Original Article

# Comparison of Intrauterine Versus Per-Rectal Misoprostol in the Prevention of Postpartum Haemorrhage During Caesarean Section



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## ABSTRACT

**Objective:** Current study is aimed to compare the frequency of postpartum haemorrhage in high-risk females undergoing caesarean sections who receive either intrauterine or per-rectal misoprostol.

**Study Design:** Prospective observational study

**Place and Duration of Study:** This study was conducted at the Sandeman Provincial Hospital Quetta during March 2022 till October 2022.

**Methods:** In this study, a total of 170 women undergoing caesarean section were randomly distributed into two study groups. Group A received 400 mg of intrauterine misoprostol, while Group B received 400 mg of per-rectal misoprostol. Maternal outcomes such as blood loss, haemoglobin difference, duration of surgery, and need for blood transfusion were compared. Neonatal outcomes and adverse events like fever, nausea, shivering, and headache were also assessed.

**Results:** The mean value of lost blood was significantly lesser in Group A (670 ± 190 mL) compared to Group B (750 ± 210 mL) (p = 0.04). The haemoglobin change was also less in Group A (0.85 ± 0.65 g/dL) versus Group B (1.05 ± 0.75 g/dL) (p = 0.03). Adverse events like shivering were more common in Group A (19% vs. 4%, p = 0.001).

**Conclusion:** There were no significant differences between the groups in terms of the need for blood transfusion or neonatal outcomes. Misoprostol effectively managed PPH via both administration routes, but intrauterine misoprostol significantly reduced intraoperative and postoperative blood loss compared to the rectal route, with temporary shivering as the only notable side effect.


**Key Words:** Postpartum Hemorrhage (PPH), Intrauterine Misoprostol, Rectal Misoprostol, Cesarean Section (CS)

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## INTRODUCTION

Postpartum haemorrhage (PPH) is defined as blood loss over 1000 millilitres during and after cesarean section (CS)[1]. Even in high-income nations, PPH, the most frequent type of significant obstetric haemorrhage, continues to be a major global reason of the morbidity and mortality of mothers[2,3]. PPH develops from numerous reasons, including uterine atony[4].

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PPH has a prevalence incidence of 6–10.8% worldwide, making it the leading cause of maternal fatalities (a quarter of all maternal deaths)[5]. PPH is the cause of more than one-third of maternal deaths in Asia and Africa[6]. A significant contributing factor to morbidity and mortality of mothers, particularly in low-resource nations where it accounts for about 25% of all deaths of mothers globally, is excessive bleeding during and after CS[7]. Furthermore, an increase in the rate of CS has been partially ascribed to the fact that the rate of PPH is rising in industrialised nations as well. PPH prevalence following CS is expected to be 3% (0.6–6.4%).

Preventive steps should be done to lower intraoperative blood waste during CS in order to lower the risks of blood transfusion and post-operative morbidity. As soon as the foetus is delivered, oxytocin is regularly administered. However, because it can result in tachycardia and hypotension, oxytocin might not be the best medication for preventing PPH in women with preeclampsia, prolong labor, or cardiac illness[8]. Furthermore, oxytocin needs to be kept refrigerated, which is impractical in developing nations because it is

light- and heat-sensitive. Prostaglandins are frequently used in obstetric medicine for the prevention and, more specifically, the management of postpartum haemorrhage. They also have uterotonic effects[8]. The most widely prescribed prostaglandin used off-label for preventing postpartum haemorrhage is misoprostol, an analogue of prostaglandin E1, because of its many benefits, which include low cost, simplicity of administration through different routes, and thermal stability (easy storage)[8]. But there is still conflicting information on both its safety and effectiveness, especially when it comes to the best way to administer it. There are several ways to deliver misoprostol, including intrauterine, per-rectal, buccal, oral, and sublingual. These routes have been investigated the most for preventing postpartum haemorrhage following caesarean sections. Certain studies support per-rectal delivery of misoprostol, whereas others demonstrate that intrauterine misoprostol dramatically lowers PPH rates [9]. The purpose of this research is to compare the incidence of postpartum haemorrhage in females undergoing caesarean sections who received intrauterine versus per-rectal misoprostol. The aim of current study is to add local data to the existing knowledge and offer support for applying these interventions in regional clinical practice. Current study is aimed to compare the frequency of postpartum haemorrhage in high-risk females undergoing caesarean sections who receive either intrauterine or per-rectal misoprostol.

