COMPARATIVE STUDY OF RECTALLY ADMINISTERED MISOPROSTOL AFTER SPINAL ANAESTHESIA VERSUS ROUTINE INTRAMUSCULAR OXYTOCIN FOR REDUCING BLOOD LOSS IN CAESAREAN SECTION

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ABSTRACT

BACKGROUND

Postpartum haemorrhage is a major cause of mortality and morbidity in pregnant women in developing countries. Caesarean section is associated with increased blood loss. Misoprostol is used as potent uterotonic agent that has been thoroughly studied in the prevention and treatment of PPH after vaginal delivery. However, role of preoperative rectal misoprostol in caesarean section for reducing blood loss is not studied much, hence this study was undertaken.

MATERIALS AND METHODS

This randomised controlled trial was performed between Jan 2017 - July 2017 on 200 high-risk pregnant women coming to labour room of Department of Obstetrics and Gynaecology, Karnataka Institute of Medical Sciences, Hubli, divided into two groups. The Group A (n= 100) received 400 µg of misoprostol. The Group B (n= 100) received 10U IM oxytocin after delivery as per hospital protocol. The primary outcome measures were amount of blood loss and change in haemoglobin level 24 hrs. after surgery.

RESULTS

The mean intraoperative blood loss was significantly lower in Group A (389 ± 172.56 mL) than Group B (445 ± 180.42 mL). The difference between the preoperative and postoperative haemoglobin value was also significantly lower in the misoprostol group (0.84) than the oxytocin group (1.10) with (p= 0.0300). Admissions to the neonatal intensive care unit were comparable between the two groups.

CONCLUSION

Preoperative administration of 400 µg rectal misoprostol significantly reduced blood loss compared to oxytocin in caesarean section without significant side effects and it can be used as an alternative to oxytocin.

KEYWORDS

Misoprostol, Oxytocin, Caesarean Section, Postpartum Haemorrhage (PPH).

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BACKGROUND

Worldwide, Caesarean delivery is the most frequently performed major surgical procedure.⁽¹⁾ Bleeding is still the major cause of mortality and morbidity in postpartum period. World Health Organisation (WHO) has reported 585,000 maternal deaths each year. 25% of cases die from postpartum bleeding. Mean amount of blood lost is 500 mL during normal vaginal delivery, 1000 mL in caesarean section and 3500 mL during caesarean hysterectomy.⁽²⁾ Caesarean delivery is associated with an increased risk of blood loss and need for blood transfusion. Major risk factors for PPH are obstructed labour, anaemia, hypertensive disorder of pregnancy, multiple pregnancy, polyhydramnios, grand multiparity, antepartum haemorrhage, prolonged and augmented labour.⁽³⁾

Misoprostol is a synthetic PGE-1 analogue with strong uterotonic properties and it is one of the most useful drugs in obstetrics.⁽⁴⁾ Ease of its administration through various routes, good safety profile, low cost and stable at room temperature make it a good option in resource-poor settings,⁽⁵⁾ and in patients under anaesthesia who are vomiting, unable to take medications. Rectal misoprostol is associated with slower absorption, longer duration of action and minimal side effects, hence considered as best route for patient undergoing caesarean delivery. Rectal misoprostol administration has mean T-max of 40 - 65 minutes^(6,7) and recent study showed T-max of 20 minutes which is much shorter.⁽⁸⁾ If rectal misoprostol administered before caesarean section, the maximum effect was obtained by the end of surgery, as there is slower rate of absorption which is useful.^(7,9) As there is wide gap of controversy in the results of many studies about the use of misoprostol for prevention of postpartum haemorrhage with caesarean section and also route of misoprostol administration was not fully studied; Hence this study was conducted to compare the effects of preoperative administration of rectal misoprostol with IM oxytocin on reducing blood loss in caesarean section and to study side effects.

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Objective

To compare the effects of preoperative administration of rectal misoprostol with IM oxytocin on reducing blood loss in caesarean section and to study side effects.

MATERIALS AND METHODS

This randomised controlled trial was performed between January 2017 - July 2017 on high-risk pregnant women coming to labour room of Department of Obstetrics and Gynaecology, Karnataka Institute of Medical Sciences, Hubli.

Total of 200 women of high risk pregnancy undergoing caesarean section in whom postpartum haemorrhage (PPH) anticipated were included in study, and patients were randomized in two groups, 100 in misoprostol Group and 100 in oxytocin Group using random number table generated online

(<http://www.graphpad.com/quickcalcs/randomize1/>).

