Original Research Article

A Prospective Study of "Effect of preoperative rectal misoprostol on cesarean section related blood loss and on APGAR score"

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Abstract

Aim and Objectives: To evaluate the effect of preoperatively administered 600 microgram misoprostol via rectal route on cesarean section related intraoperative and postoperative blood loss at 24 hours and its effect on APGAR score at 1 min and 5 min in cesarean section.**Materials and Methods**: A randomized controlled trial was conducted among 200 women scheduled for cesarean delivery who did not have any risk factor for postpartum hemorrhage. The study group (n= 100) received 600 microgram of misoprostol. The control group(n=100) received placebo. Misoprostol was administered rectally just after spinal anaesthesia. Primary outcome measured were amount of intraoperative blood loss, blood loss at 24 hour postoperative and difference between APGAR scores in both groups at 1 min and 5 min.**Results:** The mean intra operative and postoperative blood loss at 24 hour was significantly lower in the study group than the control group (440 ±252 ml versus 635±360 ml: p=0.03)(174 ±78 ml versus 310±152 ml; p=0.001). Admission to the neonatal intensive care unit and APGAR scores at 1 and 5 min were comparable between 2 groups. {7.4±1.4 and 7.9 ±1.4 at 1 min (p=0.28) and 9.0±0.7 and 8.8±0.6 at 5 min (p=0.24)}. The incidence of shivering was higher in study group.**Conclusion:** Preoperative treatment with rectal administration of 600 microgram misoprostol significantly reduces blood loss related to cesarean delivery. However, occurrence of transient side effect such as shivering was noted more frequently with the use of misoprostol.

Key Words: Cesarean section, Misoprostol, Intraoperative and postoperative blood loss, APGAR score.

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Introduction

Pregnancy and childbirth are physiological process, but by no means risk free. Among all the stages of labor, third stage of labor is the unforgiving stage and associated with maximum maternal morbidity and mortality. The normal case can, within a minute, become abnormal and successful delivery can swiftly turn into disaster. PPH is the most dreaded complication of third stage of labor. A hard fact about mortality from PPH is that it is different from other major obstetric causes of death. If not managed appropriately, antepartum hemorrhage (APH) can cause death in 8-12 hours, obstructed labor in 2 days, sepsis in 6 days, but severe PPH, if not promptly managed, a women can die in just 1 hour after delivery. Globally, PPH contributes 25% of maternal deaths while in India it is responsible for 38% of all maternal deaths, which is considerably high, given the Indian maternal mortality rate (MMR) of 212/100,000[1]. The achievement of safe childbirth by cesarean section (CS) was one of the greatest medical advances of the 20th century. CS is the most common major surgical procedure performed on women worldwide. Its rate is increasing continuously. According to WHO data CS rate in developed countries is 30% or more, while in developing countries like India it is 20-25%[2,3].

The overall intraoperative complication rate has been reported as 12-15%, the rate being significantly greater with emergency compared to elective cesarean sections. Most frequent intraoperative and postoperative complication is haemorrhage [4]. Average blood loss in a vaginal delivery is about 500ml while in CS it is twice of vaginal delivery that is 1000ml[5]. Hematocrit falls by 10% and blood transfusion is required in 6% of women undergoing CS as compared with 4% of women who have a vaginal birth[6]. Haemorrhage can be primary or secondary. Increased blood loss after CS is due to several factors, including surgical incisions, lack of uterine contraction (especially in elective CS), and manual removal of placenta rather than waiting for its spontaneous separation after placental bed retraction[7]. Minimizing blood loss during delivery, whether vaginal or CS, is an important preventive health objective aimed at reducing postpartum anemia and related morbidity. It has been reported that the prevalence of postpartum anemia in low-income countries is approximately 50%–80%[8]. The major cause of postpartum anemia is blood loss at delivery, especially in presence of antepartum anemia. Postpartum anemia constitutes an appreciable health problem among women of reproductive age and is associated with reduced quality of life, impaired cognition, emotional instability, and depression[8].Primary hemorrhage due to extension of uterine incision or laceration needs to be repaired surgically, whereas uterine atony is primarily managed with uterotonics. Most of the obstetric

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units use intravenous bolus or infusion of oxytocin to prevent uterine atony and blood loss during and after cesarean section but 10%–40% of women receiving oxytocin requires additional uterotonic agents.Misoprostol, a prostaglandin E1 (PGE1) analogue, has

- potent uterotonic action,
- is cheap and stable at room temperature, and
- has few adverse effects.

Rationale Of the Study:-

- Misoprostol has been extensively studied in the prevention and treatment of PPH after vaginal delivery however; its use in conjunction with Cesarean section has not been investigated as much.
- Notwithstanding the large number of studies conducted on doses and infusion rates of oxytocin; the doses and routes of administration of misoprostol, the ideal practice remains controversial.

