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A Study to Assess the Safety and Efficacy of Preoperative vs Postoperative Per Rectal Misoprostol in Lower Segment Cesarean Section to Prevent Postpartum Hemorrhage

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Abstract: ***Background**: Many global gains in reducing maternal mortality can be attributed to the developments in preventing and treating postpartum hemorrhage (PPH). Misoprostol, a synthetic PGE1 analog has been extensively studied in the prevention and treatment of PPH after vaginal delivery, however, its use in conjunction with cesarean delivery has not been investigated as much. The study aimed to assess the effect of rectally administered misoprostol on blood loss before and after cesarean delivery. **Material and Methods**: This was a prospective comparative study done in our obstetrics and gynecology department at Sarojini Naidu Medical College, Agra. It involved a total of 150 women who were found to be eligible for the study after meeting the inclusion criteria. Its objective was to compare the effectiveness of the rectally administered 600µg misoprostol pre - operatively versus post - operatively in minimizing intraoperative blood loss and prevention of PPH in cesarean delivery. The outcomes studied were intraoperative and postoperative blood loss, changes in hemoglobin concentration, and hematocrit, maternal adverse effects, need for additional uterotonics and surgical interventions. The level of significance was set at <0.05. **Results**: The mean blood loss in the preoperative misoprostol group was 404.25ml whereas, in the postoperative misoprostol group, there was 441.25 ml of blood loss. The difference between the total blood loss in the two groups was found to be statistically significant. (p<0.05) Only 2 patients in group A had PPH whereas 4 patients suffered from PPH in group B. **Conclusion**: In our study, we witnessed a marked reduction in intraoperative and postoperative blood loss with a decreased fall in the hematocrit indices in the subjects that received preoperative misoprostol. Preoperative rectally administered misoprostol proved to be of greater efficacy than postoperative rectally administered misoprostol in reducing blood loss due to postpartum hemorrhage in cesarean section.*

Keywords: postpartum hemorrhage, misoprostol, preoperative misoprostol, postoperative misoprostol

1. Introduction

Postpartum hemorrhage has been a major cause of maternal death and morbidity for as long as physicians have studied and written about childbirth. Despite considerable advances in medical care in the last centuries, postpartum hemorrhage is still a frequent cause of death in many parts of the world and continues to plague obstetricians even in developed countries. Nowadays, the incidence is 4 - 8% in the developed world while it runs up to 19% in developing countries. According to the World Health Organization (WHO) estimates, more than 585, 000 women die every year from the pregnancy - related cause, of which 25% were due to PPH. [1] Hence, more than ever, research in the prevention and treatment of postpartum hemorrhage, including recovery measures for women developing life - threatening hemorrhage.

The definition of PPH has been recently revised by ACOG to be the cumulative blood loss greater than or equal to 1000ml or blood loss accompanied by signs and symptoms of hypovolemia within 24 hours after the birth process regardless of route of delivery. [2]

The etiologies of PPH are classically divided into four different categories, known as the four T's – Tone, Trauma, Tissue, and Thrombin. The majority of cases are traditionally attributed to atony. Uterine atony remains the most common cause of PPH representing about 80% of all causes of postpartum hemorrhage. [3, 4]

Cesarean delivery is the most common major surgical procedure performed on women worldwide and its rate continues to rise steadily in both developed and developing countries. Intrapartum and early postpartum blood loss are also increased in conjunction with cesarean delivery.

Active management of the third stage of labor by administration of uterotonic drugs reduces the risk of postpartum hemorrhage, and postpartum anemia as well as the need for blood transfusion. The most commonly used uterotonic drugs include oxytocin, methylergometrine, carbetocin, and prostaglandins.

Misoprostol is a synthetic prostaglandin E1 analog; widely used for the management of the third stage of labor and intractable postpartum hemorrhage. It has a potent uterotonic effect, low cost, stable at room temperature, easily administered, and has few adverse effects. It is well absorbed when administered by oral, vaginal, rectal, and sublingual routes. [5, 6, 7] The role of misoprostol, a prostaglandin E1 analog, in the prevention and treatment of PPH has evolved over to its long shelf life and multiple routes of administration, which make it more suitable for low - resource settings with limited skilled providers.

