

Prophylactic Effect of Misoprostol Versus Tranexamic Acid in Conjunction with Oxytocin in Reduction of Post-Partum Hemorrhage After LSCS: A Prospective Randomized Study

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Keywords : Blood loss, PPH, tranexemic acid, misoprostal, LSCS

ABSTRACT

AIM : The aim of this study is to compare the prophylactic efficacy of sublingual misoprostol (800 µg) versus IV tranexamic acid (1gm), each administered in conjunction with oxytocin, in reducing blood loss during LSCS

METHOD: Hospital based prospective randomised study over a period of one year. The women undergoing LSCS who met the inclusion criteria were included. Total 182 patients were included and divided into three groups- control group, miso group and TXA group and comparison done by calculating the amount of blood in gauze used (approx.10cc) and the amount in the suction catheter, comparing pre and post-op Hb, and additional uterotonic agent used.

RESULTS : Among 3 groups, Group C (oxytocin + TXA) had noticeably less blood loss with a mean of 395.57 ± 143.02 , compared to Group A(oxytocin only) with a mean of 502.00 ± 112.17 , and Group B(oxytocin + miso) with a mean of 470.49 ± 110.38 which was statistically significant with a p-value of less than 0.001. In Group A, 60.0% needed additional uterotonic agents, whereas In Group B,39.3% needed additional agents,and In Group C, 32.8% needed additional uterotonic agents, but 67.2% didn't. Group A only 16.7% had PPH,In Group B only 9.8% saw PPH, while in Group C only 6.6% of cases had PPH.

CONCLUSION : Combining oxytocin with Misoprostol or Tranexamic acid might be more effective in reducing occurrences of PPH than using oxytocin alone.

INTRODUCTION

Postpartum Hemorrhage (PPH), affecting approximately 2% of deliveries globally, is a leading cause of maternal mortality in economically disadvantaged regions and contributes significantly to severe maternal morbidity and long-term health consequences. Manifestations of this condition include shock, organ dysfunction, and other critical states resulting from substantial blood loss. Epidemiologically, PPH remains the primary contributor to morbidity and mortality in childbirth, impacting an estimated 1% to 6% of all deliveries.

Uterine atony, characterized by inadequate uterine contraction postpartum, leading to increased bleeding, poses a significant risk during and after Cesarean section (C-section). The rising rate of C-sections correlates with heightened blood loss, influenced by procedural intricacy and technique. Factors such as maternal health status and conditions like placenta previa or placenta accreta elevate bleeding risk during C-sections. Emergency C-sections, particularly those prompted by labor complications, entail greater blood loss compared to planned procedures due to limited preparation time.

Following childbirth, uterine contractions aid in hemostasis. The selection of prophylactic measures to mitigate PPH risk post-LSCS (Lower Segment Cesarean Section) significantly impacts maternal safety and outcomes. Complementary to oxytocin, Misoprostol and tranexamic acid (TXA) emerge as promising pharmacological options, each offering distinct mechanisms of action and potential benefits. Misoprostol, an oral prostaglandin analog, induces robust uterine contractions, reducing postpartum blood loss, with advantages including room temperature stability and cost-effectiveness, particularly beneficial in resource-limited settings. Conversely, TXA, an antifibrinolytic agent, inhibits fibrin clot breakdown, thereby diminishing bleeding. Combining these agents with oxytocin may yield synergistic effects in minimizing blood loss during the critical postpartum period.

This study seeks to comprehensively evaluate and compare the prophylactic efficacy of misoprostol versus tranexamic acid, administered alongside oxytocin, in preventing PPH following LSCS.

METHODOLOGY

The present prospective randomised controlled study was conducted in the Dept. of Obstetrics and Gynaecology, Santosh medical college and hospital, Ghaziabad, U.P over the period of one year from January 2023 to December 2023.

Clearance was taken from the ethical committee of the institute. Among women undergoing LSCS who attended obstetrics 182 women were selected based on inclusion and exclusion criteria.

INCLUSION CRITERIA

Consenting women between the ages of 18 and 39 years with singleton pregnancy undergoing emergency or elective cesarean section, irrespective of indication, previous cesarean or high-risk factors for PPH like induced/ augmented labor, hypertensive disorders, gestational diabetes, obesity, premature rupture of membranes, chorioamnionitis, and antepartum hemorrhage

EXCLUSION CRITERIA

Multiple pregnancies
Age <18 or >39 years
Associated renal/hepatic disorders
Thromboembolic/bleeding disorders
Cesarean section under general anesthesia
Known hypersensitivity to misoprostol or TXA.

