

Effect of Intravenous Tranexamic Acid and Sublingual Misoprostol on Reducing Post Cesarean Section Bleeding

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ABSTRACT

Background and Aim: Cesarean section rates are rising around the globe and are considered as the major surgical procedure conducted on females. Cesarean-related hemorrhage contributes to increasing mortality rates around the world. Due to the rise in cesarean rate and its associated complications, post-cesarean severe bleeding without proper management is a major concern. Therefore, the present study aimed to assess the intravenous tranexamic acid (TA) and sublingual misoprostol effect on reducing post-cesarean section bleeding.

Materials and Methods: This cross-sectional study was conducted on 146 term pregnant women undergoing emergency or elective cesarean section at the Department of Obstetrics and Gynaecology, Qazi Hussain Ahmad Medical Complex, Noshehra during the period from 7th September 2020 to 6th March 2021. All the participants were randomly categorized into two groups. Each group comprised of 73 participants whereas groups I and II received sublingual misoprostol (600 µg) and 500 mg intravenous tranexamic at card clamping respectively. Both groups were administrated for postoperative 48 hours and blood loss was measured. The packed cell volume and postoperative Hb were evaluated and compared with initial values before surgery. The need for blood transfusion, drug side effects, and additional uterotonics was evaluated. SPSS version 20 was used for data analysis.

Results: The mean age of groups I and II were 28.32±4.73 and 28.17±4.83 years whereas the overall mean age was 28.25±4.78 years. A higher reduction of hemoglobin level was observed in an intravenous tranexamic group compared to the sublingual group (-2.39±0.93 versus -2.09±1.28g/dL) (p=0.001). Moreover, the intravenous tranexamic group had significantly higher blood suction and gauze usage than sublingual misoprostol (256.73± 83.25 versus 189.68± 102.4 cubic centimeter (cc) and 4.59±1.43 versus 3.19±1.27) for a significant value of 0.001. The decrease in mean blood pressure during the cesarean section procedure was significant in intravenous tranexamic than sublingual misoprostol (p=0.001).

Conclusion: Our study concluded that sublingual misoprostol significantly reduced total bleeding when compared to tranexamic acid. Furthermore, hemodynamic variables were stabilized more in the misoprostol group than in the tranexamic acid group.

Keywords: Cesarean Section Bleeding; Intravenous Tranexamic acid; Sublingual misoprostol.

INTRODUCTION

Cesarean section rates are rising around the globe and are considered as the major surgical procedure conducted on females. Cesarean-related hemorrhage contributes to increasing mortality rates around the world [1, 2]. Due to the rise in cesarean rate and its associated complications, post-cesarean severe bleeding without proper management is a major concern. Regardless of the mode of delivery, Obstetric hemorrhage is the prominent cause of maternal death globally. The prevalence of cesarean section rates varied from 20% to 30% in developed countries [3]. Pakistan exemplifies the magnitude of the problem. During caesarean section, average blood loss is two time higher than vaginal delivery, the rising prevalence of caesarean section has contributed to postpartum hemorrhage (PPH) [4]. Though oxytocin value in post-vaginal birth PPH reduction is well established, little attention has been given to their value cesarean section. The benefits of oxytocin are observed during vaginal birth have been assumed to apply to cesarean section. However, it was discovered that 10 to 42% of women receiving oxytocin required additional oxytocin agents, such as prostaglandins and ergot alkaloids [5]. Furthermore, in patients with prolonged labour, preeclampsia, or cardiac disease, oxytocin may not be the best agent for PPH prevention [6, 7]. Additionally, heat sensitive and light oxytocin necessitating cold storage, limiting its applications in low-resources countries [8].

Misoprostol, an injectable uterotonic agent, is used to prevent post-partum hemorrhage regardless of delivery mode (CS or vaginal) [9]. It is well absorbed when taken orally, sublingually, buccally, rectally, and vaginally [10]. When compared to other routes, a pharmacokinetic study discovered that sublingual misoprostol has the shortest time to peak concentration, the highest peak concentration, and the highest bioavailability. Following the oral and sublingual administration after 30 minutes, Peak concentration reached approximately, and 75 minutes after

vaginal administration. This is because of the rapid absorption through the sublingual mucosa and the avoidance of first-pass metabolism via the liver. The abundant blood supply under the tongue, as well as the relatively neutral pH in the buccal cavity, could be factors. However, when compared to other routes, sublingual administration, produces the utmost Cmax, is likewise allied with the higher prevalence of side effects [11].

Another popular approach is to use the antifibrinolytic agent tranexamic acid prophylactically to reduce perioperative bleeding intravenous tranexamic. Intravenous tranexamic is a synthetic lysine derivative that acts as an antifibrinolytic agent by reversibly blocking the lysine-binding sites on plasminogen molecules. Intravenous tranexamic injection considerably reduced post placental deliveries blood loss to postpartum (2 hours) lacking thrombosis impediments, as per studies [12, 13]. Other studies, however, have shown that when compared to routine uterotonic agents, severe PPH is caused by highly risky oral misoprostol [14]. There are limited studies regarding intravenous tranexamic and misoprostol effectiveness in post-cesarean section bleeding reduction. Therefore the present study aimed to assess the intravenous tranexamic acid (TA) and sublingual misoprostol effect on reducing post-cesarean section bleeding.