Women were eligible for inclusion if they were undergoing emergency caesarean section under spinal anaesthesia and had at least one risk factor for PPH (Multiple pregnancy, polyhydramnios, prolonged labour, augmented labour, obesity, grand multiparity, severe preeclampsia/eclampsia, anaemia, previous caesarean section).

Women with any contraindication for the use of misoprostol (e.g. known hypersensitivity) and those with cardiovascular, hepatic or haematologic disorders were excluded. Conversion to general anaesthesia also made women ineligible. The protocol was approved by the Institutional Ethical Committee of Karnataka Institute of Medical Sciences, Hubli.

Eligibility was assessed by interview, clinical examination and review of recent investigations among women scheduled for emergency caesarean. Patients who fulfilled the selection criteria were approached for participation and written informed consent was obtained from willing participants.

Women taken up for caesarean section were given preoperatively tablet misoprostol 400 micrograms per rectum after spinal anaesthesia before painting and draping was done in Group A and in Group B IM Inj. oxytocin 10 units given after delivery of baby as per hospital protocol.

Haemoglobin level was measured before and 24 hours after the operation. Shivering, number of nausea and vomiting along the operation and up to 2 hours after it was recorded. Temperature was monitored routinely and noted in the data sheet when greater than 37.5°C. When surgeon requested additional uterotonic agents on the basis of clinical findings during surgery, it was noted. Addition of oxytocin was considered as additional uterotonic intervention for the purpose of data analysis in misoprostol group. Inj. carboprost 250 ug IM and Inj. Methylergometrine 0.2 mg IM were used as secondary uterotonic agents when required. Estimation of blood loss during caesarean section was determined by measuring the amount of blood collected in suction bottles after delivery of placenta plus weight of soaked towels and postpartum blood loss during the first 24 hours after surgery was assessed by weighing pads and clots. Preoperative and postoperative haemoglobin were estimated 1 hour before surgery, 24 hours after surgery respectively. The neonatal outcome including: APGAR score, the need for Neonatal Intensive Care Unit (NICU) admission and neonatal death

were assessed. The side effects of postoperative fever, vomiting and shivering were recorded. After Data collection, data entry was done in Excel sheet, statistically analysed by SPSS 15 Software version. Quantitative data were shown as a mean and standard deviation and qualitative data as frequency. Independent t-test, chi-square test and Fisher's exact test were used for data analysis. $P \leq 0.05$ was considered statistically significant.

RESULTS

200 women meeting inclusion criteria were enrolled in the study. The baseline demographic and obstetric characteristics were similar in the two groups (Table 1).

Demographics	Misoprostol Group N=100	Oxytocin Group N=100	Total
Maternal Age [21-32] in Years	24.63±4.05	24.75±4.06	p=0.8344
Gravida [1-3]	1.83±0.67	1.70±0.67	p=0.1721
Gestational Age in Weeks [37-42]	38.98±1.26	39.09±1.23	p=0.5323

Table 1. Demographic and Obstetrics Characteristics of Participants

Risk factors for PPH were also found to affect similar proportions of participants in both groups (Table 2).

Risk Factors	Misoprostol Group	Oxytocin Group	Total	P-value
Abruption	5	5	10	1.0000
Anaemia	27	25	52	0.7150
Gestational Hypertension	3	12	15	0.0170*
Severe Preeclampsia	13	15	28	0.7050
Antepartum Eclampsia	5	2	7	0.2480
Polyhydramnios	4	0	4	0.0420*
Previous Caesarean Delivery	40	37	75	0.6220
Obstructed Labour	2	4	6	0.4140
Total	100	100	200	

Table 2. Risk Factors for PPH

*p < 0.05

The estimated blood loss (M ± SD) during caesarean section in misoprostol group was 389.00 ± 172.56 mL, in oxytocin group was 445.00 ± 180.42 mL (p= 0.001). There was statistically significant decrease in the estimated blood loss with the misoprostol group over oxytocin group (p= 0.0260) (Table 3).

Variables	Misoprostol Group		Oxytocin Group		T-value	P-value
	Mean	SD	Mean	SD		
Blood loss in mL	389.00	172.56	445.00	180.42	-2.2431	0.0260*

Table 3. Mean Blood Loss

*p < 0.05

The mean difference in preoperative and postoperative haemoglobin after 24 hours was significantly less among women who received misoprostol (0.84 gm) than among those who received oxytocin (1.10) ($p = 0.001$) (Table 4).