Aims and Objectives:-The aim of present study was to evaluate the effect of preoperative 600ug rectal misoprostol

- On intraoperative blood loss in cesarean section.
- On postoperative blood loss in cesarean section at 24 hours.
- On APGAR score at 1min and 5 min in cesarean section.

Material and Methods

The present study was a prospective randomized controlled trial, conducted on 200 cases of elective and emergency CS, from November 2013 to October 2014, at Panna Dhai Mahila Rajkiya Chikitsalaya, attached to RNT Medical college Udaipur, Rajasthan.

Inclusion criteria

1. Hemoglobin 10gm/dl or more
2. Coagulation profile within normal range
3. 36 or more completed weeks of pregnancy
4. Uncomplicated singleton pregnancy
5. Cases operated under spinal anaesthesia

Exclusion criteria

1. Hemoglobin<10gm/dl
2. Coagulopathy
3. Hypersensitivity to prostaglandins
4. Cases with risk factor for PPH- multiple gestations, polyhydraminos, fetal macrosomia.
5. APH
6. Obstructed labor
7. 2 or more previous CS
8. LSCS for cord prolapse or gross fetal bradycardia
9. Maternal chronic disease
10. Cases requiring General anesthesia
11. Eclampsia
12. History of previous uterine surgeries like myomectomy, hysterotomy etc.

Women who fulfilled the eligibility criteria, written consent was obtained from them for CS, and then participants were randomized in a 1:1 ratio into 2 groups. Women in the study group received a total preoperative dose of 600ug of misoprostol, administered as 3 individual 200ug tablets, while women assigned to the control group, received 3 placebo tablets. Misoprostol tablets were inserted rectally after giving Spinal anesthesia. The packets containing Misoprostol were sealed and opaque, and not identified by the surgeons and anesthetist. The randomization was done by the residents using computer generated tables, and the preparation and allocation of packets and confidential record maintained by staff in charge of the operation theatre.

The baseline demographic and obstetric data comprising age, parity, duration of gestation, and indication for cesarean delivery were recorded. Hemoglobin, coagulation study and ultrasound for determination of amniotic fluid index (AFI) were performed in all cases immediately before the operation. All of the operations were performed under spinal anesthesia. The standard technique of transperitoneal lower segment cesarean was adopted. To avoid bias related to surgical skill, a group of 4 surgeons from a particular obstetric unit performed all of the operations. All participants received 10 IU of oxytocin in 500 mL lactated Ringer solution, which was infused over a period of 30 minutes (i.e. at a rate of 340 mIU per minute) after cord clamping. The placenta was removed by control cord traction and uterine compression. The uterus was exteriorized and compressed during closure, which was done by continuous sutures in 2 layers using Ethicon Vicryl 0 suture. Peritoneum was closed by continuous sutures and muscle was closed by interrupted sutures using plain catgut 01suture and the sheath was closed using vicryl 0 suture material. Additional oxytocic administered at the request of the surgeon if uterine tone is inadequate. Methylergometrine was the preferred additional oxytocic. When methylergometrine was ineffective or contraindicated, 15-methyl-PGF-2α was considered as alternative.Blood loss during the operation was estimated by adding the volume of the contents of the suction bottle (a) to the difference in weight (1 g is equivalent to 1 mL) between dry (b) and soaked linen savers and mops (c) used during the operation to obtain the approximate blood loss [A=a+(c – b)]. Amniotic fluid volume was estimated by multiplying AFI by 30 mL (d) . Estimated blood loss (B) was calculated by subtracting amniotic fluid volume from approximate blood loss (B=A – d). Any complications occurring during the postoperative period was recorded. Postoperative blood loss during the first 24 hours after surgery was assessed by weight difference between dry and wet pads.

Outcome Measured

Primary outcomes

A. Volume of blood loss during intraoperative period
B. Volume of blood loss in postoperative period at 24 hours
C. APGAR score at 1min & 5min

Secondary outcomes

A. The need for additional uterotonic,
B. The incidence of adverse effects and complications,
C. The need for blood transfusion,
D. NICU admission

Statistical Analysis: Statistical analysis of the data was performed using SPSS version 20.0 (IBM, Armonk, NY, USA). Student ***t test*** was used to compare inter group measurements if normally distributed otherwise Mann and Whittney test was used . For categorical variables and proportions ***Chi square test*** was used. $p<0.05$ was considered statistically significant.

Results

The present study was conducted on 200 patients undergoing either elective or emergency cesarean section at Department of Obstetrics and Gynecology, Panna Dhai Mahila Chikitsalaya attached to RNT Medical College, Udaipur. The study and control groups were comparable with respect to baseline variables like demographic data, pre-gestational variables, and pregnancy variables(Table 1).The interval between drug administration and cord clamping was 6.33±3.65 minutes in the study group and 5.85±4.15 minutes in control group (P=0.12).

