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Impact of Preoperative Rectal Versus Intraoperative Sublingual Misoprostol on Blood Loss during Cesarean Section: A randomized clinical trial

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ABSTRACT

Objectives: To compare blood loss between immediate preoperative rectal administration of misoprostol with intraoperative sublingual administration during elective cesarean section (CS).

Materials and Methods: The patients were randomized either to receive rectal misoprostol 400 mg preoperative just after induction of anaesthesia or the same dose intraoperative sublingual. The primary outcome was estimated blood loss measurement. Secondary outcomes were change in hemoglobin concentration, need of excess oxytocin, maternal adverse effects, APGAR scores and need of admission to neonatal intensive care unit (NICU).

Results: A total of 460 cases were included (230 in each group). The estimated blood loss was lower in preoperative group in comparison with intraoperative group (545 ± 232 ml versus 753 ± 256 ml). There were less reduction in hemoglobin and haematocrit value in preoperative group (0.71 ± 0.6 g/dl, 1.4 ±1.2%) when compared with intraoperative group (1.02 ± 0.8 g/dl, 1.7 ±1.3%). Also the need for oxytocin was observed in only 22.2% in preoperative group compared to 36.1% in intraoperative group. There were no differences in APGAR scores and rate of admission to NICU in both groups.

Conclusion: Preoperative rectal administration of misoprostol after induction of anesthesia during elective CS was effective in decreasing blood loss with no obvious neonatal complication.

Keywords: misoprostol, cesarean section, blood loss.

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Introduction

Postpartum hemorrhage is a major preventable cause of maternal morbidity and mortality in developing countries[1]. 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[2].

Misoprostol, a prostaglandin E1 analogue with strong uterotonic properties, has been suggested as an alternative or in addition to injectable uterotonic agents for preventing postpartum hemorrhage following vaginal or cesarean deliveries[3-5].

Rectal and vaginal administration of misoprostol have slower onset of action and delayed peak effect when compared to sublingual route[6]. However, the rates of shivering and fever have been shown to be higher following oral and sublingual routes of administration compared with rectal and vaginal routes[7]. Early rectal administration (after induction of anesthesia and before skin incision) may overcome the problem of delayed onset of action.

The study aimed to compare blood loss between immediate preoperative rectal administration of misoprostol with intraoperative sublingual administration during elective cesarean section (CS).

Patients and Methods

This was randomized controlled study that was done at Department of Obstetrics and Gynecology of Sohag university hospital from March 2017 to February 2019. During study periods, all women who delivered by elective CS were candidates to participate in the study. Patients with fetal distress, patients in active phase of labour, multiple pregnancies, placenta previa, coagulation defect, previous two or more CS and patients refusal to participate were excluded. Local ethical committee approved the study and the written informed consent was taken.

The patients were randomized using a computer generated random numerical table to prepare sealed opaque envelopes containing a group assignment. Two groups of envelopes were given to a third party (a nurse), who was unaware of the contents into two groups. The 1st group received 2 tablets of misoprostol 200 mg (Misotac 200 mg, Sigma pharmaceutical Co.) rectally immediately after induction of anesthesia and insertion of urinary catheter and before skin incision. The second group received the same dose of sublingual misoprostol intraoperative just after delivery of the fetus. The application of misoprostol carried by assistant (rectal) or by anesthetist (sublingual). The two groups received 10 units of oxytocin after delivery of fetus. Any additional oxytocin was given if needed according to surgeon request and was recorded.

All patients were subjected to full history taking and detailed clinical and ultrasonographic examination to detect any exclusion criteria or presence of active labour pain. Cesarean deliveries were performed under spinal anesthesia through pfannenstiel incision by senior obstetricians. The uterus was closed in two layers using delayed absorbable sutures.

Maternal hemoglobin and hematocrit values were measured before CS and at 24 hours postpartum. Also amount of intraoperative blood loss was estimated by weighing the towels before and after CS taking in consideration that those towels were introduced after delivery of the fetus and drainage of amniotic fluids. Postoperative 24 hours external blood loss was estimated by weighing the soaked towels placed in the vulvar area. The postoperative blood loss was calculated (weight difference of towels placed in the vulvar area). The overall blood loss was calculated.

The primary outcome was intrapartum and postpartum blood loss. Secondary outcomes were change in hemoglobin concentration and hematocrit value 24 hours postpartum, need of excess oxytocin (more than 10 units of oxytocin), maternal adverse effects (fever more than 38°C, shivering, etc), APGAR scores of neonates and need of admission to neonatal intensive care unit (NICU).

