass


