Original Article

Intrauterine Misoprostol Versus Intravenous Oxytocin for the Prevention of Primary Postpartum Hemorrhage During Cesarean Section: A One-Year Randomized Controlled Trial

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Abstract

***Background**: Postpartum haemorrhage (PPH) is the major cause of maternal death worldwide, significantly in poor countries, like Asia, Africa. In our country PPH is the major cause of maternal mortality (about 80%). Global studies for decades showed that maternal mortality following PPH is due to uterine atony following vaginal delivery, caesarean section delivery and use of uterotonic drugs are the choice for both prevention and treatment of PPH. This study aims to evaluate the use and efficacy of intrauterine misoprostol versus oxytocin alone, in controlling postpartum haemorrhage due to atonic uterus amongst women with undergone Caesarean section in a tertiary care hospital setting of Bangladesh. **Material and Methods:** This randomized clinical trial was done in the Department of Obstetrics & Gynecology, Eastern Medical college Hospital, Cumilla, Bangladesh between January 2022 to December 2022. A total of 100 participants were randomly selected from all patients who admitted for elective cesarean section within this period. In this, the study group (Group A=50), received only intrauterine misoprostol after placental delivery. On the other hand, in control group (Group B=50) received routine intravenous Oxytocin alone. **Results**: There were no significant differences in baseline characteristics between the two groups. Group A (misoprostol) showed significantly lower pre-operative, post-operative, and total blood loss compared to Group B (oxytocin). Post-operative hemoglobin and hematocrit levels were significantly higher in Group A ($p<0.01$ and $p<0.001$, respectively). Additionally, Group A required fewer additional uterotonics and had a lower incidence of side effects, with no major differences in the type of adverse effects between the groups. **Conclusion**: This study concluded that intrauterine misoprostol is more effective than intravenous oxytocin in reducing blood loss and maintaining better postoperative hemoglobin and hematocrit levels during cesarean section, with fewer additional uterotonic requirements and minimal side effects.*

Keywords: Intrauterine Misoprostol, Intravenous Oxytocin, Postpartum Hemorrhage, Cesarean Section, Randomized Controlled Trial.
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Introduction

Postpartum hemorrhage (PPH) continues to be the leading cause of maternal deaths worldwide[1]. It is responsible for over one-third of maternal fatalities in Asia and Africa[2,3]. Uterine atony is the primary cause of PPH and can occur after both vaginal and cesarean births[4]. PPH is defined as a blood loss of 500 mL or more after vaginal delivery, or 1000 mL or more following a cesarean section[5,6]. Uterine atony occurs when uterus does not contract (or tighten) properly during or just after delivery[7]. For decade, Oxytocin has been routinely used to prevent uterine atony and excess uterine bleeding during cesarean section (CS).

Misoprostol is a synthetic analogue of natural prostaglandin E (PGE1). It is an effective anti-ulcer agent[8] and also used in medical abortion, medical management of miscarriage, induction of labor, cervical ripening before surgical procedures, and the treatment of postpartum hemorrhage. It can be used in different routes effectively including oral, vaginal, sublingual, buccal, or rectal[9,10]. One research study by Quiroga-Díaz, et al[10] proved the efficacy of the intrauterine use of misoprostol (800 µg) versus placebo for the prevention of PPH after CS delivery.

This current Randomized control trial was done to compare the efficacy and safety of intrauterine misoprostol versus intravenous oxytocin in the prevention of primary postpartum hemorrhage during cesarean section.

Materials and Methods

This Prospective Randomized control trial was conducted in the Department of Obstetrics & Gynaecology, Eastern Medical College Hospital, Comilla, Bangladesh between January 2022 to

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December 2022. A total of 100 pregnant woman at term (37-40 weeks) have been selected as per inclusion criteria from all patients those who admitted for elective cesarean section within this period. Informed written consent was taken from all participants after discussing the nature and aim of the study. Exclusion criteria included women with anemia (Hb <8 g/dL), cardiac disease, renal disease, liver disease, twin pregnancy, antepartum hemorrhage (such as placenta previa or abruptio placentae), coagulopathy, hypertension, known hypersensitivity to prostaglandins, and those who did not provide consent.

All women were undergone randomization by random sampling into two groups. The study group (A=50) received 600µg (300 +300) of misoprostol as intrauterine insertion at each cornual part bilaterally, after placental delivery and after exploring the uterine cavity. The other group, control group (B=50) received 10 units of Oxytocin infusion. The main outcome measurements were per-operative palpation of uterine tonicity, volume of intraoperative blood loss, and measurement of hemoglobin/hematocrit levels comparing preoperative and post-operative period. Intraoperative blood loss was measured by standardized visual estimation method, after operation by blood collected in the suction apparatus and weighting the used abdominal mop and gauzes per-operatively. All women were followed up postoperatively for 24 hours. Secondary outcome measured by the requirement of additional uterotonic agent, misoprostol related side effects.