The sample size was determined by using G* power version.1.9.2 for windows for power analysis. We estimated 230 patients in each group, would be needed to show a 5% difference in estimated blood loss between the two groups with statistical power

95% and 0.05% as an alpha error.

SPSS 10.0 for Windows (Statistical Package for the Social Sciences; SPSS Inc., Chicago, IL, USA) was used for all statistical analysis. The chi square test was used to compare the association between categorical variables in both groups and the Fisher exact test was used when necessary. The student t test was used to compare means of quantitative variables in parametric data.

Results

A total of 528 cases undergoing an elective CS were assessed for eligibility to participate; 68 of them were excluded (Fig 1). 460 cases were included into 2 equal groups. Patients' characteristics in both groups are shown in Table1.

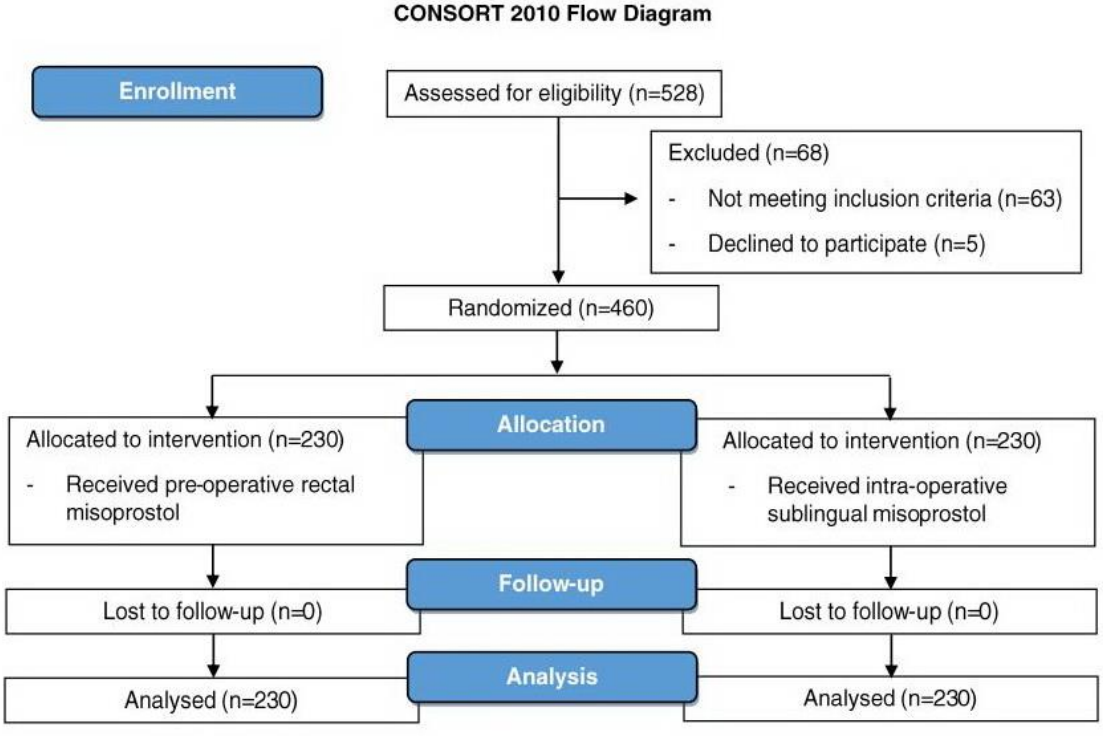

Fig 1. Patients flow chart.

Table 1. Patients' characteristics in both groups.

	Preoperative rectal group	Intraoperative sublingual group	p value
Age (years)	27.8 ± 8.9	28.6 ± 8.3	0.37
Parity	2.7 ± 1.4	2.4 ± 1.6	0.19
Preoperative hemoclobin (g/dl)	10.9 ± 1.2	10.7 ± 1.5	0.26
Preoperative hematocrit (%)	32.3 ± 3.2	31.7 ± 2.9	0.33

The estimated blood loss was significantly lower in the preoperatively rectally administered misoprostol group (545 ± 232 ml) when compared to the intraoperative sublingual group (753 ± 256 ml) with p value 0.014 (Table 2). Similarly, more patients in group 2 than in group 1 needed additional

oxytocin, p value 0.001. There was a significant decrease in hemoglobin and hematocrit values in intraoperative sublingual group (1.02 ± 0.8 g/dl and 1.7 ± 1.3%) when compared to preoperative rectal group (0.71 ± 0.6 g/dl and 1.4 ± 1.2%) as shown in (Table 2).

