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Per-rectal Misoprostol for Prophylaxis of Postpartum Hemorrhage

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Abstract:

Background: *Postpartum hemorrhage (PPH) remains a leading cause of maternal deaths globally, particularly in low-resource settings. Misoprostol, a heat-stable and easy-to-administer uterotonic, offers potential advantages over oxytocin for PPH prevention.*

Aim of the study: *This study aimed to evaluate the effectiveness and safety of per rectal misoprostol compared to intramuscular oxytocin for preventing PPH.*

Methods: *A cross-sectional study was conducted on 100 women undergoing vaginal deliveries at Bangabandhu Sheikh Mujib Medical University, Bangladesh. Participants were randomly assigned into two groups: Group A (n=50) received 600 µg of misoprostol rectally, while Group B (n=50) received 10 IU of oxytocin intramuscularly. Outcomes measured included blood loss, the incidence of PPH, side effects, and the need for additional interventions.*

Result: *Both groups showed similar blood loss (misoprostol: 260.8±41.4 ml, oxytocin: 280.4±47.5 ml). Misoprostol had higher incidences of mild fever (30%) and shivering, while oxytocin resulted in a higher need for transfusions (4%).*

Conclusion: *Misoprostol is as effective as oxytocin in preventing PPH, with some mild side effects, making it a practical option in resource-limited settings.*

Keywords: *Postpartum hemorrhage, misoprostol, oxytocin, maternal health, and PPH prevention.*

1. INTRODUCTION

The birth of a healthy child is one of the most significant moments in a woman's life; however, it also presents substantial risks to her health. The World Health Organization (WHO) estimates that approximately 500,000 women die annually due to pregnancy-related complications, with at least 98% of these deaths occurring in developing countries [1]. The third stage of labor is often regarded as the most dangerous for the mother, with postpartum hemorrhage (PPH) posing the greatest threat [2]. PPH is commonly defined as blood loss exceeding 500 ml or any bleeding that leads to hemodynamic instability. However, research suggests that normal blood loss during vaginal delivery may range between 500 to 1000 ml [3,4]. Prendiville et al. (1988) proposed that a more clinically relevant definition of PPH should include blood loss exceeding 1000 ml [5]. PPH remains the leading cause of maternal

mortality, accounting for 14.9% of maternal deaths in regions with high maternal mortality and less than 10% in developed nations [6]. Numerous trials have investigated strategies to reduce blood loss, comparing active management with expectant management during labor. Most studies focus on bleeding from the placental bed, where physiological changes in pregnancy cause denuding of the muscular layer of the spiral arteries. Active management, by inducing uterine contractions, compresses these arteries and significantly reduces blood loss. Adequate management of the third stage of labor is essential to prevent PPH in vaginal deliveries. In the Bristol Third Stage Trial, Prendiville et al. (1988) reported a postpartum bleeding incidence of 5.9% in the actively managed group compared to 17.9% in the physiologically managed group, concluding that active management significantly reduced blood loss during the third stage [5]. Various pharmacological agents are used to prevent PPH, including oxytocin, ergometrine, and syntometrine (a combination of oxytocin and ergometrine). Prostaglandin F2α has also been employed. Routine oxytocin administration has proven effective in lowering PPH incidence, though no single drug has emerged as the definitive "drug of choice." The WHO recommends intramuscular oxytocin during the third stage of labor. While ergometrine is also effective, its use is often associated with side effects like nausea, vomiting, and hypertension [6,7]. Prostaglandin F2α has been successfully used in active management, administered intramuscularly [8]. Misoprostol, a prostaglandin E1 analogue, is a potent uterotonic with rapid effects on the postpartum uterus [3]. Its potential as an alternative to standard oxytocics, particularly in both low-risk and high-risk pregnancies, has gained attention. In many developing countries, approximately 90% of deliveries occur at home, often without skilled birth attendants. The lack of trained personnel to administer parenteral oxytocin, combined with high rates of anemia during pregnancy, limited availability of safe blood transfusions, and the absence of refrigeration for oxytocin storage, exacerbates the incidence of PPH. Recent studies have explored the use of oral and rectal misoprostol for managing the third stage of labor. Misoprostol offers several advantages, including stability at room temperature, low cost, ease of administration, and fewer side effects. This study aims to assess the efficacy of per rectal administration of misoprostol as an alternative to oxytocin for preventing postpartum hemorrhage. Misoprostol has already been administered prophylactically at a dose of 600 µg per rectum in tertiary hospitals in our country, and this study seeks to evaluate the effectiveness of this dosage.

