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Original Research Article

A COMPARATIVE STUDY OF INTRAOPERATIVE INTRAUTERINE MISOPROSTOL ADMINISTRATION AFTER DELIVERY OF PLACENTA WITH POSTOPERATIVE PER RECTAL MISOPROSTOL ADMINISTRATION FOR THE PREVENTION OF POSTPARTUM HAEMORRHAGE IN WOMEN UNDERGOING CESAREAN SECTION

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Abstract

Background: Postpartum hemorrhage (PPH) accounts for 25% of maternal deaths worldwide, making it the leading cause of maternal deaths

Objective: the objective of this study is to investigate the efficacy and safety of intrauterine misoprostol administration during cesarean section compared to postoperative per rectal administration for the prevention of PPH

Material and Methods: A randomized controlled trial was conducted on a cohort of pregnant women undergoing cesarean delivery. A comprehensive count of 200 pregnant women at full term (37-40 weeks of gestation), slated for either elective or emergency cesarean delivery, were included in the study all the 200 pregnant who have undergone elective or emergency LSCS were divided into two groups randomly: Group A receiving intrauterine tablet misoprostol 800 mg after delivery of the placenta, and Group B receiving postoperative per rectal tablet misoprostol 800mg. The primary outcome measured was the incidence of PPH, while secondary outcomes included hemoglobin levels, the requirement for blood transfusion, and adverse events.

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Results: Average blood loss was 534±150ml in group A and 660±190ml in group B. Preoperative hemoglobin was 11.3±2.5gm in group A and 11.4±2gm in group B which was compared with a fall in post-operative hemoglobin which was 10.5± 1.5 gm in group A and 10.2 ±2.0gm with an average difference in hemoglobin level to be 0.7± 0.50 gm in group A and 1.2±0.93gm in group B. The PPH rate in Group B is 7.52 % whereas the PPH rate in Group A is only 2.04%. Only 3.09 % required need for other interventions such as intrauterine balloon tamponade or uterine artery ligation whereas its incidence is 5.26% in group B. In group A 6 women and in group B 9 women required need for administration of additional uterotonics. The average duration of surgery was similar in both groups which was 40-45±10 minutes. In this study out of 100 only 5 women required a need for blood transfusion in group A and this rate was slightly higher in group B i.e. 8 out of 100 in group B.

Conclusion: Our current investigation indicates that the administration of 800 mcg of misoprostol through the intrauterine route in addition to oxytocin infusion seems to be more effective than that of per rectal 800mg misoprostol administration

1. Introduction

4 million women annually, with a higher prevalence in low-income nations.[1] Those who manage to survive this condition frequently require immediate surgical procedures to manage the bleeding, which can lead to enduring reproductive issues and emotional distress. Target 3.1 of the Sustainable Development Goals strives to decrease the worldwide maternal mortality ratio to below 70 per 100,000 live births [3]

Severe maternal complications, leading to organ dysfunction or even death, are often a result of significant blood loss, jeopardizing maternal hemodynamic stability. Globally, uterine atony stands as the most frequent cause of postpartum haemorrhage (PPH), contributing significantly to maternal mortality from PPH [3]. Other factors that can lead to PPH include genital tract trauma (such as vaginal or cervical lacerations and uterine rupture), retained placental tissue, or maternal bleeding disorders. While PPH can occur in any woman, certain risk factors like grand multiparity, prolonged labour, previous history of PPH, and multiple gestations are associated with an elevated risk of post-birth bleeding [4]. Additionally, anaemia often exacerbates the condition [5]. Fortunately, most PPH-related complications can be mitigated through the use of prophylactic uterotonics during the third stage of labour, which refers to the time between the delivery of the baby and the complete expulsion of the placenta.

One uterotonic agent used for prophylaxis of PPH is misoprostol, which is a prostaglandin E1 analogue. Misoprostol is water-soluble, heat-stable, and gets absorbed within 9–15 minutes, with a half-life of approximately 20–40 minutes[7]

The administration routes of misoprostol offer different advantages: oral and sublingual routes provide a rapid onset of action, while the vaginal and rectal routes lead to extended activity and higher bioavailability[7]. The World Health Organization (WHO) recommends misoprostol as a uterotonic option for the prevention of postpartum hemorrhage, particularly in settings where oxytocin is unavailable.