Notwithstanding the large number of studies conducted on doses and infusion rates of oxytocin, and doses and routes of misoprostol, the ideal practice remains controversial. The study aimed to assess the effect of rectally administered misoprostol on blood loss during and after cesarean delivery.

2. Material and Methods

This study was a prospective comparative study conducted in the department of obstetrics and gynecology at Sarojini Naidu Medical College, Agra. A total of 150 women were included in the study, who met the inclusion criteria after taking informed consent. Ethical clearance was taken from the institutional ethical committee of the college.

All patients were randomly allotted into two groups. The study group (group A) received misoprostol 600µg rectally after regional anesthesia and shortly before the skin incision. (n=76) whereas the control group (group B) received misoprostol 600µg rectally at the end of the cesarean section. (n=74)

Inclusion criteria
All uncomplicated singleton pregnancies of gestational age more than 34 weeks were included in the study.

Exclusion criteria
Multiple pregnancies, maternal hypertension**,** maternal anemia (severe and moderate anemia) coagulation disorders, scarred uterus.

Caesarean section was performed under spinal anaesthesia. The abdominal skin incision was given. the rectus fascia was opened and the rectus muscles were separated and dissected off the peritoneum which was picked up between two tissue forceps and opened longitudinally. The uterus was opened through a transverse lower segment incision. Both groups received 10 IU oxytocin intramuscularly after delivery of the foetus.

All the towels were weighed before and after CS, and the weight difference was calculated, the amount of intraoperative blood loss was estimated in the suction apparatus in ml and every 1 gm increase in the weight of towels was equated with 1 mL blood loss. The total amount of intraoperative blood loss was calculated (blood loss in suction apparatus plus weight difference of used towels).

A trained nurse was responsible for postoperative external blood loss measurement during the first 24 hours after surgery 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. Another blood picture was obtained 24 hours postoperatively to detect changes in Hb level.

3. Results

76 patients in the study group and 74 patients in the control group were included in this study.

Maximum patients in both groups belonged to the age group of 23 - 27 years (45% of the patients in the study group and 47% in the control group).

About 75% of the patients in both groups belong to rural areas.

Maximum number of patients in our study in both groups were primigravida followed by second gravidas. Maximum parity observed was 3 in Group A and 4 in Group B in our study.

Maximum number of patients were 37 - 39 weeks of gestation at the time of presentation. Maximum gestational age was 41 weeks in group A and 42 weeks in group B. The mean gestational age was 37.68±1.4weeks in the preoperative misoprostol group and 37.54±1.6weeks in the postoperative misoprostol group. There was no difference found statistically between the two groups. The sociodemographic characteristics of the patients has been discussed in table 1. No significant difference was found between these factors.

Table 1: Distribution based on socio - demographic characteristics

Socio - demographic factor	Variables	Preoperative Misoprostol (Group A)	Postoperative Misoprostol (Group B)	P - value
Age	18 - 22	21	19	0.4
	23 - 27	34	35	
	28 - 32	17	17	
	33 - 35	4	3	
Domicile	Rural	57	56	0.4
	Urban	19	18	
Parity	0	56	52	0.2
	1	15	14	
	2	3	4	
	>2	2	4	
Gestational Age	Mean ± SD	37.68±0.52	37.54±0.47	0.08
BMI	Mean ± SD	26.97±0.82	26.82±0.8	0.1

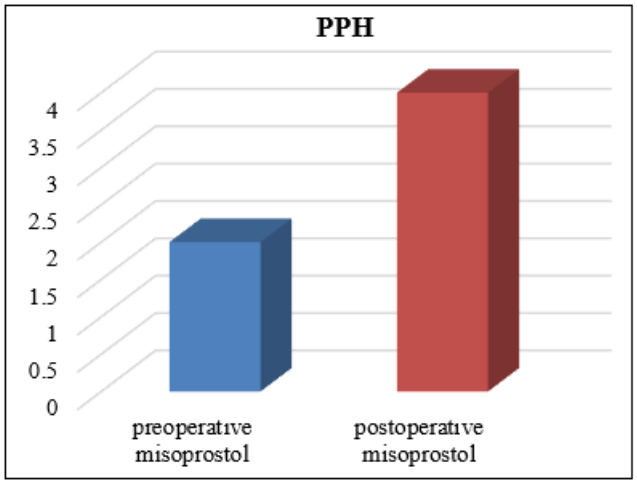
The hematocrit variables have been discussed in table 2. In our study mean haemoglobin at the time of admission was 9.921±1.18 g/dl in the preoperative misoprostol group and 9.939±1.17 g/dl in the postoperative misoprostol. Mean PCV in preoperative misoprostol group was 30.5% whereas in postoperative misoprostol group mean PCV at the time of admission was found to be 30.7%.