The patient’s detailed clinical history including demographic details, obstetrics history, past and present history, assessment of vitals, general, systemic, and local examination including per abdomen, per speculum, and per vaginum examination was done as per proforma (Annexure III). Laboratory investigations including pre and post-op Hb were taken. Patients were divided into three groups randomly To evaluate and compare intraoperative blood loss by calculating the amount of blood in gauze used (approx.10cc) and the amount in the suction catheter, To evaluate perioperative Hb fall by comparing pre- and post-48hr Hb decline and To evaluate the need for additional uterotonic agents intra-op during the procedure

Group A: patients received only oxytocin 10U in 500ml saline at the time of LSCS at the time of cord clamping.
 Group B: patients received sublingual Misoprostol 800mcg at the time of cord clamping along with regular oxytocin (10U in 500ml saline)
 Group C: patients received intravenous Tranexamic acid 1gm at the time of cord clamping along with regular oxytocin (10U in 500ml saline)

STATISTICAL ANALYSIS

The observations were methodically described in terms of their respective proportions. During the analysis, the data was meticulously compiled and subjected to rigorous statistical scrutiny. Various tests, including the chi-square test and the Student's T-test, were applied where deemed applicable to the data under investigation. Throughout this analytical process, a p-value of less than 0.05 was adopted as the criterion for establishing statistical significance, ensuring a robust and reliable foundation for the conclusions drawn from the data.

OBSERVATIONS AND RESULTS

Distribution of Study Subjects according to occurrence of PPH

A comparative analysis was conducted among three groups (A, B, and C) receiving different drug combinations (oxytocin only, oxytocin + Misoprostol, and oxytocin + Tranexamic acid) for managing postpartum hemorrhage (PPH). Group A exhibited a 16.7% incidence of PPH, while Groups B and C showed lower rates at 9.8% and 6.6% respectively. Conversely, the absence of PPH was notably higher in Groups B and C with percentages of 90.2% and 93.4%, compared to Group A with 83.3%. These findings suggest potential benefits associated with the oxytocin + Misoprostol and oxytocin + Tranexamic acid combinations in reducing PPH occurrences. Amongst the two combination groups, the oxytocin + TXA combination was found to be more effective in reducing PPH occurrence.

Table 1.

PPH	GROUP A (oxytocin only)	GROUP B (oxytocin + miso)	GROUP C (Oxytocin + TXA)
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	Frequency(n)	Percentage(%)	Frequency(n)	Percentage(%)	Frequency(n)	Percentage(%)
yes	10	16.7	6	9.8	4	5.6
No	50	83.3	55	90.2	57	93.4
Total	60	100	61	100	61	100

Distribution of Study Subjects according to the need for additional agent

In evaluating the necessity for additional agents among three groups receiving different treatments—Group A (Oxytocin only), Group B (Oxytocin + Misoprostol), and Group C (Oxytocin + Tranexamic acid)—it was observed that 60.0% of Group A participants required additional agents, whereas 39.3% of Group B and 32.8% of Group C participants needed them. These findings substantiate the fact that oxytocin used alone for the prevention of PPH is least effective and requires additional uterotonic agents whereas the combination of oxytocin with tranexamic acid is most effective for the prevention of post-LSCS PPH and does not require additional agents. Table 2.

NEED FOR ADDITIONAL AGENT	GROUP A (oxytocin only)	GROUP B (oxytocin+miso)	GROUP C (oxytocin + TXA)
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	Frequency(n)	Percentage(%)	Frequency(n)	Percentage(%)	Frequency(n)	Percentage(%)
Yes	36	60.0	24	39.3	20	32.8
No	24	40.0	37	60.7	41	67.2
Total	60	100.0	61	100.0	61	100.0

Comparison of Blood loss and post-op Hb between three groups

The study evaluated the effects of different medication combinations on variables including blood loss, post-operative hemoglobin levels, and hemoglobin difference across three groups: Results indicate that Group C exhibited significantly lower blood loss compared to Groups A and B (395.57 ± 143.02 vs. 502.00 ± 112.17 and 470.49 ± 110.38 , respectively; $p < 0.001$). These findings suggest that the addition of tranexamic acid to oxytocin may effectively reduce blood loss in comparison to misoprostol or oxytocin alone. Table3.