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Numerous randomized controlled trials have investigated the effectiveness of intraoperative misoprostol administered through various routes in reducing blood loss and preventing postpartum hemorrhage. These studies have shown that the use of misoprostol yields comparable efficacy to oxytocin. [8-12] However, Zhao et al. Indicated that misoprostol demonstrated greater effectiveness in reducing blood loss compared to oxytocin [13] .
This research article investigates the efficacy and safety of intrauterine misoprostol administration during cesarean section compared to postoperative per rectal administration for the prevention of PPH. A randomized controlled trial was conducted on a cohort of pregnant women undergoing cesarean delivery, divided into two groups: Group A receiving intrauterine misoprostol, and Group B receiving postoperative per rectal misoprostol. The primary outcome measured was the incidence of PPH, while secondary outcomes included hemoglobin levels, the requirement for blood transfusion, and adverse events.

2. Material and Method

This prospective randomized controlled study was carried out at Atal Bihari Vajpayee govt medical college and hospital Vidisha (M.P.). Following approval from the college ethical committee at A.B.V.G. Medical College, A comprehensive count of 200 pregnant women at full term (37-40 weeks of gestation), slated for either elective or emergency cesarean delivery, were included in the study. Informed consent was obtained from all participants. ***The exclusion criteria*** were:-

- Anemia (Hemoglobin < 8 g),
- Cardiac disease,
- Renal disease,
- Liver disease,
- Pregnancy with obstetric hemorrhages such as placenta previa, placental abruption, and vasa previa,
- Pregnancy with coagulopathy or thrombocytopenia or blood dyscrasias,
- And Pregnancy-Induced Hypertension (PIH) with Hemolysis, Elevated Liver Enzyme, And Low Platelets (HELLP) syndrome,
- History of prostaglandin allergy and duration of surgery more than 120 minutes

All women who gave consent for the study were assigned randomly to one of two study groups A and group B. LSCS was performed under spinal anaesthesia in all 200 women. The first group received 800 micrograms of misoprostol intrauterine inserted at the cornual part bilaterally, divided on each side after placental delivery in addition to the standard practice of administering oxytocin infusion (20 IU oxytocin dissolved in 500 ml of Ringer lactate solution, administered at a rate of 125 ml/h over a span of 6 hours) Other group received 800 micrograms of misoprostol per-rectally after completion of caesarean section.
The primary measurements taken into account were the quantity of blood loss during the surgical procedure and the variations in hemoglobin/hematocrit levels before the surgery and

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24 hours post-surgery. The measurement of intraoperative blood loss involved collecting the blood in the suction device following the procedure and accounting for the varying weights of abdominal swabs and gauzes before and after the surgery. One gauze soaks around 250-300 ml of blood. The decrease in hemoglobin /hematocrit levels after surgery was computed as the difference between the preoperative values (recorded upon admission of the women) and the measurements taken 24 hours after the operation from the central laboratory.

Initial demographic and obstetric information, comprising age, parity, gestational age, history of prior cesarean section, reason for the present cesarean section, and infant birth weight, were documented. Additional aspects such as the requirement for supplementary oxytocic treatment, duration of the operation, volume of intraoperative infusion, necessity for blood transfusion, adverse effects of the experimental drug, and any notable postpartum health issues were also meticulously recorded.

3. Result

A total of 200 full-term pregnant women who consented to the study and were eligible for the study after fulfilling inclusion and exclusion criteria were enrolled in this study. These 200 women were randomly divided into two groups of 100 in each group. One group (group A) received an intrauterine tablet of misoprostol 800 micrograms in each cornua after delivery of placenta in addition to routine oxytocin infusion, other group (group B) received perrectal tablet of misoprostol after completion of cesarean section . Maternal age and gravidity were found to be statistically significant, there were no statistically significant differences observed between the two groups in terms of body mass index, blood pressure, gestational age, and duration of the cesarean section. There was no requirement for the conversion of spinal anaesthesia into general anaesthesia in all cases. Most patients were in the age group of 20-30 years of age in both groups. The most common indication for cesarean section was fetal distress in group A and group B.

Average blood loss was 534±150ml in group A and 660±190ml in group B. Preoperative hemoglobin was 11.3±2.5gm in group A and 11.4±2gm in group B which was compared with a fall in post-operative hemoglobin which was 10.5± 1.5 gm in group A and 10.2 ±2.0gm with average difference in hemoglobin level to be 0.7± 0.50 gm in group A and 1.2±0.93gm in group B. The PPH rate in Group B is 7.52 % where as the PPH rate in Group A is only 2.04%. Only 3.09 % required need for other interventions such as, intrauterine balloon tamponade or uterine artery ligation whereas its incidence is 5.26% in group B. In group A 6 women and in group B 9 women required need for administration of additional uterotonics. The average duration of surgery similar in both groups which was 40-45±10 minutes. In this study out of 100 only 5 women required a need for blood transfusion in group A and this rate was slightly higher in group B i.e. 8 out of 100 in group B. The chi-square statistic is 28.6634. The p-value is < 0.00001. The result is significant at $p < .05$(table 3).