The mean blood loss in preoperative misoprostol group A was 404.25ml whereas in postoperative misoprostol group there was 441.25 ml of blood loss. The mean blood was significantly lower in the preoperative misoprostol group.

Table 2: Distribution of the basis of haematocrit variables

Variables (Mean ± SD)	Preoperative Misoprostol (Group A)	Postoperative misoprostol (Group B)	P - value
Preoperative Haemoglobin (g/dl)	9.921±1.18	9.939±1.17	**0.4**
Preoperative PCV	30.5±2.44	30.7±2.24	**0.3**
Intraoperative blood loss (ml)	330.6±72.4	358.8±64.8	**0.01**
Postoperative blood loss (ml)	73.65±20.2	82.4±24.6	**0.01**
Total blood loss (ml)	404.25±97.75	441.20±125.6	**0.2**
Postoperative haemoglobin (g/dl)	9.7±0.92	8.4±0.94	**0.001**
Postoperative PCV	28.7±2.08	28.2±2.14	**0.07**
Mean fall in Haemoglobin (g/dl)	0.24±0.45	0.45±0.8	**0.02**
Mean fall in PCV	2.23±1.24	2.68±1.8	**0.03**
Duration of 3rd stage of labor (mins)	2.34±0.75	2.68±1.05	**0.01**

Table 3 shows the distribution of patients according to the outcomes studied. Postpartum haemorrhage occurred in 2 patients (2.6%) in the groups that received preoperative misoprostol that could be managed easily with medical management. PPH occurred in 4 patients (5.4%) in postoperative misoprostol group. Balloon tamponade was required to control bleeding in 1 patient.



In our study a total of 8 out of 76 patients i. e., 10.5% patients needed additional uterotonics in preoperative misoprostol group whereas in postoperative misoprostol group 14 out of 74 i. e., 18.9% patients required additional uterotonics. Similarly, requirement for blood transfusion was also found to be lower in the patients who received misoprostol preoperatively. Only 1 patient required blood transfusion postoperatively in the preoperative misoprostol group while in the postoperative misoprostol group 4 patients needed blood transfusion.

Table 3: Distribution on the basis of primary and secondary outcomes

Variables	Preoperative Misoprostol (Group A)	Postoperative Misoprostol (Group B)
PPH diagnosed	2 (2.63%)	4 (5.41%)
Need of additional oxytocin	3 (3.94%)	5 (6.75%)
Need of additional ergometrine	2 (2.63%)	3 (3.94%)
Need of carboprost	2 (2.63%)	4 (5.26%)
Need of additional misoprostol	1 (1.31%)	2 (2.63%)
Need for blood transfusion	1 (1.31%)	4 (5.4%)
Need of manual removal of placenta	2 (2.6%)	4 (5.4%)
Need for surgical intervention	0	1 (1.31%)
Mean birth weight (kg)	2.75±0.75	2.72±0.76
Duration of hospital stay (>5 days)	2 (2.6%)	6 (8.1%)

No significant difference was found in maternal and perinatal complications between the two groups. Shivering was seen as the commonest side effect in both groups.

There was no requirement for admission to the intensive care unit or maternal death.

4. Discussion

Postpartum haemorrhage is known to be the leading cause of maternal morbidity and mortality. World Health Organization statistics show that 40.1% of pregnant women worldwide are anaemic. The condition is prominent in Southeast Asian countries where about half of all global maternal deaths are due to anaemia and India contributes to about 80% of the maternal death due to anaemia in South Asia. The majority of these deaths are preventable. Prevention of PPH can be considered the key to reducing maternal mortality and morbidity.