Data Collection and Analysis: The study protocol was reviewed and approved by the ethical Review Committee of Eastern Medical College and hospital, Cumilla, Bangladesh. Data was coded and entered using SPSS v25 for analysis. Quantitative data described by mean and standard deviation and comparison was done between the two groups by Unpaired 't' tests. p-value <0.05 was taken as significant.

Results

The study reveals that the mean age of Group-A, who received misoprostol, was 25.46 with SD 5.24 while the mean age of Group-B who received oxytocin was 25.74 with SD 5.28. However, the average BMI of the women in the Group A was 22.98 with SD 1.48 whereas the average BMI of the women in the Group-B was 23.12 with SD 2.00. Interestingly, the menstrual cycle of 98.0% women of Group-A was found regular, whereas that cycle of 100.0% women of Group-B was found regular. Furthermore, most (64.0%) of the women of Group-A as well as most (66.0%) of the women of Group-B were Multiparous. Interestingly most (40.0%) women of Group-A were with multi gravidity, followed by 36.0% with 1st gravidity and 24.0% with 2nd gravidity. On the other hand, among the women of Group-B, 34.0% each were with 1st and 2nd gravidity while only 32.0% were with multi gravidity. However, the average gestational age of the women in the Group-A was 38.46 with SD 1.11 whereas the average gestational age of the women in the Group-B was 38.62 with SD 1.03. There was no statistical difference between the two groups concerning maternal age, body mass index, parity, gestational age (Table-I).

Table-II showed that the average pre-operative blood loss among the women in the Group-A was 289.1 ml with SD 49.61 whereas the average pre-operative blood loss among the women in the Group-B was 399.1 ml with SD 46.81. The pre-operative blood loss among the women of Group-A was significantly lower than that among the women of Group-B. On the other hand, the average post-operative blood loss among the women in the Group A was 90.30 ml with SD 47.78 whereas the average post-operative blood loss among the women in the Group-B was 181.80 ml with SD 44.57. The post-operative blood loss among the women of Group-A is significantly lower than that among the women of Group-B. However, the average total blood loss among the women in the Group-A was 379.30 ml with SD 85.91 whereas the average total loss among the women in the Group-B was 580.7 ml with SD 79.54. The total blood loss among the women of Group-A is significantly lower than that among the women of Group-B.

Table-III showed that the average pre-operative mean hemoglobin in Group-A was 12.00 gm/dl with SD 0.86 whereas the average pre-operative mean hemoglobin in Group-B was 11.96 gm/dl with SD 0.67. The difference was not statistically significant (p>0.05). Similarly, the average of post-operative mean hemoglobin in Group-A was 11.3 gm/dl with SD 0.89 whereas the average post-operative mean hemoglobin in Group-B was 10.44 gm/dl with SD 1.59. The average post-operative mean hemoglobin in Group-A was significantly higher than that of Group-B (p<0.01). On the other hand, the average pre-operative mean hematocrit in Group-A was 36.1% with SD 2.47 whereas the average of pre-operative mean hematocrit in Group-B was 35.92% gm/dl with SD 2.22. The difference was not statistically significant (p>0.05). Besides, the average of post-operative mean hematocrit in Group-A was 33.8% with SD 2.31 whereas the average of post-operative mean hematocrit in Group-B was 30.80% gm/dl with SD 2.33. The mean hematocrit in Group-A was significantly higher than that of Group-B (p<0.001).

Table-I: Background information of the study population (n=100)

Variable	Group-A (n=50)	Group-B (n=50)	Significance
Age (years), (mean ± SD)	25.46 ± 5.24	25.74 ± 5.28	p>0.05
BMI (Kg/m^2), (mean ± SD)	22.98 ± 1.48	23.12 ± 2.00	p>0.05
Gravidity (%) 1st 2nd Multi	 36.0% 24.0% 40.0%	 34.0% 34.0% 32.0%	p>0.05
Parity (%) Nulliparous Multiparous	 36.0% 64.0%	 34.0% 66.0%	p>0.05
Gestational age (weeks), (mean ± SD)	38.46 ± 1.11	38.62 ± 1.03	p>0.05

Table-II: Comparison of per-operative and post-operative blood loss between two groups (n=100)