# METHODS

This prospective observational study was conducted at Sandeman Provincial Hospital Quetta during March 2022 till October 2022. A total of 170 patients undergoing cesarean delivery were enrolled using non-probability consecutive sampling, with 85 patients allocated to each study group. The sample size was determined to detect a clinically significant difference in the prevention of postpartum hemorrhage (PPH) between two methods of misoprostol administration, with a 5% significance level ($\alpha = 0.05$) and 80% power ($\beta = 0.2$). The sample size was calculated using the following formula:

$$n = \left( \frac{Z_{\alpha/2} + Z_{\beta}{}^{2} \times p1(1-p1) + p2(1-p2)}{(p1-p2)^{2}} \right)$$

Where, $Z_{(\alpha/2)}$ is the critical value at a 95% confidence interval (1.96), $Z_{\beta}$ presents 80% power (0.84), $p1$ and $p2$ are the expected proportions of PPH in both groups based on previous studies [15]. A total sample size of 170 patients (85 in each group) was calculated. Patients were divided into two groups using the lottery method. Group A consisted of 85 patients who received 400 mg of intrauterine misoprostol placed at the uterine fundus immediately after placental delivery during uterine suturing. Group B included 85 patients who received 400 mg of misoprostol administered per-rectal immediately after placental delivery. Patients in both groups were monitored for 24 hours postpartum, and blood loss was measured six hours after delivery. PPH was defined as blood loss exceeding 1000 mL within the first 24 hours postpartum, assessed using a combination of suction volume and gauze saturation by a visual analogue method. Written informed consent was obtained from all participants before inclusion in the study, ensuring they fully understood the purpose, procedures, and potential risks involved.

Women undergoing cesarean delivery, both elective and emergency, for single or multiple gestations at term (37–40 weeks) were included. The study also included patients with a history of previous cesarean sections. Women with known hypersensitivity to prostaglandins, liver or coagulation disorders, heart disease, renal disease, a history of uterine rupture, or contraindicated for the use of prostaglandins were no included in the study.

Data were collected through a structured questionnaire and hospital records, supplemented by consultations with healthcare providers. Information on patient demographics, reproductive history, pregnancy details, labor and delivery characteristics, and maternal and neonatal outcomes were collected. Hemoglobin levels were measured pre-operatively and 24 hours post-operatively to evaluate blood loss. The primary outcome was the occurrence of PPH, while secondary outcomes included changes in hemoglobin levels, the need for additional uterotonic agents, blood transfusion requirements, and adverse effects of the study drug.

Data were analyzed using SPSS version 27. Descriptive statistics were used to summarize patient characteristics, and differences between the two groups were assessed using the independent t-test for quantitative variables and the chi-square or Fisher's exact test for categorical variables. A p-value of less than 0.05 was considered statistically significant.

# RESULTS

Table 1 provides a summary of the maternal and neonatal demographic statistics for both groups. There were no discernible differences between the two groups when age, parity, gestational age, history of prior caesarean sections, and neonatal birth weight were analyzed. Table 2 lists each group's indications for a CS.

**Table No. 1: Demographic characteristics of the women.**

| Variable | Group-A (n=85) | Group B (n = 85) | T-stat/ p-value |
|---|---|---|---|
| Age (mean±SD) (years) | 27.4 ± 4.3 | 28.0 ± 4.5 | –0.78, 0.43 |

| | | | |
|---|---|---|---|
| Parity | | | |
| Primigravida | 39 (45.9%) | 40 (47.1%) | 0.11, 0.95 |
| Multigravida | | | |
| 1 | 35 (41.2%) | 30 (35.3%) | |
| 2 | 8 (9.4%) | 10 (11.8%) | |
| 3 | 2 (2.4%) | 5 (5.9%) | |
| Previous LSCS | 17 (20.0%) | 19 (22.4%) | 0.13, 0.72 |
| Mean gestation in weeks (mean± SD) | 38.4 ± 1.5 | 38.3 ± 1.3 | 0.45, 0.65 |
| Weight of baby at birth (mean± SD KGs) | 2.7 ± 0.4 | 2.75 ± 0.5 | –0.51, 0.61 |

LSCS: lower segment cesarean section; Group A received intrauterine misoprostol (400 mg); Group B received per-rectal misoprostol (400 mg). A p-value of <0.05 is considered significant.