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Table 1: Basic characteristics

Basic characteristics (Mean ± SD)		**Intrauterine Misoprostol group (n=100)**	**Per-rectal misoprostol Group n=100**	**Chi - square (X2)**
Maternal age	<20 20-30 30-35 >35	9 82 7 2	7 79 11 3	< 0.00001
Booked status	Booked Unbooked	36 64	29 71	.290607
Gravidity	Primigravida Multipara Grandmultipara	56 40 4	48 50 2	< 0.00001
Emergency/ elective	Emergency c s Elective cs	10 90	15 85	.285049
Body mass index	<18 18-24 >24	23 48 29	19 57 24	.443952
Gestational age	Early term Full-term Late-term	2 89 9	5 78 17	.106896

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Blood pressure	SBP	120±100mmhg	128±116mmhg	.830504
	DBP	88±30mmhg	90±30mmhg	
Birth weight (kilograms) (mean, SD)	<2kg 2-3.5kg >3.5kg	9 70 21	11 69 12	.31154

Table 2- indication of caesarean section

Indications		**Intrauterine Misoprostol group (n=100)**	**Per-rectal misoprostol Group n=100**	**Chi -square (X2)**	**Chisquare (X2)**
Foetal distress		15	18		
Meconium stained liquor		9	9		
Bad obstetric history		3	2		
Breech		7	9		
Non-progress of labour		3	4		
Preeclampsia		8	6		
Previous 2 LSCS		7	5		
Previous 1 LSCS		12	9		
Twin gestation		6	4	.035275	.022414
Placenta previa		2	3		
Cephalopelvic disproportion		10	12		

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Failed induction		4	5		
Obstructed labour		6	4		

Table 3: Caesarean section blood loss determinants among the groups

	Intrauterine Misoprostol group (n=100	**Per-rectal misoprostol Group n=100**	**Chi -square (X2)**
Postpartum hemorrhage	2	7	< 0.00001
No Postpartum hemorrhage	98	93	
PPH rate	2.04%	7.52%	
Need other interventions	3 (3.09%)	5(5.26%)	
Need for additional uterotonics	6(6.38%)	9(9.89%)	

Table 4: Side effect profile

Variable		**Intrauterine Misoprostol group (n=100)**	**Per-rectal misoprostol Group n=100**	**Chi -square (X2)**	**Chi-square (X2)**
Fever		03	05		
Nausea, vomiting		13	14		

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Shivering		14	17		
Headache		03	02	.105207	.532384
Metallic taste		01	03		
Giddiness		00	02		

Table 5: Incidence of postpartum hemorrhage

Variable		**Intrauterine Misoprostol group (n=100)**	**Per-rectal misoprostol Group n=100**	**Chi -square (X2)**	**Chisquare (X2)**
Blood loss (mL)		450±200ml	580±190ml		
Preoperative Hb (gm%		11.2±2.5gm	11.4±2gm		
Postoperative Hb (gm%		10.5± 1.5 gm	10.2 ±2.0gm	.000947	< .00001
Hb difference		0.7± 0.50 gm	1.2±0.93gm		
Duration of surgery (min)		38±10min	42±12min		
Need of blood transfusion		05	08		

Side effect profile

Adverse side effects were also taken into consideration (table no – 4). The most common side effects noted were nausea, vomiting, headache, metallic taste, shivering, giddiness, and fever. Out of all 200 cases most patients complained of shivering which was present in 14 patients in group A, and 17 patients in group B, nausea and vomiting were the second most common side effects which were present in 13 patients in group A and 14 patients in group B respectively.

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4. Discussion

It is commonly known that a cesarean section is becoming more commonplace throughout the world in both developed and developing nations. To prevent uterine atony during surgery, oxytocin is frequently used. To stop bleeding, however, more uterotonic medications were added in some places.

One of the main causes of maternal morbidity and mortality, particularly in nations with inadequate medical resources, is excessive blood loss during and after delivery. It is the cause of nearly 25% of maternal deaths globally. Postpartum hemorrhage has been demonstrated to be effectively controlled by misoprostol. The World Health Organization (2012) recommends misoprostol at doses of 600 mg orally and 800 mg sublingually for the prevention and treatment of PPH. In addition, ACOG (2017) suggests that misoprostol be administered orally, sublingually, or rectally in doses between 600 and 1000 mg to treat PPH without causing serious side effects.

