



EFFECT OF PREOPERATIVE SUBLINGUAL MISOPROSTOL IN REDUCING INTRA AND POST-OPERATIVE BLOOD LOSS IN CESAREAN SECTION - A DOUBLE BLIND RANDOMIZED PLACEBO CONTROLLED TRIAL

Gynaecology

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ABSTRACT

INTRODUCTION: Postpartum hemorrhage and intra-operative blood loss during cesarean delivery is a major concern to all obstetrician. Maternal mortality is unacceptably high worldwide. About 830 women die from pregnancy or child -birth related complications around the world everyday. It was estimated that in 2015, roughly 303000 women died during and following pregnancy and child birth. PPH is the leading cause of maternal mortality in low income countries, and the primary cause of nearly one quarter of all maternal deaths globally.

AIMS & OBJECTIVE: To measure the efficacy and safety of pre-operative sublingual misoprostol for decrease of blood loss during and after the cesarean sections.

MATERIALS AND METHOD: There after subject recruitment was done form July 2018 to June 2019. Effect of sublingual misoprostol prior to cesarean section just before skin incision to decrease bleeding during and after cesarean sections. Patients admitted for delivery in the Gynecology & obstetrics department of SSKM Hospital.

RESULT AND ANALYSIS: Our study showed in Control Group, 4(4.3%) patients had needed Blood Trans fusion. Association of Blood Trans fusion needed was statistically significant ($p=0.0431$) between two groups. In SUB LINGUAL MISOPROSTOL Group, 7(7.6%) patients had DIARRHOEA, 9(9.8%) patients had NAUSEA, 8(8.7%) patients had SHIVERING, 8(8.7%) patients had TEMPERATURE RISING and 6(6.5%) patients had VOMITING. Association of Adverse effects was statistically significant ($p<0.0001$) between two groups. In Control group,

SUMMARY AND CONCLUSION: We found that Total blood loss (After delivery of baby and 24 hrs Post- op) was less in sub lingual misoprostol groups compared to control group which was statistically significant. Hard tone of Uterus during CS was higher in sub lingual misoprostol group in compared to control group which was statistically significant.

KEYWORDS

sublingual misoprostol, blood loss, cesarean section, double blind, placebo controlled

INTRODUCTION

Postpartum hemorrhage and intra-operative blood loss during cesarean delivery is a major concern to all obstetrician. Maternal mortality is unacceptably high worldwide. About 830 women die from pregnancy or child -birth related complications around the world everyday. It was estimated that in 2015, roughly 303000 women died during and following pregnancy and child birth.¹ PPH is the leading cause of maternal mortality in low income countries, and the primary cause of nearly one quarter of all maternal deaths globally.² Cesarean delivery is the most common major surgical procedure performed on women worldwide and its rates continue to rise steadily in both developed and developing countries.¹ In 2007, the global cesarean delivery rate was estimated to be 15%. Postpartum hemorrhage is a major contributor to maternal mortality, mainly in developing countries. Recent studies from developed countries report an increase in the rate of postpartum hemorrhage, which has been attributed (at least in part) to a rise in the rate of cesarean delivery.³ Large population- and hospital-based cohort studies have attributed this to uterine atony after vaginal or cesarean deliveries.³ Cesarean delivery, often performed because of —dystocia , may predispose a patient to uterine atony. This has been traditionally attributed to either myometrial fatigue or impaired contractility at the site of the uterine incision. According to the World Health Organization, postpartum hemorrhage (PPH) continues to be the most significant cause of maternal morbidity and mortality worldwide. Average blood loss during delivery is progressively more with the type of delivery, vaginal delivery (500 ml), cesarean section (1000 ml), and emergency hysterectomy (3500 mL). A reduction of blood loss during cesarean delivery has a great benefit to decrease postoperative morbidity and mortality and decrease the rate of blood transfusion and the risks associated with it. Excessive blood loss is estimated by a 10% drop in the hematocrit value post delivery or by need for blood transfusion. Postpartum hemorrhage following a cesarean delivery has been defined as blood loss over 1000 ml.⁴ Recent studies have estimated that

the prevalence of postpartum hemorrhage after cesarean delivery ranges from 0.6% to 6.4% (median, 3%), although the frequency depends on the criteria used to define this condition and the method used to calculate blood loss and approximately 4% in a case of vaginal delivery. PPH is the leading cause of preventable maternal mortality in the developing world, and its prevention is assumed to be an important and rational strategy, and has been identified as a key component of safe motherhood.