Blood loss	Group-A (n=50)	Group-B (n=50)	Significance
Per-operative blood loss (ml), Mean ± SD	289.1 ± 49.61	399.1 ± 46.81	p<0.001
Post-operative blood loss (ml), Mean ± SD	90.3 ± 47.78	181.8 ± 44.57	p<0.001
Total blood loss	379.3 ± 85.91	580.7 ± 79.54	p<0.001

Table-III: Pre-operative and post-operative hemoglobin and hematocrit values between two groups (n=100)

Variables	Group-A (n=50)	Group-B (n=50)	Significance
Pre-operative hemoglobin (gm/dl), Mean ± SD	12.0 ± 0.86	11.9 ± 0.67	p>0.05
Post-operative hemoglobin (gm/dl), Mean ± SD	11.3 ± 0.89	10.4 ± 1.59	p<0.01
Pre-operative HCT (%), Mean ± SD	36.1 ± 2.47	35.9 ± 2.22	p>0.05
Post-operative HCT (%), Mean ± SD	33.8 ± 2.31	30.8 ± 2.33	p<0.001

Table-IV: Comparison of additional uterotonic requirement, incidence and distribution of side effects between two groups (n=100)

Variables	Group-A (n=50)	Percentage (%)	Group-B (n=50)	Percentage (%)
Need for additional utero-tonics	Yes No	8.2% 91.8%	Yes No	76.0% 24.0%
Need other additional interventions	Yes No	0.0% 00.0%	Yes No	14.0% 86.0%
Incidence of side effects	Yes No	10.00% 90.0%	Yes No	24.0% 76.0%
Distribution of side effects Headache Fever Shivering Vomiting		 60.0% 0.0% 20.0% 20.0%		 41.7% 8.3% 16.7% 33.3%

In this study Group-A required significantly fewer additional uterotonics and had a lower incidence of side effects compared to Group-B, with no major differences in the type of adverse effects observed between the groups (Table-IV).

Discussion

Excessive blood loss during and after delivery represents the main cause of maternal mortality and morbidity. It accounts for almost 25% of maternal death worldwide[11]. It is well known fact that cesarean section is a major obstetrics interference that invariably causes severe PPH. Oxytocin is used routinely to prevent uterine atony during surgery[12]. Methyl ergometrine, once widely used, is now discouraged due to its adverse effects on the heart and peripheral blood vessels[12,13]. Following oxytocin, misoprostol administered via various routes has been proven in numerous studies to be a highly effective uterotonic agent for the prevention of PPH[14,15].

In this study, we chose the intrauterine route of misoprostol because it is the most convenient way to put misoprostol during cesarean section than other routes such as oral, sublingual, buccal, or rectal. In addition, misoprostol is an autacoid substance, so its effect is stronger if it is closer to target organ to contract the uterine muscle[16]. It binds to myometrial cells to cause strong myometrial contractions that

start at the fundus near a cornu and propagate down to the body of the uterus[17,18]. Several studies and meta-analyses have demonstrated that misoprostol, administered through various routes (oral, sublingual, or rectal), is effective in reducing postpartum hemorrhage; however, no single route of administration has been proven to be superior to the others[19-21]. But in this study, intrauterine administration proved much efficacy than intravenous administration group. Most previous studies reported significant adverse effects, primarily shivering and fever[22-24], however, in our study, the majority of women in both groups did not experience any side effects.

Surprisingly, this study showed that the mean estimated blood loss was statistically significantly lower in the misoprostol group. Mean Hemoglobin and Hematocrit level changed was also statistically significantly lower. And the results from the study consistently showed that women in Group A had significantly better outcomes in terms of both blood loss (pre-, post-, and total) and post-operative blood parameters (hemoglobin and hematocrit) compared to Group B. These differences are not only statistically significant but also clinically relevant, suggesting that the interventions or conditions associated with Group A are more effective in managing blood loss and supporting post-operative recovery. Our findings are consistent with those of several other similar studies[22-25].

Conclusion

This study concluded that intrauterine misoprostol (600 µg) is more effective than intravenous oxytocin (10 IU) in controlling postpartum hemorrhage during cesarean section. Misoprostol significantly reduced the incidence of PPH and blood loss without increasing the need for additional uterotonics, blood transfusions, or interventions. It was associated with minimal side effects, mainly mild fever and transient shivering. Unlike oxytocin, which has a short half-life, requires cold storage, and is more expensive, misoprostol is cost-effective, stable at room temperature, and easy to administer, making it a practical option for PPH prevention.

Conflict of Interest

The authors declared that they have no conflicts of interest.

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