VARIABLES	GROUP A (oxytocin only)	GROUP B (oxytocin + miso)	GROUP C (oxytocin + TXA)	Df, pvalue
BLOOD LOSS	502.00 ± 112.17	470.49 ± 110.38	395.57 ± 143.02	<0.001
POST-OP Hb	9.48 ± 1.33	9.38 ± 1.20	9.80 ± 1.31	0.16
Hb Difference	0.40 ± 0.27	0.50 ± 0.54	0.55 ± 0.42	0.16

Comparison of Pre to post-op Hb in 3 groups individually

In a comparative analysis of three groups undergoing different uterotonic regimens (Group A: Oxytocin only, Group B: Oxytocin + Misoprostol, Group C: Oxytocin + Tranexamic acid), mean pre-operative hemoglobin levels (Hb) varied, Following surgery, all groups experienced a decrease in Hb levels which was statistically significant in all the groups(mean difference: 0.50 gm/dl, t-value: 7.17, $p < 0.001$). Notably, all paired t-tests revealed significant differences in Hb levels pre- and postoperatively across the three groups, underscoring the impact of different uterotonic regimens on perioperative hemoglobin fluctuations. Table 4.

Hb (g/dl).	Mean + SD	Mean difference	T-value (paired t-test)	P=value
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GROUP A (oxytocin only)

PRE-operative	9.88 ± 1.18	0.40	11.31	<0.001
Post-operative	9.48 ± 1.33			

GROUP B (oxytocin +misoprostal)

PRE-operative	9.89 ± 1.14	0.50	7.17	<0.001
Post-operative	9.38 ± 1.20			

GROUP C (oxytocin + tranexemic acid)

PRE-operative	10.35 ± 1.26	0.55	10.04	<0.001
Post-operative	9.80 ± 1.31			

DISCUSSION

In the present investigation, it was observed that within Group A, which exclusively received Oxytocin, 16.7% encountered Postpartum Hemorrhage (PPH), while 83.3% remained unscathed by such complications. Conversely, Group B, administered both Oxytocin and Misoprostol, exhibited a PPH incidence of only 9.8%, with 90.2% remaining unafflicted. Similarly, Group C, receiving Oxytocin concomitantly with Tranexamic acid, demonstrated a PPH rate of 6.6%, leaving 93.4% unaffected by this condition. A comparison across the three cohorts unveiled Group A's highest PPH incidence (16.7%), whereas Groups B and C showcased lower rates at 9.8% and 6.6%, respectively. Remarkably, Groups B and C exhibited substantially higher rates of PPH prevention, standing at 90.2% and 93.4%, respectively, in contrast to the 83.3% observed in Group A. These findings underscore the potential efficacy of amalgamating Oxytocin with either Misoprostol or Tranexamic acid in mitigating PPH occurrences, thereby shedding light on the prospect of adjunctive agents alongside Oxytocin for PPH prophylaxis. Notably, Group C, where Oxytocin was combined with TXA, displayed enhanced outcomes in PPH prevention among the study cohorts, which aligns with findings from a concurrent study conducted by Assis et al.

Within the study cohort, it was noted that within Group A, exclusively managed with Oxytocin, 60.0% necessitated supplementary uterotonic agents, while 40.0% did not require such interventions. Conversely, Group B, administered both Oxytocin and Misoprostol, depicted a requirement for additional agents in 39.3% of cases, with 60.7% managing without supplementation. Similarly, Group C, receiving Oxytocin and Tranexamic acid, showcased a need for additional uterotonic agents in 32.8% of cases, leaving 67.2% without such requirements. These variances in treatment responses underscore the imperative for tailored medical interventions. Comparison with Vasquez DN et al.'s study on similar treatments revealed that 60.0% of Group A necessitated supplementary interventions, contrasting with 39.3% in Group B and 32.8% in Group C. Conversely, 40.0% of Group A, 60.7% of Group B, and

67.2% of Group C did not necessitate supplementary uterotonic agents for PPH prophylaxis during LSCS, highlighting the superior effectiveness of combination therapies over Oxytocin monotherapy.