Variables	Misoprostol Group		Oxytocin Group		T-value	P-value
	Mean	SD	Mean	SD		
Preoperative Hb	10.56	1.44	10.26	0.81	1.8140	0.0712
Postoperative Hb	9.72	1.31	9.16	0.83	3.5684	0.0005*
Changes in Hb	0.84	0.70	1.10	0.94	-2.1861	0.0300*

Table 4. Comparison of Change in Haemoglobin (gm/dL) in Two Groups

* $p < 0.05$

Additional uterotonic drugs were given to fewer women in the misoprostol group (12) than in the oxytocin group (17) ($p = 0.004$) and need for blood transfusion was less in the misoprostol group (18) compared to oxytocin group (22) (Table 5).

Outcome Measures	Misoprostol Group	Oxytocin Group	Total	P-value
No. of patients requiring blood transfusion	18	22	40	0.4795
Additional uterotonic agent	12	17	29	0.3153
NICU admissions	7	7	14	1.0000

Table 5. Comparison of Outcome Measures

Shivering (11), vomiting (5) and pyrexia (3) were the most frequent adverse effects noted more frequently among women receiving misoprostol. No maternal death was recorded in either group (Table 6).

Side Effects	Misoprostol Group N=20	Oxytocin Group N=8	Total N=28
Hypertension	1	0	1
Shivering	11	5	16
Pyrexia	3	1	4
Vomiting	5	2	7

Table 6. Side Effects

In one case of misoprostol group, hypertension was noted. Overall, the incidence of adverse effects was higher among women who received misoprostol. However, most adverse effects were self-limiting and subsided with simple measures such as covering women with blankets for shivering and cold sponging for pyrexia. Pharmacological agents were not required for any of these conditions.

DISCUSSION

In this study, we compared rectal misoprostol with an intramuscular injection of oxytocin administration in assessing blood loss in caesarean section. We found there is significant difference ($p < 0.05$) of intraoperative blood loss and change in post-operative haemoglobin level in misoprostol group compared to oxytocin group. Our study was similar to study done by Alwani M et al from India, Fazel MR et al from Iran. Fazel et al 2 compared rectal misoprostol with IV oxytocin usage in caesarean section, blood loss was 578 ± 185 mL and 630 ± 213 mL respectively. Change in haemoglobin level in two groups was not statistically significant. Alwani M et al⁽¹⁰⁾ compared rectally administered 600 ug misoprostol after spinal anaesthesia with intramuscular oxytocin during caesarean section, found no significant difference in two groups regarding change in postpartum haemoglobin, need for blood transfusion and incidence of PPH, no significant difference in any side effects. K Aruna Kumari et al assessed the impact of pre-operative 200 µg per rectal misoprostol on blood loss during and after caesarean delivery found mean intraoperative and postpartum blood loss was lower in the study group than the control group: 374 ± 69.9 mL and 131 ± 31.8 mL versus 401 ± 79.9 and 145 ± 35.6 mL respectively and concluded that preoperative administration of 200 µg rectal misoprostol significantly reduced blood loss related to elective caesarean delivery. Hesham M Borg et al⁽¹¹⁾ compared the effectiveness of the rectally administered misoprostol pre-operative with post-operative period in minimising intraoperative blood loss and prevention of postpartum haemorrhage in caesarean delivery found estimated blood loss (M $\pm$ SD) in preoperative group was 372.33 ± 25.997 mL, in postoperative group was 722 ± 34.089 mL ($p = 0.001$) and haematocrit value after caesarean section was also significantly lower in postoperative group than in preoperative group I ($p < 0.001$) and both groups were not different in terms of side-effects. Vimala et al⁽¹²⁾ compared sublingual misoprostol 400 µg with oxytocin found that oxytocin group has significantly more intraoperative bleeding and there was no significant differences in post-

operative haemoglobin level. In our study, shivering was observed in 11% of cases in misoprostol group and 5% in oxytocin group. Alwani M et al showed shivering in 7% of patients in misoprostol and 1% in oxytocin group. Fazel et al reported shivering was significantly more common in misoprostol group. Vimala et al reported shivering in 26% and 4% in patients with 400 µg of sublingual misoprostol group and oxytocin group respectively. Chaudhuri et al reported 8.3% and 1.1% in the misoprostol and oxytocin groups respectively. Shivering is of different rate due to use of different routes of administration of drugs, operation room temperature and fluids used during the procedure. In our study vomiting was seen in 5% of patients who received misoprostol and 2% with oxytocin, pyrexia was seen in 3% in misoprostol group and 1% with oxytocin group. The differences were statistically not significant. Previous studies have reported similar findings.

CONCLUSION

Rectal misoprostol is a good alternative uterotonic for patients undergoing caesarean section for prevention of PPH with minimal side effects and longer duration of action, especially in resource poor countries with high maternal mortality and morbidity.

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