The outcome variables are presented in Table 2,3. The mean intra-operative blood loss was significantly lower in the study group than in the control group (429±234 mL versus 620±375 mL; P=0.001). The mean postpartum blood loss was also lower in the study group than in the control group (185±95 mL versus 324±167 mL; P=0.001), as was the difference between the preoperative and postoperative hematocrit values (4.6±2.5 versus 8.2±3.8; P=0.02).

By contrast, the percentage of cases requiring additional oxytocics was significantly higher in the control group than in the study group (18% versus 7%; P=0.001).Transient postpartum fever (temperature ≤38 °C) developed during the first 24 hours after delivery in 11 women (5.5%) from the study group and 13 women (6.5%) from the control group (P=0.20).With regard to neonatal outcome, the mean Apgar score at 1 and5 minutes was 7.8±1.8 and 9.2±0.6 in the study

group and 8.1±1.6 and 9.0±0.8 in control group (Table 2). These values were not significantly different between the 2 groups. In all, 6 neonates(3.0%) from the study group and 9 (4.5%) from the control group were admitted to the neonatal intensive care unit (NICU). The main reason for admittance to the NICU was transient tachypnea of the newborn (TTN): the incidence was 3.0% in study group and 4.0% in control group (data not shown). One neonate from the control group spent 1 week in the NICU owing to congenital pneumonia.

Table 1: Baseline charactreristics

Variable	Study group (n=100)	Control group (n=100)	p value
Age, y	25.58 ±4.09	25.48± 4.17	0.864
Gravida	1.83± 1.06	1.91± 0.91	0.56
No of prev CD	27 ±1.5	27± 1.18	0.60
Time until delivery	6.68 ±1.32	6.1± 1.21	0.14
Preoperative Hb	10.95± 0.60	10.87± 1.26	0.56
Pregnancy duration	37.44± 1.21	37.14± 1.17	0.073
Birth weight	2.82± 0.48	2.73± 0.48	0.19

Table 2 :Study Outcomes: Primary

Primary outcome	Study group (n=100)	Control group (n=100)	P value
Intraoperative blood loss	450 ± 252 ml	635 ± 360 ml	0.03
Postoperative blood loss	174 ± 78ml	310 ± 152 ml	0.001
APGAR at 1 min	7.4 ± 1.4	7.9 ± 1.4	0.28
APGAR at 5 min	9.0 ± 0.7	8.8 ± 0.6	0.24

Table 3: Secondary Outcomes

Variable	Study group (n=100)	Control group (n=100)	P value
Additional uterotonic	3 (3%)	9 (9%)	0.01
Shivering	7(7%)	1(1%)	0.02
Pyrexia	2 (2%)	3 (3%)	0.20
Vomiting	2 (2%)	4 (4%)	0.30
NICU admission	2 (2%)	3 (3%)	0.24
BT	0	1 (1%)	0.23

Discussion

The present randomized controlled trial conducted at tertiary care center of Rajasthan showed results in favour of early (preoperative) rectal administration of 600ug misoprostol for reduction of blood loss related to cesarean section. When blood loss was classified into four categories according to amount (200-400 ml, 401-600ml, 601-800 ml and 801-1000 ml), significantly more patients in the study group were in the 200-400 ml category as compared with patients in control group (58% vs 26%). None of the patient in study group belonged to blood loss category 801-1000ml, whereas, in control group 44% patients belonged to 801-1000 ml blood loss category, which is significantly different.Elsedeek et al report similar observations in a study where authors investigated the value of preoperative administration of rectal misoprostol at cesarean delivery. They observed decreased intraoperative and postpartum blood loss, resulting in lesser drop in hemoglobin in the misoprostol group compared with the placebo group. However, the main disadvantage of the study was the use of only towel weighing to estimate blood loss.Our study also found that the percentage of cases requiring additional uterotonics was significantly higher in control group than in misoprostol group. The similar observations are reported by recent studies.[8,4,15]The baseline characteristics, primary and secondary outcomes in our study are comparable to previous studies by Mervat S-E-A Elsedeek and Chaudhari P et al as shown in Table 4

Table 4: Comparison with other studies

Outcomes	Mervat S-E-A Elsedeek trial	Chaudhari P et al	Present study
Time taken from insertion to cord clamping	6.33 min	104.62 sec	6.68
Intraoperative blood loss	429 ml	502 ml	450 ml
Postoperative blood loss	185 ml	74 ml	185 ml
APGAR at 1 min	7.8	-	7.6
APGAR at 5 min	9.2	-	8.7
Shivering	-	9	7

Conclusion

- Preoperative treatment with rectal administration of 600-microgram misoprostol significantly reduces blood loss related to cesarean delivery.
- However, occurrence of transient side effect such as shivering was noted more frequently with the use of misoprostol.
- There were no significant differences on the effect on neonatal outcome.

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