2. Methodology & Materials

This cross-sectional descriptive study was conducted at the Department of Obstetrics and Gynecology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, over a one-year period from January to December 2016. A purposive sampling technique was employed to select 100 pregnant women who met specific inclusion and exclusion criteria. The participants were divided into two groups:

- **Group A (N=50)**: Comprised of 50 patients who received 600 µg of misoprostol administered rectally.
- **Group B (N=50)**: Comprised of 50 patients who received 10 IU of oxytocin administered intramuscularly.

Inclusion Criteria:

- Pregnancies between 36-42 weeks.
- Normal vaginal deliveries (NVD).

Exclusion Criteria:

- Instrumental deliveries (e.g., Ventouse, forceps).
- Coagulation disorders.
- Antepartum hemorrhage.
- History of asthma or known allergies to prostaglandins.
- Placenta previa.
- Intrauterine fetal death.
- Grand multiparity.

All participants were provided with detailed information about the study's objectives, procedures, and aims, and written informed consent was obtained prior to their participation. Baseline demographic data were collected, ensuring strict confidentiality. Study variables included nausea, vomiting, shivering, temperature changes, labor induction, and labor augmentation. Ethical approval for the study was obtained from the institutional ethics

committee.Group A participants received 600 µg of misoprostol rectally after the delivery of the placenta and membranes. Oxytocin was not routinely administered during the active management of the third stage of labor but was kept ready for use if clinically indicated. In cases where labor induction or augmentation with oxytocin was required, the oxytocin drip was discontinued after the baby's delivery, and misoprostol was given rectally following placental delivery. In Group B, 10 IU of oxytocin was administered intramuscularly for active management of the third stage of labor. The placenta was delivered via controlled cord traction. If blood loss exceeded 500 ml or if the patient's hemodynamic condition deteriorated, active management included an intravenous infusion of oxytocin (4 amps per 1000 ml of Hartmann's solution) and an intramuscular injection of 1 ampoule of Ergometrine.

Statistical Analysis

The data were systematically structured into appropriate tables and figures, each supplemented with detailed descriptions to facilitate understanding. Statistical analyses were conducted using SPSS software (version 26) on a Windows platform. Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequencies and percentages. Group comparisons for continuous variables were carried out using the Student's t-test, whereas categorical variables were analyzed using the chi-square test. Statistical significance was determined with a threshold p-value of less than 0.05.

3. RESULT

The table compares the distribution of age, parity, gestational age, and the nature of onset in two groups (Group A and Group B), each consisting of 50 individuals. The age distribution is similar across both groups, with the majority of participants falling between 26-30 years (34% in Group A and 36% in Group B). In terms of parity, 40% of each group had one child, while 60% had 2-3 children. Most participants had a gestational age of 38-39 weeks (60% in Group A, 62% in Group B), with smaller percentages below 38 weeks or at 40 weeks or more. The nature of onset was predominantly spontaneous, occurring in 86% of Group A and 92% of Group B, with induced onset being less frequent. Figure 1 shows the percentage distribution of patients across two groups (A and B) based on whether they experienced labor augmentation. In Group A, 88% of patients had no augmentation, while 12% did. In Group B, 74% had no augmentation, and 26% had labor augmentation. The data indicates that a higher proportion of patients in Group A did not undergo augmentation compared to Group B, which had a relatively higher rate of labor augmentation. Table 2 presents the duration of labor for two groups (Group A and Group B), each consisting of 50 participants. The mean duration of the first stage of labor was 7.5±2.25 hours for Group A and 7.4±2.21 hours for Group B, showing very similar times between the groups. The second stage of labor had a mean duration of 30.8±22.25 minutes for Group A and 29.51±21.31 minutes for Group B, again indicating minimal differences. In the third stage, the mean duration was 8.5±6.11 minutes in Group A and slightly longer at 9.5±5.22 minutes in Group B. Figure 2 compares the percentage of subjects in Groups A and B who either did or did not receive additional oxytocin. In Group A, 82% of the participants did not receive additional oxytocin, while 18% did. In Group B, 80% of the participants did not receive additional oxytocin, while 20% did. Figure 3 illustrates a comparison between Group A and Group B regarding the percentage of cases with blood loss exceeding 500 ml and less than 500 ml. In Group A, 16% of individuals experienced blood loss greater than 500 ml, whereas in Group B, 18% did. Conversely, the majority of cases in both groups had blood loss below 500 ml, with Group A having 84% and Group B showing 82% in this category. Table 3 presents a comparative analysis of symptomatology between the two groups. Group A reported no occurrences of nausea, vomiting, or diarrhea, while Group B exhibited low frequencies of these symptoms, with nausea at 8% and vomiting at 6%. Shivering was observed in 16% of Group B participants, highlighting a notable difference, although the P-value for this comparison is not significant. Importantly, a higher percentage of participants in Group A (30%) experienced elevated temperatures (≥38° C) compared to Group B (16%) (P <9.05). In Table 4, the analysis of hemoglobin levels reveals no significant differences between the two groups, both pre- and post-delivery. Group A had a mean hemoglobin level (Hb %) of 10.4±1.2 pre-delivery and 9.8±0.92 post-delivery, while Group B recorded mean values (Hb %) of 10.5±1.1 pre-delivery and 9.9±1.01 post-delivery. Table 5 compares the average blood loss between the groups, showing that