The effectiveness percentage is dependent on the dosage, mode of administration, and side effects. For example, when 600 µg is applied orally during vaginal deliveries, the percentage of cases with bleeding falls to 6%, vomiting to 8%, and diarrhea to 3%. Postpartum hemorrhage is reduced to 41.8 per cent when misoprostol 400 µg is administered rectal. Misoprostol, an autocoid substance whose effect intensifies with proximity to contracting receptors, was administered intrauterine in this study in an amount of 800 µg. This was done because it is a more comfortable to administer mesoprostol while performing a cesarean section. Since it has been demonstrated that misoprostol in combination with conventional oxytocin does not result in significant side effects, this treatment was administered to all patients. A comparative study was done intrauterine vurses perrectal mode of tablet mesoprostol administration . In our study PPH rate was 2.04%in group A which was 7.52% in group B.total blood loss was calculated which was 534±150ml in group A and 660±190ml in group B . Preoperative hemoglobin level was compared with post operative hemoglobin level in both the group . There was hemoglobin difference of 0.7± 0.50 gm in group A andslightly higher i.e. 1.2±0.93gm in group B.

Bahadur et al. Conducted A retrospective data analysis was carried out on 160 women who had lower segment cesarean sections. After giving birth, 85 out of 160 women (53%) received an intrauterine tablet containing 800 mg of misoprostol in addition to their usual oxytocin infusion (group A), and 75 out of 160 women (47%) received only oxytocin (group B). It shows that During the caesarean section, group A experienced a mean blood loss of 680 ± 202 ml, while group B experienced 740 ± 228 ml (p ¼ .08). In comparison to group A (0.93 ± 0.68 gm percent), group B had a higher Hb difference (1.03 ± 0.83 gm percent) (p ¼ .41). In both groups, no patient needed extra oxytocic medication, and no patient experienced postpartum hemorrhage. There is a statistically significant decrease in intraoperative and postoperative blood loss when misoprostol is administered intrauterine in addition to routine oxytocin infusion during cesarean sections. P Q Diaz et al randomized clinical trial involving 200 caesarean section patients was carried out. They were split up into two groups of 100 women each, and after the birth of their child, group A received an intrauterine placebo, and group B

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received 800 µg of misoprostol. Comparisons were made between the side effects, loss of hematocrit and hemoglobin, and requirement for additional uterotonics. Findings: group B experienced a 50% reduction in the need for additional uterotonics and a 39% decrease in hemoglobin loss. Thirteen versus three percent of the patients in group A had hemoglobin losses greater than three grams. Hematocrit's loss was decreased by forty-six percent. Seven versus one percent of the cases had patients whose hematocrit dropped by more than ten percent. Tiwari et al Enrolled 150 pregnant women scheduled for either an elective or emergency caesarean delivery at term (37–40 weeks gestation). Participants were randomly assigned to one of two groups: Group I consisted of women who received an intravenous infusion of 10 IU oxytocin after giving birth, while Group II consisted of women who received 400mcg intrauterine misoprostol in addition. It was discovered that there was a highly significant difference in the postoperative hematocrit and hemoglobin between the two groups (10.12 ± 1.55 vs. 9.24 ± 1.52; p). < 0.01) and (2.48 ± 1.38 vs 3.75 ± 1.77; $p < 0.001$) respectively. Estimated blood loss in two groups was found to be very highly significant (440.19 ± 257.75 vs 677.38 ± 343.04; $p < 0.001$). Intraoperative blood loss was significantly lower in the group I compared to group II (408.27 ± 123.34 vs 486.04 ± 135.84; $p < 0.001$). Blood loss during the first 6 hours after delivery was also lower in the group I (58.87 ± 9.86 ml vs 63.29 ± 12.39 ml; $p < 0.05$). Fewer women in the intrauterine misoprostol group needed additional uterotonics (7 vs 11; $p > 0$ points, five. The two groups' differences in side effects were determined to be statistically nonsignificant.

5. Conclusion

The use of misoprostol via intrauterine administration during caesarean section has received less attention in research. However, when combined with standard oxytocin infusion, it demonstrates a significant reduction in both intraoperative and postoperative blood loss, which holds clinical importance. In conclusion, when compared to various studies employing different routes or doses of misoprostol, our current investigation indicates that the administration of 800 mcg of misoprostol through the intrauterine route in addition to oxytocin infusion seems to be more effective than that of per rectal 800mg misoprostol administration.

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