**Table No. 2: Reasons of cesarean surgery.**

| Indications | Group A (n = 85) | Group B (n = 85) |
|---|---|---|
| Fetal distress | 12 (14.1%) | 10 (11.8%) |
| Meconium-stained liquor | 5 (5.9%) | 7 (8.2%) |
| Bad obstetric history | 2 (2.4%) | 3 (3.5%) |
| Breech | 6 (7.1%) | 4 (4.7%) |
| Non-progress of labor | 8 (9.4%) | 9 (10.6%) |
| Preeclampsia | 5 (5.9%) | 7 (8.2%) |
| Previous LSCS | 10 (11.8%) | 9 (10.6%) |
| Twin gestation | 2 (2.4%) | 3 (3.5%) |
| Cephalopelvic disproportion | 4 (4.7%) | 3 (3.5%) |
| Failed induction | 7 (8.2%) | 6 (7.1%) |
| Oligohydramnios | 3 (3.5%) | 5 (5.9%) |

Group A received intrauterine misoprostol (400 mg); Group B received per-rectal misoprostol (400 mg).

No patients required a switch from local to general anesthesia during the surgical procedures. The average loss of blood was significantly lesser in the Group A (650 ± 190 mL) compared to Group B (740 ± 220 mL), with a statistically significant difference (p = 0.02) as shown in Table 3. The mean hemoglobin (Hb) levels before and after surgery were comparable between the two groups, with Group A showing a change of 0.85 ± 0.60 gm/dL and Group B showing 1.00 ± 0.85 gm/dL (p = 0.26). However, Group A had a statistically significant lower requirement for additional oxytocics during the procedures, with only 5 patients (5.9%) needing extra doses compared to 12 patients (14.1%) in Group B (p = 0.04).

The mean length of surgery duration was comparable between Group A (65.5 ± 12.0 minutes) and Group B (66.3 ± 11.5 minutes) (p = 0.45). Additionally, there was no significant difference in the requirement for blood transfusions between the two groups, as detailed in Table 3.

**Table No. 3: Outcome measures.**

| Variable | Group-A (n=85) | Group-B (n=85) | T-statistic, p-value |
|---|---|---|---|
| Blood volume (mL) | 650 ± 190 | 740 ± 220 | 2.44, 0.02 |
| Before CS hemoglobin in gm% | 11.75 ± 1.30 | 11.65 ± 1.45 | 0.56, 0.58 |
| After CS hemoglobin in gm% | 10.90 ± 1.25 | 10.60 ± 1.50 | 1.05, 0.30 |
| Hemoglobin difference | 0.85 ± 0.60 | 1.00 ± 0.85 | 1.08, 0.26 |
| Length of surgery in minutes | 65.5 ± 12.0 | 66.3 ± 11.5 | 0.45, 0.45 |
| Need for additional oxytocics | 5 (5.9%) | 12 (14.1%) | 4.12, 0.04 |
| Need for blood transfusion | 4 (4.7%) | 5 (5.9%) | 0.04, 0.84 |

Group A received intrauterine misoprostol (400 mg); Group B received per-rectal misoprostol (400 mg). Hb: hemoglobin. A p-value of <0.05 is considered significant.

Maternal side effects are detailed in Table 4. The usual side-effects observed, were nausea/vomiting, headache, hyperthermia, metal-like taste, and dizziness, were similar between the two groups. But, the occurrence of shivering was greater significantly in Group A (20%) compared to Group B (3%), with a p-value of 0.001 (OR = 9.0, 95% CI: 2.5–32.3).