MATERIAL AND METHODS

This cross-sectional study was carried out on 146 term pregnant women undergoing emergency or elective cesarean section at the Department of Obstetrics and Gynaecology, Qazi Hussain Ahmad Medical Complex, Noshehra during the period from 7th September 2020 to 6th March 2021. All the participants were randomly categorized into two groups. Each group comprised of 73 participants whereas groups I and II received sublingual misoprostol (600 µg) and 500 mg intravenous tranexamic at card clamping respectively. Both groups were administrated for postoperative 48 hours and blood loss was measured. The packed

cell volume and postoperative Hb were evaluated and compared to initial values before surgery. The need for additional uterotonics, blood transfusion, and drug side effects was evaluated. PPH after CS was compared between misoprostol (group-I) and intravenous TA (group-II). All the individuals with a CS indications, age's from 18 to 40 years, singleton pregnancy, gestational age (37–40 weeks), spinal anesthesia, and inferior segment incision based CS were enrolled. All the women with heart, pulmonary, kidney, liver, etc. diseases, TA allergic, coagulation complaints, severe preeclampsia, abnormal placenta, PPH risk factors were excluded.

The data was statistically analyzed using SPSS version 20 software. For variables with a normal distribution, the Student's t test and the paired t test were used. The repeated-measures analysis of variance test was used to examine the effect of time on the hemodynamic parameters. To compare qualitative variables between groups, the Chi-square test was used. P values less than 0.05 were deemed significant.

RESULTS

The mean age of groups I and II were 28.32 ± 4.73 and 28.17 ± 4.83 years whereas the overall mean age was 28.25 ± 4.78 years. A higher reduction of hemoglobin level was observed in an intravenous tranexamic group compared to the sublingual group (-2.39 ± 0.93 versus -2.09 ± 1.28 g/dL) ($p=0.001$). Moreover, the intravenous tranexamic group had significantly higher blood suction and gauze usage than sublingual misoprostol (256.73 ± 83.25 versus 189.68 ± 102.4 cubic centimeter (cc) and 4.59 ± 1.43 versus 3.19 ± 1.27) for a significant value of 0.001. The decrease in mean blood pressure during the cesarean section procedure was significant in intravenous tranexamic than sublingual misoprostol ($p=0.001$).

Table-1 Different variables with their outcomes

Features	Sublingual Misoprostol (n=73)	Intravenous tranexemic (n=73)	P-value
Age (year)	28.32 ± 4.73	28.17 ± 4.83	0.796
Gestational Age (wks)	39.56 ± 1.2	39.36 ± 2.2	0.512
Hemoglobin before intervention (g/dL)	12.92 ± 1.3	13.26 ± 0.83	0.034
Systolic blood pressure (mmHg) before surgery	123.75 ± 16.7	127.38 ± 11.21	0.213
Diastolic blood pressure (mmHg) before surgery	76.34 ± 8.72	75.36 ± 9.81	0.859
Pulse rate before intervention	91.47 ± 7.32	96.28 ± 11.52	0.042
Duration of intervention	39.26 ± 1.68	37.93 ± 2.3	0.07

Table-2 Demographic details of Participants

Features	Sublingual Misoprostol (n=73)	Intravenous tranexemic (n=73)	P-value
Gauze used	3.19 ± 1.27	4.59 ± 1.43	<0.001
Blood suction cc	189.68 ± 102.4	256.73 ± 83.25	<0.001
Hemoglobin level after 48 hours (g/dL)	10.72 ± 1.53	10.71 ± 0.98	0.967
Hemoglobin reduction (g/dL)	-2.09 ± 1.28	-2.39 ± 0.93	<0.001
Additional uterotonics required	3 (3.8%)	4 (5%)	0.9

There was no significant difference in demographic details of both groups. The gestational age and hemodynamic features before intervention showed substantial similarities with a 5% level of significance. Duration of surgery and hemoglobin levels before and after the intervention is shown in Table-1. The intravenous tranexamic group had reduced hemoglobin level significantly as compared to the sublingual misoprostol group, which shows

insignificant differences after 48 hours of surgery. Additionally, as shown in Table-2 sublingual misoprostol group utilized a lower number of gauze and had blood suction compared to intravenous tranexamic. Mean blood pressure decreased significantly in the TA group as compared to sublingual misoprostol group ($F = 6.5$ (4, 514), $P = 0.001$), whereas pulse rate show similar results for both groups as shown in Table 3. Furthermore, there were no substantial dissimilarities in regards of vomiting, fever, nausea, and blood transfusion as shown Figure-1.