The current study unveiled that within Group A, solely administered with Oxytocin, the mean pre-surgical hemoglobin (Hb) level stood at 9.88 ± 1.18 gm/dl, significantly dropping to 9.48 ± 1.33 gm/dl post-surgery ($p < 0.001$). Similarly, in Group B, receiving Oxytocin alongside Misoprostol, the pre-operative mean Hb level was 9.89 ± 1.14 gm/dl, decreasing significantly to 9.38 ± 1.20 gm/dl post-operatively ($p < 0.001$). Likewise, in Group C, where Oxytocin was combined with Tranexamic acid, the pre-operative mean Hb level was 10.35 ± 1.26 gm/dl, significantly declining to 9.80 ± 1.31 gm/dl post-surgery ($p < 0.001$). These outcomes highlight the diverse effects of different drug combinations on postoperative Hb levels, underscoring the necessity to account for these variations in clinical management. Comparison with findings from a study by Tabatabaie et al., analyzing three groups subjected to various uterotonic regimens, revealed distinct mean pre-operative Hb levels across the groups, with Group C displaying the highest level (10.35 ± 1.26 gm/dl). Subsequent to surgery, all groups exhibited a reduction in Hb levels, with Group B demonstrating the most pronounced decline (mean difference: 0.50 gm/dl, $p < 0.001$). Notably, significant disparities were observed in pre- and post-operative Hb levels across all three groups, highlighting the influence of diverse uterotonic regimens on perioperative Hb fluctuations.

CONCLUSION

Postpartum Hemorrhage (PPH): The incidence of postpartum hemorrhage was lowest in Group C and highest in Group A. This indicates that patients who were given oxytocin alone (Group A) experienced the highest rates of PPH, suggesting the necessity of additional agents to mitigate the incidence of post-LSCS PPH.

Requirement for Additional Agents: Group A required the highest use of additional pharmacological agents, while Group C needed the least. This implies that oxytocin alone is not as effective in reducing the incidence of PPH, necessitating the use of other uterotonics such as misoprostol and tranexamic acid (TXA).

Postoperative Hemoglobin Levels: Postoperative hemoglobin levels decreased across all groups. Statistically significant reductions were observed in both Group A and Group B, as indicated by paired T-tests, highlighting the need for additional agents to manage blood loss effectively.

REFERENCES

1. Dawoud M, Al-Husseiny M, Helal O, Elsherbini M, Abdel-Rasheed M, Sediek M. Intravenous tranexamic acid vs. sublingual misoprostol in high-risk women for postpartum hemorrhage following cesarean delivery; a randomized clinical trial. *BMC Pregnancy Childbirth*. 2023;23:611. doi: 10.1186/s12884-023-05935-5.
2. Assis IC, Govêia CS, Miranda DB, Ferreira RS, Riccio LGC. Analysis of the efficacy of prophylactic tranexamic acid in preventing postpartum bleeding: systematic review with meta-analysis of randomized clinical trials. *Brazilian Journal of Anesthesiology*. 2022. doi: 10.1016/j.bjane.2022.08.002.
3. Pakniat H, Chegini V, Shojaei A, Khezri MB, Ansari I. Comparison of the effect of intravenous tranexamic acid and sublingual misoprostol on reducing bleeding after cesarean section: A double-blind randomized clinical trial. *J Obstet Gynaecol India*. 2019 Jun;69(3):239–245. doi: 10.1007/s13224-018-1181-x.
4. Moradan S, Mahdavi Anaraki R, Mirmohammadkhani M. Prophylactic effect of misoprostol versus tranexamic acid in conjunction with oxytocin in reduction of post-partum hemorrhage after cesarean section: A randomized clinical trial. *Koomesh*. 2018;20(4):620-625.
5. Tabatabaie SS, Alavi A, Bazaz M. Comparison of the effect of tranexamic acid and misoprostol on blood loss during and after cesarean section: A randomized clinical trial. *RIJM*. 2021; doi: 10.30483/RIJM.2021.249741.0.

5. Sahu J, Mishra N. Role of intravenous tranexamic acid in reducing blood loss during cesarean section: Study at tribal-dominated area hospital in Chhattisgarh, India. *J Obstet Gynaecol.* 2019; doi: 10.1111/jog.13915.
6. Chaudhuri P, Mandi S, Mazumdar A. Rectally administrated misoprostol as an alternative to intravenous oxytocin infusion for preventing post-partum hemorrhage after cesarean delivery. *J Obstet Gynaecol Res.* 2013 Sep;40(9):202330. doi: 10.1111/jog.12464.
7. Othman ER, Fayez MF, Abd El Aal DM, Mohamed HSD, Abbas AM, Ali MK. Sublingual misoprostol versus intravenous oxytocin in reducing bleeding during and after cesarean delivery: A randomized clinical trial. *Taiwan J Obstet Gynecol.* 2016 Dec;55(6):791-795. doi: 10.1016/j.tjog.2016.02.019.