To measure the efficacy of sublingual misoprostol given during cesarean section just before skin incision in decreasing blood loss during and after cesarean sections, cesarean sections just before skin incision, on tone of uterus during and after the procedure. Safety and tolerability of sublingual misoprostol given prior to cesarean section just before skin incision. Effect of sublingual misoprostol prior to cesarean section just before skin incision on neonate. Compare the hematocrit level and Hb% by giving sublingual misoprostol prior to cesarean section just before skin incision.

MATERIALS AND METHOD

Study setting:

Department of Obstetrics & Gynecology (indoor setting) of IPGME&R & SSKM. Hospital

Period of study: Study was initiated after approval from the IEC. There after subject recruitment was done form July 2018 to June 2019

Definition of problem- Effect of sublingual misoprostol prior to cesarean section just before skin incision to decrease bleeding during and after cesarean sections.

INCLUSION CRITERIA:

Women with pregnancy who have been advised to undergo cesarean sections with the following criteria:

1. Women with age between 18-35 years with uncomplicated

singleton pregnancies of 36-40 weeks gestation and up to gravid 3 scheduled for elective lower segment cesarean delivery via a Pfannenstien incision under spinal an aesthesia.

2. Women willing to give written informed consent to participate in the study.

EXCLUSION CRITERIA:

1. Women having risk factors for post partum hemorrhage, such as, multiple pregnancy, polyhydramnions, fetal macrosomia, antepartum hemorrhage, obstructed labour, haemoglobin < 8 gm%, haematocrit < 30%, severe pre eclampsia and coagulopathy; 57
2. active thromboembolic disease, eg., deep vein thrombosis, pulmonary embolism, cerebral thrombosis, history of thrombosis or thromboembolism, intrinsic risk for thrombosis eg thrombogenic vulvar disease, thrombogenic cardiac disease, cardiovascular, renal and liver disorders, hypercoagulopathy, thrombophilia etc.
3. History of previous cesarean deliveries and history of any intra abdominal surgery.
4. bronchial asthma.
5. hypersensitivity to misoprostol.

RESULT AND ANALYSIS

In our study, 92(50.0%) patients were in Control and 92(50.0%) patients were in SUB LINGUAL MISOPROSTOL. In Control Group, 6(6.5%) patients were ≤ 20 years old, 51(55.4%) patients were 21-25 years old, 21(22.8%) patients were 26-30 years old and 14(15.2%) patients were 31-35 years old. In SUB LINGUAL MISOPROSTOL Group, 6(6.5%) patients were ≤ 20 years old, 52(56.5%) patients were 21-25 years old, 24(26.1%) patients were 26-30 years old and 10(10.9%) patients were 31-35 years old. Association of Age in years was not statistically significant ($p=0.8311$) between two groups. In Control Group, 50(54.3%) patients were gravida 1, 39(42.4%) patients were gravida 2 and 3(3.3%) patients were gravida 3. In SUB LINGUAL MISOPROSTOL Group, 56(60.9%) patients were gravida 1, 34(37.0%) patients were gravida 2 2(2.2%) patients were gravida 3. Association of gravida was not statistically significant ($p=0.6434$) between two groups. In Control Group, 13(14.1%) patients had Firm uterus, 75(81.5%) patients had Hard uterus and 4(4.3%) patients had Soft uterus. In SUB LINGUAL MISOPROSTOL Group, 3(3.3%) patients had Firm uterus and 89(96.7%) patients had Hard uterus. Association of Tone of Uterus during was statistically significant ($p=0.0033$) between two groups. In Control Group, 92(100.0%) patients had hard uterus. In SUB LINGUAL MISOPROSTOL Group, 92(100.0%) patients had Hard uterus.

Our study showed in Control Group, 4(4.3%) patients had needed Blood Trans fusion. Association of Blood Trans fusion needed was statistically significant ($p=0.0431$) between two groups. In SUB LINGUAL MISOPROSTOL Group, 7(7.6%) patients had DIARRHOEA, 9(9.8%) patients had NAUSEA, 8(8.7%) patients had SHIVERING, 8(8.7%) patients had TEMPERATURE RISING and 6(6.5%) patients had VOMITING. Association of Adverse effects was statistically significant ($p<0.0001$) between two groups.

