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Original Research Article

Sublingual Misoprostol as an Adjunct to Oxytocin During Cesarean Delivery in Women at Risk of Postpartum Hemorrhage

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ABSTRACT

Objective: To assess the efficacy of sublingual misoprostol as an adjunct to parenteral oxytocin in preventing blood loss during and after surgery in patients with high risk for postpartum hemorrhage.

Method: One hundred seventy-five women who were high risk for postpartum hemorrhage and undergoing emergency cesarean delivery were assigned randomly to receive either 400 µg misoprostol or placebo sublingually at the time of cord clamping. All participants received an intravenous infusion of 20 units of oxytocin. The primary outcome measures were intraoperative and postoperative blood loss.

Results: Mean intraoperative blood loss was significantly less in misoprostol group as compared with placebo group (595 ± 108 vs. 651 ± 118 ml, P = 0.025). Perioperative Hb fall was significantly less in misoprostol group (0.87 ± 0.29 vs. 1.01 ± 0.26 g, P = 0.0018).

Conclusion: Misoprostol as an adjunct to oxytocin is more efficient in preventing blood loss as compared to oxytocin alone.

Keywords: Oxytocin; Postpartum Hemorrhage; Sublingual Misoprostol.

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INTRODUCTION

Postpartum hemorrhage (PPH) is one of the most common obstetric maternal complications and is among the three most common etiologies of maternal death worldwide.[1] Its incidence is increasing and it affects 1–5% of all deliveries.[2,3] The risk of PPH is further increased in the presence of risk factors such as multiple pregnancy, polyhydramnios, grand multiparty, severe pre-eclampsia, prepartum hemorrhage, prolonged and obstructed labor, augmented labor, obesity, and anemia.[4-6] It is a preventable complication and its prevention is considered to be vital and logistic means for bringing down maternal mortality rate and thus accepted as a key component of safe motherhood. Atony is the main cause of PPH and is responsible for about 80% of PPH events.[7]

Oxytocin is a time tested and standard uterotonic agent to prevent and treat uterine atony and excessive uterine bleeding during delivery, operative or otherwise. However, various studies[8,9] have challenged its role and 10–40 % of women need additional uterotonic therapy.[10,11] Misoprostol a prostaglandin E1 analogue with good uterotonic properties has been evaluated as an alternative to oxytocin[12-15] during cesarean delivery, and has also been used in combination with oxytocin.[16-19] Misoprostal has found a good place in obstetrics in view of its availability, low cost, long shelf life, ease of administration and often mild and self-limited adverse effects. Various studies[20,21] have reported that misoprostol is more effective than oxytocin and methylergometrine in the treatment of PPH. While some studies have considered it as first-line therapy in the treatment of PPH where oxytocin is not available[22], other studies have not confirmed that misoprostol is more effective than oxytocin in the prevention of PPH. Majority of these studies didn't focus or even excluded the high risk group who are expected to get benefitted from such adjuvant agents.

The present study was conducted to study the role of combination of misoprostol and oxytocin in prevention of bleed during and after cesarean section in high risk patients.

MATERIAL AND METHODS

This is a prospective, randomized, double-blind study conducted in the Post graduate Department of Obstetrics and Gynaecology of Sheri-Kashmir Institute of Medical Sciences, a tertiary care teaching hospital in Jammu and Kashmir. Women undergoing

emergency cesarean under spinal anesthesia and who had at least one risk factor for PPH (multiple pregnancy, polyhydramnios [defined as amniotic fluid index more than 24 cm], prolonged labor or dystocia [according to the partogram], grand multiparity [parity ≥4], prepartum hemorrhage, severe pre-eclampsia/eclampsia, anemia [hemoglobin <8.0 g/L and known previous PPH) were included in this study. All the patients were evaluated properly and after qualifying the eligibility, consent was taken.

Women were assigned randomly to receive either 400 µg misoprostol or placebo sublingually at the time of cord clamping. Randomization was done by computer-generated random numbers (blocks of size eight). For blinding the study clinicians, investigators, data analysts, and participants were masked to the treatment allocation. All cesareans were performed under spinal anesthesia and uterine incisions were low transverse type. The medication was placed in the patient's sublingual space by the anesthesiologist at cord clamping. Simultaneously, for all women, an intravenous infusion of oxytocin 20 U in 1,000 ml saline solution was started at 10 ml/min for 30 min, which was followed by 2.0 ml/min for 6 h. Further use of any other intervention was at the discretion of the obstetrician. The blood loss during intraoperative period was calculated by measuring blood in the suction apparatus and sterile drapes before irrigation and by evaluating the blood in abdominal swabs and gauzes. Postoperative blood loss was assessed by weighing the soaked pads. Hemoglobin was measured preoperatively and 24 hours after delivery. Baseline characteristics and all other outcome variables were recorded on data sheets. Perioperative fall in Hb was calculated from preoperative and second postoperative day's Hb estimation.

Table 1: Patient characteristics in the two groups

Variable	Misoprostol(n=110)	Oxytocin alone(n=110)
Maternal Age	26.5 ± 5.5	24.5 ± 6.5
Primipara	98(89.09)	96(87.27)
Multipara	12(10.90)	14(12.72)
Pregnancy Duration	38.0 ± 1.5	37.9 ± 1.6
Preop Hb	9.62± 1.5	9.53± 1.2
No. of Risk Factors		
1	97(80.16)	101(91.81)
≥2	13(11.81)	09

RESULTS

There were no significant difference in both the groups in terms of demographic, obstetrics and risk factors.(Table 1)

The total blood (mean) loss was significantly lower in misoprostol group (545±110) as compared to oxytocin alone group (630±108). Also proportion of women with blood loss <500, 500-1000 and even with >1000 was higher in oxytocin group. Fewer patients in misoprostol group needed additional urotonic agents (20.90% vs 40.90%) and blood transfusion (2.72% vs 3.6%).