Group B experienced slightly higher blood loss (280.4±47.5 ml) compared to Group A (260.8±41.4 ml), although this difference was not statistically significant. Table 6 addresses blood transfusion requirements, indicating that 4% of participants in Group B required transfusions, whereas none in Group A needed this intervention, reflecting a lower necessity for blood transfusions in Group A.

Table1. *Demographic profile and clinical presentation of patients (N=100).*

Variables	Group A (N=50)		Group B (N=50)	
	n	%	n	%
Age (years)				
20-25	15	30.00	14	28.00
26-30	17	34.00	18	36.00
31-35	12	24.00	12	24.00
36-40	6	12.00	6	12.00
Parity				
1	20	40.00	20	40.00
2-3	30	60.00	30	60.00
Gestational age (weeks)				
< 38	8	16.00	9	18.00
38-39	30	60.00	31	62.00
≥ 40	12	24.00	10	20.00
Nature of onset				
Spontaneous	43	86.00	46	92.00
Induced	7	14.00	4	8.00

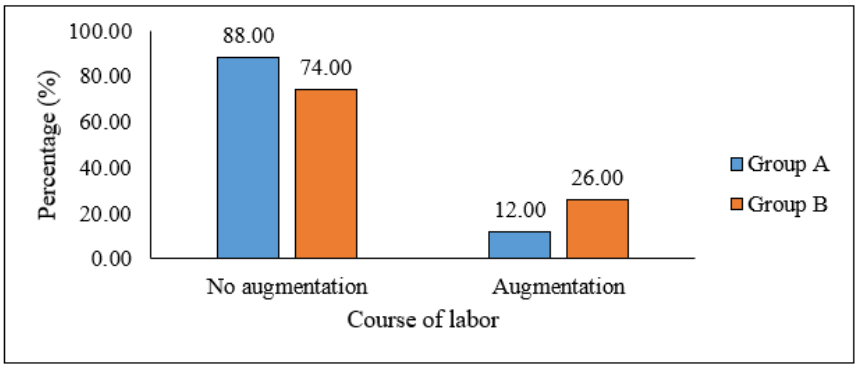

Figure1. *Distribution of patients depending on augmentation during labor (N=100).*

Table2. *Duration of labor (N=100).*

Duration of labor	Group A (N=50)	Group B (N=50)
	Mean±SD	Mean±SD
1st stage (hour)	7.5±2.25	7.4±2.21
2nd stage (minute)	30.8±22.25	29.51±21.31
3rd stage (minute)	8.5±6.11	9.5±5.22