Table-3 details of hemodynamic details

Features	Sublingual Misoprostol (n=73)	Intravenous tranexemic (n=73)	P-value
Mean Blood Pressure (mmHg)	91.92 ± 9.84	92.69 ± 9.43	0.634
5 min before spinal anesthesia	88.35 ± 9.69	81.93 ± 12.67	0.01
5 min after spinal anesthesia	83.46 ± 9.38	78.8 ± 10.81	<0.001
10 min after spinal anesthesia	81.78 ± 8.87	76.23 ± 10.42	<0.001
20 min after spinal anesthesia	81.64 ± 8.57	75.8 ± 10.32	<0.001
Recovery room values			
Pulse Rate			
5 min before spinal anesthesia	91.82 ± 6.71	94.89 ± 10.89	0.051
5 min after spinal anesthesia	89.43 ± 6.69	94.46 ± 13.08	0.038
10 min after spinal anesthesia	87.90 ± 6.32	94.42 ± 14.17	0.002
20 min after spinal anesthesia	88.73 ± 6.23	94.35 ± 14.73	0.002
Recovery room values	87.32 ± 6.67	93.36 ± 10.83	0.001

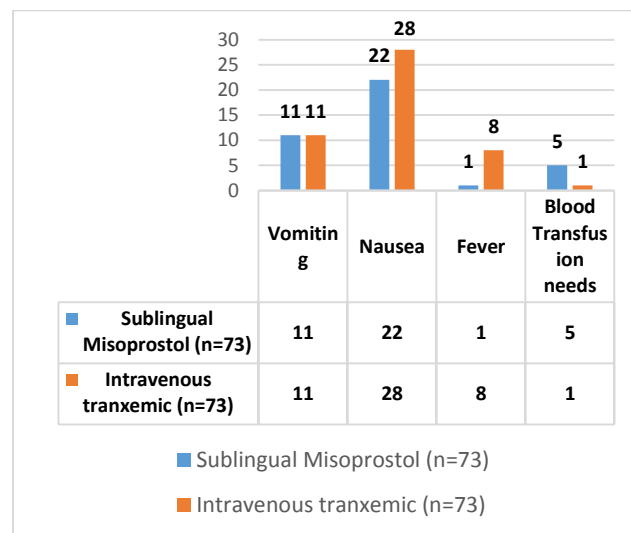


Figure-1 Prevalence of side effects in sublingual and intravenous tranexemic groups

DISCUSSION

Caesarean section is a major intervention carried out on pregnant women worldwide. Despite the oxytocin used on routine basis during CS, hemorrhage and uterine atony may experience in high risk pregnant women with severe complications. Maternal mortality can be reduced with any treatment modality. Due to widespread accessibility, economical, and room temperature stability, Misoprostol is alternative uterotonic agents [17]. Intravenous TA has been used for reducing hemorrhage after intervention and demonstrated effectiveness in patients undergoing CS [18, 19]. Blood loss at caesarean is difficult to assess accurately. A study found that visual assessment of blood loss was 33% less accurate

than drape estimation, with the drape estimate correlating well with hot spectrometry [20]. To overcome the mentioned limitation, Hb level changes before intervention for few days were measured in the current study to assess blood loss indirectly.

Sahhaf et al. [21] findings contradicting the present study and found that haemoglobin levels and bleeding volume were similar in both misoprostol after 6–12 hours and intravenous TA. The disparity could be attributed to alterations in the sort and dosage of misoprostol managed. Abdel Aleem et al. [22] showed that administering misoprostol significantly reduced blood loss 10 minutes before CS matching our study findings. Sentu rk et al. [23] validated the misoprostol effects on reducing blood loss without thrombosis, which is similar to the findings of this study. According to another study conducted by Al-Sawaf et al. [24], intravenous TA appears to be less effective than intramuscular oxytocin in the prevention of PPH; however, it has the potential advantage of being easily administered, cost-effective, and stable at room temperature.

Ugwu et al. [25] found that sublingual misoprostol (200 lg and 400 lg) had no effect on blood loss or PPH occurrence but the 200 lg dose reduced hostile effects. Although sublingual misoprostol different dosages of were not utilized, it was discovered that the efficacy of sublingual misoprostol better than TA in reducing post-caesarean section bleeding loss. In future, however, researchers should increase the sample sizes to evaluate the best dose. Atukunda et al. [26] verified that at 600 lg sublingual misoprostol is inferior for primary PPH protection compared to oxytocin at 10 IU. Chaudhuri et al. [27] demonstrated that oxytocin and sublingual misoprostol both appeared to reduce PPH more efficiently as compared to oxytocin alone. Additionally, Ugwu et al. [28] found that combining intravenous oxytocin with sublingual misoprostol decreased requirement of additional uterotonics and reduced post intervention blood loss. This combination was associated with an increased risk of shivering and fever [28].

Okonofua et al. reported in another recent study that, while sublingual misoprostol is efficient in reducing certain PPH bleeding loss but not in all PPH types. Ancillary treatments and additional uterotonics are required as they reported in their study [29]. The present study found no evidence of adverse effects increase or additional uterotonics usage.

CONCLUSION

Our study concluded that sublingual misoprostol significantly reduced total bleeding when compared to tranexamic acid. Furthermore, hemodynamic variables were stabilized more in the misoprostol group than in the tranexamic acid group.

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