Mean postoperative Hb (g) was significantly higher in the misoprostol group (9.39 ± 0.68 vs. 8.04 ± 0.56, *P* =). Perioperative Hb fall was significantly less in misoprostol group (0.23 ± 0.29 vs. 0.70 ± 0.26 g).

The most of the side effects like shivering, fever, nausea, vomiting and diarrhea very higher in misoprostol group as compared to other group. These effects were self-limiting in both the groups and didn't need any specific intervention. Also the differences were not statistically significant**.**

Table 2: PPH Risk factors in the two groups

Variable	Misoprostol(n=110)	Oxytocin alone(n=110)
Multiple pregnancy	16(14.54)	14(12.72)
Polyhydramnios	18(16.36)	19(17.27)
Prepartum hemorrhage	8(7.27)	12(10.90)
Severe preeclampsia/eclampsia	12(10.90)	11(10)
Anemia	28(25.45)	30(27.27)
Prolonged/obstructed labor	14(12.72)	11(10)
Grand multiparity	8(7.27)	6(5.45)
Known previous postpartum hemorrhage	6(5.45)	7(6.36)

Table 3: Outcome parameters in the two groups and results

Parameters	Misoprostol n=110	Oxytocin alone n=110	p-value
Estimated blood loss			
Total (ml)	545±110	630±108	< 0.001
<500ml	64(58.18)	31(28.18)	< 0.001
500-1000ml	42(38.18)	73(66.36)	< 0.001
>1000ml	04(3.6)	6(5.45)	>0.74
Additional uterotonic therapy	23(20.90)	45(40.90)	0.001
Blood transfusion	03(2.72)	04(3.6)	>0.05
Operating time (min)	40±5.2	42±5.0	0.004
Postoperative Hb (g/dl)	8.96±0.68	8.74±0.64	0.014

DISCUSSION

This study was conducted to learn the effectiveness of the misoprostol and oxytocin in prevention of post-partum hemorrhage in high risk patient. The patients with high risks for post-partum hemorrhage were randomized in two groups with 110 patients in each group. We found that the group who received misoprostol along with oxytocin had significantly decreased total mean (545±110) blood as compared to the other group who only received oxytocin (630±108). Also proportion of women with blood loss <500, 500-1000 and even with >1000 was higher in oxytocin group.

Various studies have been done to know the role of misoprostol in preventing the blood loss during and after cesarean section. Most of these studies,[12,17,23-25] have claimed the effectiveness of misoprostol in this regard, however, few have reported no difference.[16,26] The extent of the decrease in the amount of blood loss varied over a wide range among these studies. The reasons for this variation might be because of different dosage and route of misoprostol, differences in study groups, methods of estimating the loss of blood.

We in our study used 400 µg of misoprostol sublingually and an intravenous infusion of oxytocin 20 U in 1,000 ml saline solution was started at 10 ml/min for 30 min, which was followed by 2.0 ml/min for 6 h. Dose of misoprostol in various studies has ranged from 200 to 800 mcg.[27,28] Zhao et al[27,28] in their study comparing 600 µg oral misoprostol with oxytocin (20 U intrauterine plus 20 U IV). Lokugamage et al.[29] compared 500 µg oral misoprostol with 10 U IV Syntocinon and concluded that oral misoprostol could be used as an alternative oxytocic agent. Hamm et al in a placebo controlled study concluded that 200 mcg buccal misoprostol reduced the need for additional uterotonic agents. Acharya et al, Sood et al[30] and Picklu[31] et al used 400 µg of misoprostol and reported significant decrease in blood loss. Misoprostol was given by the sublingual, buccal, rectal, or intrauterine routes.

The subjects of the present study were women undergoing emergency cesarean section under spinal anesthesia who had at least one risk factor for PPH. Most of the studies done in the past didn't focus or even excluded the high risk group who are expected to get benefitted from such adjuvant agents. Of the seven previous randomized trials[16-19,23,24,30] comparing the use of misoprostol and oxytocin with the use of oxytocin alone to reduce blood loss during cesarean delivery, five excluded women with all[17,19,23,24] or some[18] of the risk factors for PPH, one[30] included both high- and low-risk women, and one[16] did not report exclusion criteria.

Perioperative Hb fall was significantly less in misoprostol group (0.23 ± 0.29 vs. 0.70 ± 0.26 g). This is similar to that reported in a recent study[17] in which concomitant oxytocin infusion was given to all women, as in the present study. In studies reporting no difference, misoprostol was either compared with oxytocin or a lower dose of misoprostol was used. In our study blood transfusion was needed in 2.72% of misoprostol group vs 3.6% in other group. This finding is consistent with previous studies.[18,19,24] Baskett et al. and Haque et al. reported no cases of transfusion need in their studies.[32,33] Fewer patients in misoprostol group needed additional urotonic agents (20.90% vs 40.90%). reduced requirement for additional uterotonic agents with the use of combined oxytocics were in agreement with some of the previous studies. While some others have reported no difference. The most of the side effects like shivering, fever, nausea, vomiting very higher in misoprostol group as compared to other group. However the differences were not statistically significant. Similar pattern of adverse effect was shown by other studies in which sublingual misoprostol was used.

CONCLUSION

Misoprostol as an adjunct to oxytocin is more efficient in preventing blood loss as compared to oxytocin alone in terms of efficacy in controlling blood loss without any significant increase in adverse effects.

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