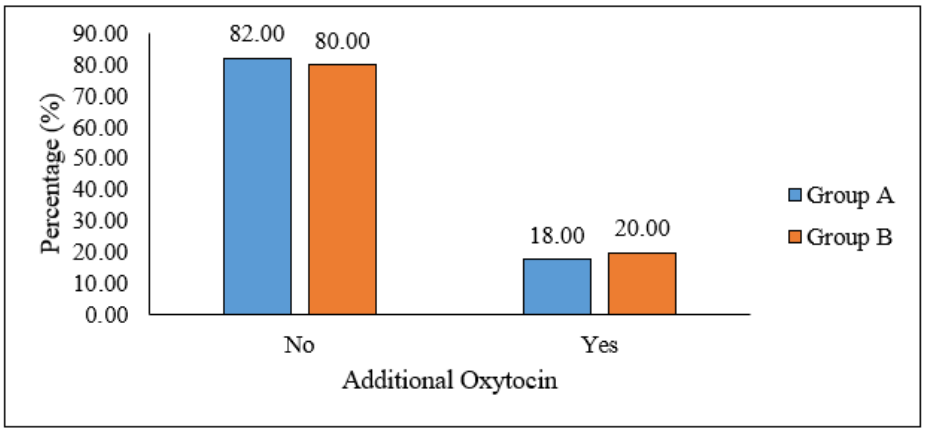

Figure2. *Use of additional Oxytocin (N=100).*

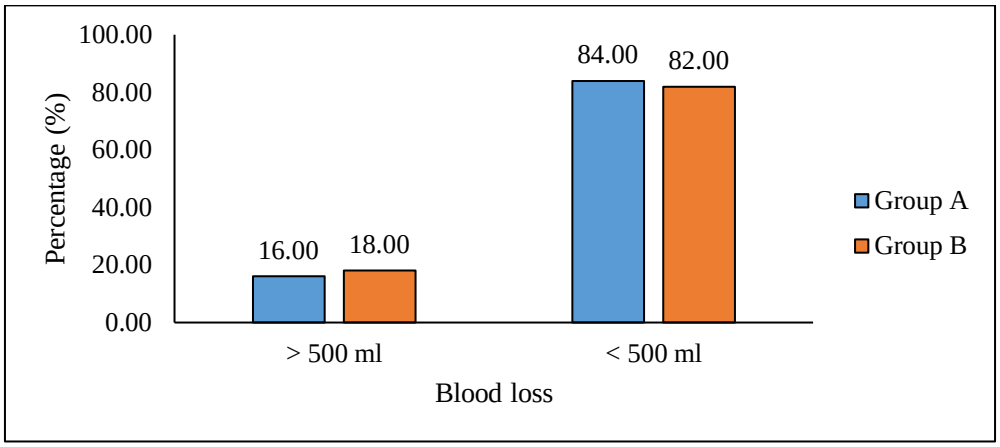

Figure3. *Amount of blood loss in groups (N=100).*

Table3. *Profile of symptomatology in study groups (N=100).*

Symptom	Group A (N=50)		Group B (N=50)		P-value
	n	%	n	%	
Nausea	0	0.00	4	8.00	NS
Vomiting	0	0.00	3	6.00	
Shivering	0	0.00	8	16.00	
Diarrhea	0	0.00	0	0.00	
Temperature (≥38° C)	15	30.00	8	16.00	< 9.05

Table4. *Comparison of changes in hemoglobin levels between groups (N=100).*

Variables	Group A (N=50)	Group B (N=50)	P-value
	Mean±SD	Mean±SD	
Pre-Delivery	10.4±1.2	10.5±1.1	NS
Post-Delivery	9.8±0.92	9.9±1.01	

Table5. *Comparison of the average blood loss between the two groups (N=100).*

Blood loss (ml)	Group A (N=50)	Group B (N=50)	P-value
Mean±SD	260.8±41.4	280.4±47.5	NS

Table6. *Comparison of blood transfusion requirements across groups (N=100).*

Blood transfusion	Group A (N=50)		Group B (N=50)	
	n	%	n	%
Required	0	0.00	2	4.00
Not required	50	100.00	48	96.00

4. DISCUSSION

Maternal mortality remains a critical concern in developing countries, with postpartum hemorrhage (PPH) being a leading cause of death. While the incidence of hemorrhage-related maternal deaths has declined in developed nations, PPH continues to pose a significant challenge in countries like Bangladesh. It is well-established that preventive measures are preferable to reactive interventions, and the routine administration of oxytocic drugs has been shown to significantly reduce the occurrence of PPH. However, oxytocics present challenges, including potential adverse effects and the need for special storage conditions, which limit their widespread use in resource-poor settings. Misoprostol has been proposed as an alternative for PPH prevention, particularly in low-risk populations, given its lower cost, stability at room temperature, and ease of administration. This study aimed to evaluate the efficacy and safety of rectally administered misoprostol for the prevention of PPH. The findings of this comparative study indicate that misoprostol, with its rapid onset of action, is as effective as oxytocin in minimizing blood loss during the third stage of labor. Additionally, misoprostol does not cause significant hypertension, unlike other uterotonics such as methergin, and lacks bronchoconstrictory effects, which enhances its safety profile [9]. A review by Sanjay B. Rao et al. demonstrated that rectal misoprostol has been compared favorably to control groups or placebos [10], while a study by Bamigboye et