DISCUSSION

In our study, 92(50.0%) patients were in Control Group and 92(50.0%) patients were in SUB LINGUAL MISOPROSTOL Group. In Control Group, 6(6.5%) patients were ≤ 20 years old, 51(55.4%) patients were 21-25 years old, 21(22.8%) patients were 26-30 years old and 14(15.2%) patients were 31-35 years old. In SUB LINGUAL MISOPROSTOL Group, 6(6.5%) patients were ≤ 20 years old, 52(56.5%) patients were 21-25 years old, 24(26.1%) patients were 26-30 years old and 10(10.9%) patients were 31-35 years old. Association of Age in years was not statistically significant ($p=0.8311$) between two groups. In Control Group, 50(54.3%) patients were gravida 1, 39(42.4%) patients were gravida 2 and 3(3.3%) patients were gravida 3. In SUB LINGUAL MISOPROSTOL Group, 56(60.9%) patients were gravida 1, 34(37.0%) patients were gravida 2 and 2(2.2%) patients were gravida 3. Association of gravida was not statistically significant ($p=0.6434$) between two groups.

In Control Group, 13(14.1%) patients had Firm uterus, 75(81.5%) patients had Hard uterus and 4(4.3%) patients had Soft uterus. In SUB LINGUAL MISOPROSTOL Group, 3(3.3%) patients had Firm uterus and 89(96.7%) patients had Hard uterus. Association of Tone of Uterus during CS was statistically significant ($p=0.0033$) between two

groups. Our study showed that in Control group, the mean BMI (mean $\pm$ s.d.) of patients was $21.0924 \pm .6775$. In SUB LINGUAL MISOPROSTOL group, the mean BMI (mean $\pm$ s.d.) of patients was 21.0533 ± 0.7039 . Difference of mean BMI was not statistically significant ($p=0.7017$) between two groups. In Control group, the mean POG at delivery (mean $\pm$ s.d.) of patients was 37.9239 ± 1.2246 . In SUB LINGUAL MISOPROSTOL group, the mean POG at delivery (mean $\pm$ s.d.) of patients was 37.9022 ± 1.2230 . Difference of mean POG at delivery was not statistically significant ($p=0.9042$) between two groups.

We found that in Control Group, 92(100.0%) patients were hard uterus after 2 hrs of cs. In SUB LINGUAL MISOPROSTOL Group, 92(100.0%) patients were Hard uterus after 2 hrs of cs. In Control Group, 8(8.7%) patients had needed Tranexanic acid. In SUB LINGUAL MISOPROSTOL Group, 2(2.2%) patients had needed Tranexanic acid. Association of Tranexanic acid needed was not statistically significant ($p=0.0510$) between two groups. In Control Group, 4(4.3%) patients had needed Blood Transfusion. Association of Blood Transfusion was statistically significant ($p=0.0431$) between two groups.

OMOZUWA ES et al ⁵ (2016) found that Blood loss estimation was done using direct measurement and weighing. Shivering, pyrexia and vomiting as the side effects of the trial drug were also analysed. Mean intraoperative blood loss was significantly less in the sublingual group as compared to the rectal group (602.87 ± 131.96 vs 705.83 ± 142.24 ml, $p=0.002$). Mean postoperative Hb (g) was higher in the sublingual group 10.00 ± 1.13 vs 9.63 ± 0.76 , $p=0.463$. Perioperative Hb fall was less in the sublingual group (1.17 ± 1.08 vs 1.49 ± 0.99 , $p=0.193$). Sublingual misoprostol was found to be more effective in reducing intraoperative blood loss at elective Caesarean section with side effects that are transient.

Aghazadeh Naini A et al ⁶ (2014) found that there was not a significant difference between two groups in terms of need to blood transfusion or the incidence of drug's side effects ($P>0.05$). Sublingual misoprostol reduces the intra-operative blood loss during cesarean section and also, the need for additional uterotonic agents; however, this reduce in blood loss does not decrease transfusion rate.

Ahmed T et al ⁷ (2017) found that Mean intraoperative blood loss was significantly less in misoprostol group as compared with placebo group (510 ± 100 vs. 670 ± 110 ml). Fewer women needed additional uterotonic agents in misoprostol group (20.2 vs. 40.5 %). Perioperative Hb fall was significantly less in misoprostol group (0.77 ± 0.25 vs. 1.05 ± 0.25 g). Conclusion: Sublingual misoprostol decreases intraoper- ative blood loss and the need for additional uterotonic agents at cesarean delivery.

Mervat SE et al ⁸ (2012) found that the main outcome measures were intra-operative blood loss, postpartum blood loss at 24 hours, and difference between preoperative and postoperative hematocrit values. The mean intra-operative and postpartum blood loss was significantly lower in the study group than the control group: 429 ± 234 mL and 185 ± 95 mL versus 620 ± 375 mL and 324 ± 167 mL, respectively ($P=0.001$ for both comparisons). The difference between the preoperative and postoperative hematocrit values was also significantly lower in the study group than the control group (4.62 ± 2.45 versus 8.15 ± 3.84 ; $P=0.02$). Admissions to the neonatal intensive care unit and Apgar scores at 1 and 5 minutes were comparable between the 2 groups.