The neonatal outcomes and drug side effects were nearly comparable in both groups apart from shivering which was more frequent in an intraoperative sublingual group, p value 0.004 (Table 3).

Table 2. Primary and secondary outcomes in both group.

	Preoperative rectal group	Intraoperative sublingual group	p value
Estimated blood loss (ml)	545 ± 232	753 ± 256	0.014
Need of excess oxytocin	51 (22.2%)	83 (36.1%)	0.001
Decrease in hemoglobin (g/dl)	0.71 ± 0.6	1.02 ± 0.8	0,023
Decrease in hematocrit (%)	1.4 ± 1.2	1.7 ± 1.3	0.037

Table 3. Maternal adverse effects of misoprostol and neonatal outcome.

	Preoperative rectal group	Intraoperative sublingual group	p value
Fever	545 ± 232	753 ± 256	0.014
Shivering	51 (22.2%)	83 (36.1%)	0.001
APGAR scores at 5 minutes	0.71 ± 0.6	1.02 ± 0.8	0,023
Admission to NICU	1.4 ± 1.2	1.7 ± 1.3	0.037

NICU: neonatal intensive care unit.

Discussion

There was less estimated blood loss and lower need of excess oxytocin in women who received preoperative rectal misoprostol when compared with those received intraoperative sublingual misoprostol.

Preoperative rectal administration succeeded to achieve best results owing to the rectal and vaginal routes have slower absorption rates and a lower peak concentration after 60 minutes[8], leading to a sustained effect. The highest bioavailability and concentration of the drug occurred at the end of the surgical procedure, thus inducing strong uterine contractions and reduced blood loss.

The above results agreed with Elsedeek, 2012[9], Abd-Ellah et al, 2014[10] and Ragab et al, 2016[11]. However, in all these studies they compared between preoperative and postoperative rectal administration in which actually the 2nd group deprived from ecbolic effect of misoprostol intraoperative so it was expected that estimated intraoperative blood loss and need of excess oxytocin would be higher in postoperative group.

The drop of hemoglobin level was significantly lower with preoperative administration of misoprostol in comparison with postoperative administration (0.71 ± 0.6 g/dl versus 1.02 ± 0.8 g/dl). Also the reduction in hematocrit value was significantly lower with preoperative rectal misoprostol as compared with intraoperative sublingual misoprostol (1.4 ± 1.2% versus 1.7 ± 1.3%). These results agreed with Elsedeek, 2012[9] who found that preoperative administration associated with less reduction oh hemoglobin level and hematocrit value.

However, our results disagreed with Sweed et al, 2018[12] who reported that sublingual misoprostol was associated with less blood loss in comparison with the same dose of rectal misoprostol. This could be

explained by timing of administration as they used sublingual misoprostol preoperative but we used sublingual misoprostol after delivery of fetus and we delayed its use to avoid the problems of its rapid absorption and rapid onset of action[6].

In the current study, the incidence of side effects of the preoperative rectal misoprostol were comparable to intraoperative sublingual misoprostol apart of shivering which occur more frequently in an intraoperative sublingual group (22.6% versus 12.6%, p value 0.004). This agreed with Sweed et al, 2018[12] and partially agree with Mansouri and Alsahly, 2011[13], they reported more frequent shivering (52%) with sublingual route. The high percentage in their results may be attributed to high dose 600 mg compared to 400 mg in our study. The two groups were comparable as regard APGAR scores at 5 minutes and admission to NICU.

The limitation of the current study represented by absence of a double-blind technique, also exclusion of patients actively in labour and multiple pregnancies who more liable to uterine atony and blood loss during caesarean delivery but we preferred to exclude these cases to avoid their effect upon our results.

Conclusion

In conclusion, preoperative rectal administration of misoprostol after induction of anesthesia during elective CS was effective in decreasing blood loss with no obvious neonatal complication. Further studies are needed to investigate the possibility of preoperative administration during CS for women in labor and women with multiple pregnancies.

Potential conflicts of interest

The authors declare no conflict of interest.

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