al. compared it with syntometrine for managing the third stage of labor. In the current study, the average duration of the third stage was 8.5 minutes in the misoprostol group and 9.5 minutes in the oxytocin group, with no statistically significant differences in mean blood loss between the two groups. Only 16% of patients in the misoprostol group experienced blood loss exceeding 500 mL, which is comparable to results observed in the oxytocin group. Furthermore, none of the patients receiving misoprostol required a blood transfusion, whereas two patients in the oxytocin group did. These findings align closely with the studies of Sanjay B. Rao et al. [10]. El Rafaey et al. (1995) also reported no significant differences between misoprostol and oxytocin in terms of hemoglobin concentration drop following administration [9]. In this study, the maximum hemoglobin drops between the two groups ranged from 5% to 6%, a difference that was not statistically significant ($P > 0.05$). However, misoprostol was associated with an increased incidence of pyrexia, which, though self-limiting and responsive to common antipyretics like diclofenac sodium or paracetamol, was an undesirable side effect. The occurrence of both shivering and pyrexia is likely attributable to the effect of prostaglandin E on the central thermoregulatory center. Lumbiganon et al. (1999) noted that while this side effect may not pose a serious clinical concern, it could lead to unnecessary diagnostic tests or antibiotic therapy, potentially complicating management [11,12]. Shivering and pyrexia were the most common side effects observed with misoprostol in this study, with a clear association between the two. Women who experienced shivering following misoprostol administration had an average temperature increase of 0.38°C higher than those who did not. In contrast, shivering in women administered oxytocin did not result in a significant rise in temperature [13]. Pyrexia occurred twice as frequently and was more severe in the misoprostol group, typically developing within 15 to 20 minutes of administration and resolving within 20 to 30 minutes. This side effect may affect the acceptability of misoprostol, as some women reported being unable to hold or breastfeed their infants immediately after delivery due to fever. Despite these side effects, misoprostol offers numerous advantages over oxytocin, including a long shelf life, stability at high temperatures (eliminating the need for refrigeration), the option for rectal administration (which avoids the use of needles), and fewer gastrointestinal side effects. Additionally, it can be safely administered to hypertensive patients, making it a suitable option for managing the third stage of labor in resource-limited settings [12]. The rectal route of administration presents further practical benefits, as it reduces the gastrointestinal side effects associated with oral misoprostol, which are dose-dependent. Further research is necessary to assess the use of misoprostol in women at high risk of PPH and in rural settings in developing countries [12,14]. The findings of this study, alongside others, may help inform health policies that promote collaboration with traditional birth attendants to improve access to life-saving treatments for PPH. In settings where skilled birth attendants are unavailable, misoprostol may be the only viable option for controlling PPH [12]. Identifying the most effective management approach for the third stage of labor, particularly in the absence of uterotonics, remains a critical area for ongoing investigation.

5. Limitations of the Study

This study has several limitations. The sample size is relatively small, which may limit the generalizability of the findings. The study was conducted in a single tertiary hospital, which may not fully represent the broader population, particularly in rural or under-resourced settings. The follow-up period was short, making it difficult to assess long-term outcomes and potential complications.

6. Conclusion and Recommendations

This study demonstrates that rectally administered misoprostol is as effective as intramuscular oxytocin in preventing PPH in vaginal deliveries. Misoprostol offers several advantages, including ease of administration, stability at room temperature, and a favorable safety profile, particularly in resource-limited settings. While both misoprostol and oxytocin effectively reduced blood loss during the third stage of labor, misoprostol showed a slightly lower need for blood transfusions. However, it was associated with higher incidences of pyrexia and shivering. Despite these side effects, misoprostol remains a viable alternative to oxytocin, especially in areas where refrigeration and skilled healthcare providers may be lacking. Further research is needed to explore its use in high-risk populations and rural settings, potentially making it a key

intervention for reducing maternal mortality from PPH in developing countries.

Ethical approval: *The study was approved by the Institutional Ethics Committee.*

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