Maged AM et al ⁹ (2019) found that to Intraoperative blood loss was significantly lower in the preoperative misoprostol group compared with the postoperative group (528.7 ± 114.8 mL vs 788.6 ± 165.8 mL; $P<0.001$). Blood loss during the first 24 hours after delivery was also lower in the preoperative group (199.3 ± 84.5 mL vs 302.9 ± 125.6 mL; $P<0.001$). Fewer women in the preoperative group needed additional uterotonics (7 vs 21; $P<0.001$). After delivery, the decrease in both hemoglobin and hematocrit levels was significantly less in the preoperative group (-6.8 vs -12.8% and -6.05 vs -17.8% , respectively; $P<0.001$). Preoperative rectal administration of misoprostol significantly reduced intraoperative and postoperative blood loss during and after elective cesarean delivery.

Our study showed that in Control group, the mean Total blood loss (After Delivery of baby and 24 hrs Post-op) (mean $\pm$ s.d.) of patients

was (915.3261± 56.0112)ml. In SUB LINGUAL MISOPROSTOL group, the mean Total blood loss (After Delivery of baby and 24 hrs Post-op) (mean± s.d.) of patients was (686.5217± 66.4597)ml. Difference of mean Total blood loss (After Delivery of baby and 24 hrs Post-op) was statistically significant ($p<0.0001$) between two groups. In Control group, the mean Pre-op Hb (before 24 hrs)(mean± s.d.) of patients was (11.5859± 1.2336)gm/dl. In SUB LINGUAL MISOPROSTOL group, the mean Pre-op Hb (before 24 hrs)(mean± s.d.) of patients was (11.6533± 1.2714) gm/dl. Difference of mean Pre-op Hb (before 24 hrs) was not statistically significant ($p=0.7156$) between two groups.

CONCLUSION

We found that Total blood loss (After delivery of baby and 24 hrs Post-op) was less in sub lingual misoprostol groups compared to control group which was statistically significant. Hard tone of Uterus during CS was higher in sub lingual misoprostol group in compared to control group which was statistically significant.

It was found that Tranexanic acid was needed more in control group compared to sub lingual misoprostol group though it was not statistically significant.

Blood transfusion was needed more in control group compared to sub lingual misoprostol group which was statistically significant.

Adverse effects like diarrhea, nausea, shivering, temperature rising and vomiting was more in sub lingual misoprostol groups compared to control group which was statistically significant.

In our study difference of mean Pre-op Hb (before 24 hrs) was not statistically significant between two groups but the mean Post-op Hb (after 24 hrs) was higher in sub lingual misoprostol groups compared to control group which was statistically significant.

Extra Uterotonic was needed less in sub lingual misoprostol groups compared to control group which was statistically significant.

Total IVF during CS and 24 hrs after CS was less in sub lingual misoprostol groups compared to control group which was statistically significant.

Table: Association between Blood Trans fusion needed: Group

GROUP			
Blood transfusion needed	Control	SUB LINGUAL MISOPROSTOL	TOTAL
No	88	92	180
Row %	48.9	51.1	100.0
Col %	95.7	100.0	97.8
Yes	4	0	4
Row %	100.0	0.0	100.0
Col %	4.3	0.0	2.2
TOTAL	92	92	184
Row %	50.0	50.0	100.0
Col %	100.0	100.0	100.0

Table: Association between Adverse effects: Group

GROUP			
Adverse effects	Control	SUB LINGUAL MISOPROSTOL	TOTAL
DIARRHOEA	0	7	7
Row% Col %	0.0 0.0	100.0 7.6	100.0 3.8
NAUSEA	0	9	9
Row% Col %	0.0 0.0	100.0 9.8	100.0 4.9
No	92	54	146
Row %	63.0	37.0	100.0
Col %	100.0	58.7	79.3
SHIVERING	0	8	8
Row %	0.0	100.0	100.0
Col %	0.0	8.7	4.3
TEMPERATURE RISING	0	8	8
Row %	0.0	100.0	100.0
Col %	0.0	8.7	4.3
VOMITING	0	6	6
Row %	0.0	100.0	100.0
Col %	0.0	6.5	3.3

TOTAL	92	92	184
Row %	50.0	50.0	100.0
Col %	100.0	100.0	100.0

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