**Table No. 4: Comparison of the Side-effects between the two groups.**

| Variable | Group A (n = 85) | Group B (n = 85) | Chi-square stat, p-value | OR (95% CI) |
|---|---|---|---|---|
| Fever | 8 (9.4%) | 4 (4.7%) | 2.13, 0.14 | 2.1 (0.60–7.21) |
| Nausea, vomiting | 9 (10.6%) | 6 (7.1%) | 0.50, 0.48 | 1.56 (0.52–4.66) |
| Shivering | 17 (20.0%) | 3 (3.5%) | 14.82, 0.001 | 9.0 (2.5–32.3) |
| Headache | 5 (5.9%) | 3 (3.5%) | 0.61, 0.43 | 1.68 (0.31–9.05) |
| Metallic taste | 4 (4.7%) | 2 (2.4%) | 0.65, 0.42 | 2.00 (0.30–13.40) |
| Dizziness | 5 (5.9%) | 4 (4.7%) | 0.11, 0.73 | 1.25 (0.31–4.93) |

Group A received intrauterine misoprostol (400 mg); Group B received per-rectal misoprostol (400 mg). A p-value of <0.05 is considered significant.

# DISCUSSION

The prevention and treatment of PPH should be given top priority for all women undergoing vaginal or caesarean deliveries, especially for those who are anaemic or having conditions like preeclampsia and unable to tolerate even a small quantity of blood loss. When it comes to managing intraoperative and postoperative bleeding, misoprostol is just as useful as oxytocin. Misoprostol plus oxytocin has also been shown to reduce intra- and post-operative haemorrhage during cardioscopy (CS) more effectively than oxytocin alone. According to Ezra Sullivan[12], misoprostol's long-lasting influence on uterine contractility after oxytocin's first, fast effect on it could be the likely cause of the decrease in bleeding.

Misoprostol has been administered during CS by oral, buccal, sublingual, intrauterine, intravaginal, and rectal routes at different dosages ranging from 400 to 800 mg, according to a literature study. However, no prior research has examined the differences between the intrauterine and rectal routes of misoprostol delivery. Our results showed that, with means of 650 ± 190 mL and 740 ± 220 mL, respectively, the intrauterine misoprostol group (Group A) had considerably less average blood loss than the per-rectal group (Group B) ($p = 0.02$). Group A also required considerably fewer additional doses of oxytocics than Group B, with just 5 patients (5.9%) requiring additional treatment, compared to 12 patients (14.1%) in Group B ($p = 0.04$). QuirogaDıaz et al.[13] brought forward the idea of using intrauterine misoprostol to prevent PPH. On the other hand, they utilised 800 mg on 200 individuals in their study. Also, they reported few unfavourable incidents. The effectiveness of misoprostol, taken orally or sublingually, in lowering the quantity of blood loss following childbirth has been the subject of multiple research. According to certain studies, misoprostol 400 mg is just as successful as syntometrine or oxytocin, if not more so[14]. When combined with oxytocin, rectal misoprostol reduced intraoperative and postoperative blood loss, the mean decline in haematocrit level, and the need for further uterotonics[15]. Misoprostol inserted directly into the uterus cavity has the potential to promote faster and more efficient ripening by increasing local concentrations of the medication and so increasing its effectiveness. Our findings are supported by the possibility that this local effect lowers blood loss during surgery and reduces the need for further uterotonics. The difference in haemoglobin levels following surgery did not achieve statistical significance ($p = 0.26$), despite the fact that the mean haemoglobin levels before and after surgery were similar between the two groups. This result implies that misoprostol administration techniques may both provide sufficient pre-operative cervical ripening without appreciably affecting haemoglobin levels or raising the risk of anaemia following surgery.

# CONCLUSION

PPH was well managed with misoprostol administered via either of the two methods. On the other hand, when compared to the rectal route of administration, misoprostol administered intrauterine during CS is linked to a clinically significant decrease in intraoperative and postoperative blood loss. Furthermore, intrauterine mode of misoprostol administration can be suitably delivered intraoperatively with the only apparent side effect being temporary shivering.

**Author's Contribution:**

| | |
|---|---|
| Concept & Design of Study: | Maryam Shoaib |
| Drafting: | Firdous Ara, Momy Gul |
| Data Analysis: | Rehana Kamal, Samia Saifullah, Arifa Inayat |
| Revisiting Critically: | Maryam Shoaib, Firdous Ara |
| Final Approval of version: | By all above authors |

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