Misoprostol a PGE1 analogue has been investigated for both prevention as well as management of postpartum haemorrhage as it causes uterine contractions. Misoprostol offers advantages like stability at room temperature (unlike oxytocin which requires refrigeration), better shelf life and can be safely used in cases like heart disease and preeclampsia. It is a well - tolerated drug with minimal self - limiting side effects. The drug's wide availability, low cost, ease of use makes it an ideal drug for use in such settings. We used 600 µg of misoprostol which was administered rectally in both groups after spinal anaesthesia before draping.

In our study, the mean blood loss in preoperative misoprostol group A was 404.25ml whereas in the postoperative misoprostol group there was 441.25 ml of blood loss. Hence, the patients that received preoperative misoprostol were associated with a lesser amount of blood loss. **Hesham M Borg et al** [8] documented total blood loss of 562.88 ± 56.447 ml in the preoperative misoprostol group whereas there was a total blood loss of 959.65±57.869 ml in the postoperative misoprostol group. **K. Aruna Kumari et al** [9] also showed that there was a significantly lower amount of blood loss in the patients who received misoprostol preoperatively. There was a total blood loss of 505±101.7 ml in the preoperative misoprostol group whereas 546.5±115.5 ml of blood loss occurred in the postoperative misoprostol group. Their result was found to be statistically significant with a p value of <0.003. **A. H. Abd - Ellah et al** [10] study also mentioned total blood loss of 620±291 ml in the preoperative misoprostol group and 898±321 ml of blood loss in the postoperative

misoprostol group. Most of the relevant studies support the view that misoprostol when administered preoperatively results in a much lesser amount of blood loss. This can be explained by the fact that, there was higher plasma concentration of misoprostol and thus higher bioavailability of misoprostol at the end of the cesarean section leading to effective uterine contractions and subsequent reduction in the blood loss.

Mean haemoglobin after caesarean in the preoperative misoprostol group in our study was found to be 9.7±0.92 g/dl and 8.4±0.94 g/dl in the postoperative misoprostol group. The difference between the mean haemoglobin after caesarean was found to be statistically significant. ($p<0.05$) Similar results were found by **A. H. Abd - ellah et al** [45] where the mean postoperative haemoglobin in the patients receiving misoprostol preoperatively was 10.5±0.67g/dl and 9.8±1.24 g/dl in the postoperative misoprostol group. The results were found to be significant in their study indicating decreased blood loss during and after caesarean section and reduced risk of postpartum haemorrhage in patients receiving preoperative misoprostol. This can be explained by the fact that high availability and higher concentration of misoprostol had occurred after the end of the surgical procedure, hence leading to strong uterine contraction and consequently resulted in the reduction of blood loss.

Misoprostol is generally a well - tolerated drug with minimal side effects. The most commonly reported adverse effects seen with misoprostol are generally mild and include shivering/chills, diarrhoea, abdominal pain, fever, nausea, vomiting, and headache.

In the present study, 21 patients in the preoperative misoprostol group and 31 patients in the postoperative misoprostol group suffered from different side effects. Other related studies also showed comparable side effects between the two groups.

All the side effects found in both the groups were statistically insignificant. ($p>0.05$)

The additional need for use of uterotonics and blood transfusion was also found to be significantly lower in the preoperative misoprostol group. Only 1 patient that received postoperative misoprostol required balloon tamponade as a surgical intervention to control postpartum haemorrhage. No patients in Group A required any surgical intervention to control PPH. In our study, no clinically significant difference was found in the neonatal outcomes.

5. Conclusion

Preoperative 600 µg per - rectal misoprostol is an effective and better option for reducing intraoperative and postoperative blood loss, thus preventing postpartum haemorrhage and reducing overall maternal mortality and morbidity. We witnessed a marked reduction in intraoperative and postoperative blood loss with a decreased fall in the haematocrit indices with the use of preoperative misoprostol. There was also a lesser requirement for additional uterotonics and surgical interventions in case of postpartum haemorrhage. There were fewer blood transfusions required. Notwithstanding the large number of studies conducted on the doses and routes of administration of misoprostol, ideal practice remains under evaluation. Larger studies are still needed to validate the efficacy of preoperative misoprostol and to find the optimal dose to prevent post - partum hemorrhage in caesarean delivery.

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