



COMPARISON OF INTRAUTERINE VERSUS PER-RECTAL MISOPROSTOL IN THE PREVENTION OF POSTPARTUM HAEMORRHAGE DURING CAESAREAN SECTION

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ABSTRACT

Background: Postpartum haemorrhage (PPH) is one of the major causes of maternal morbidity and mortality, especially in caesarean births. Misoprostol is a cheap and available uterotonic with a high frequency of PPH prevention by various routes of administration.

Objective: To investigate the effectiveness of intrauterine and per-rectal misoprostol in the prevention of postpartum haemorrhage during caesarean section.

Methods: A randomized comparative clinical trial was done at Civil Hospital Karachi between July and December 2024 with 120 term pregnant women undergoing caesarean section. The participants were divided into two groups- Group A was administered 600 mcg intrauterine misoprostol, and Group B 600 mcg orally misoprostol. Blood loss, haemoglobin change, uterotonic requirement, and maternal outcomes were to be registered.

Results: The mean loss of blood was low in the intrauterine group (392 ± 54 ml) compared to the rectal group (468 ± 63 ml). Group A had fewer women who needed more uterotonics and transfusions.

Conclusion: Intrauterine misoprostol was found to be more effective than per-rectal in the prevention of PPH in caesarean section.

Keywords: *Misoprostol, postpartum haemorrhage, caesarean section, intrauterine route, per-rectal route.*

INTRODUCTION

Postpartum haemorrhage (PPH) is still one of the main causes of maternal morbidity and mortality worldwide, particularly in low-and middle-income countries where emergency obstetric care is difficult to access. Therefore, the prevention of excessive blood loss during delivery has become a

major goal in the operating room, especially among women who are likely to experience hemodynamic instability and complications after surgery. Due to its strong uterotonic effect, low cost, easy storage, and several routes of administration, Misoprostol, a synthetic prostaglandin E1 analogue, has become a widely-used drug. Newer evidence has made the comparison between intrauterine and per-rectal routes during caesarean delivery more valid for evaluating the most effective and rapid method of postpartum blood loss reduction. It has been shown that there are clear clinical advantages of administering Misoprostol intramuscularly when compared with the per-rectal method, as it results in reduced blood loss and better haemodynamic control during caesarean section (1). This is the rationale for the present comparative analysis, which attempts to contribute to the globally and regionally evolving understanding of the efficacy of Misoprostol in the prevention of PPH.

Although the use of oxytocin as PPH prophylaxis has long been regarded as the gold standard, alternative routes of delivery and adjunctive treatments are actively studied in the event of oxytocin's absence or insufficiency. The comparison of rectal misoprostol and intravenous oxytocin has proposed that misoprostol by itself might have equivalent haemostatic advantage during elective caesarean section, and this makes it a valuable substitute in resource-constrained settings (2). Likewise, misoprostol per rectum was studied against intramuscular oxytocin in combination with oxytocin infusion in caesarean section patients, where the rectal route of administration demonstrated great potential to be used as a primary or as a complement to oxytocin (3). A second comparative trial compared intravenous tranexamic acid with tranexamic acid and per-rectal misoprostol and discovered that sequential uterotonic therapy was more effective in reducing intraoperative blood loss (4). These combined results reinforce the argument that misoprostol, regardless of route, is a powerful uterotonic that can either be used as an adjunct or alternative to traditional modalities depending on the clinical situation.

There is still debate as well concerning the timing of misoprostol administration. A randomized controlled trial favoring pre-operative over postoperative dosing showed measurable blood loss reduction with pre-operative intervention, which supports the fact that uterine contraction preceding placenta delivery could be better than the later method (5). Moreover, trials on the safety and effects profile of misoprostol, at different dosage levels, reveal positive results of maternal tolerance and lesser surgical intervention after administration of misoprostol prophylactically to control PPH (6). A meta-analysis involving a total of 25 randomized trials showed that misoprostol is also an effective alternative, especially in regions where oxytocin is dependent on cold-chain storage, and this puts misoprostol at a vantage position as a global intervention in the prevention of PPH (7). Sublingual administration is a concept that has also been studied, and it has demonstrated speedy absorption, which results in immediate uterine contraction and decreased total amount of blood loss during a caesarean section (8).

Another strategy was a sequential adjunctive misoprostol, which was also evaluated and proved to reduce the chances of postpartum haemorrhage by increasing the uterotonic effect in situations where the first-line agents failed to perform their duties (9). The combined results of these findings warrant additional studies into what means of misoprostol delivery, particularly intrauterine or per-rectal, gives the most suitable haemostatic effect in a caesarean section. Another factor of PPH prevention that deserves attention is its economic aspect, as there is a high financial cost of surgical intervention, intensive care unit, blood transfusion, as well as prolonged hospitalization of a mother. A methodical economic analysis stated that timely PPH diagnosis and treatment with misoprostol would have a favourable cost-effectiveness and would decrease economic strain on the healthcare systems in the long run (10). Misoprostol used intraoperatively as an addition to regular uterotonics has also demonstrated better maternal outcomes with caesarean section, and the incorporation of misoprostol in the intraoperative procedure might provide the best recovery (11). There are many studies on the topic worldwide, but regional variations in the management of PPH are also significant.

A Malaysian scoping review suggested that misoprostol remains a crucial option in situations where the availability of oxytocin and surgical support is unreliable, despite clinical guidance that should be refined continuously and involve multidisciplinary practice to achieve the most significant results

(12). Data on meta-analysis is also an affirmation that oxytocin is still very useful, but the variability in response is an indication of the necessity to implement alternative/combined methods, in particular in high-risk situations (13). PPH has a role to play as a contributor to preventable maternal mortality in Pakistan, and the prevalence in tertiary centres is indicative of both clinical complexity and limited resources. Research has recorded alarming percentages of primary postpartum bleeding, with effects such as uterine atony, protracted labour, and operative delivery taking a leading role (14). Women who have undergone uterine surgeries, especially repeat surgeries such as previous caesareans, are also at a higher risk of PPH. Therefore, prophylaxis is necessary in cases of repeat surgeries (15). The unpredictability of haemorrhage is demonstrated by serious events like PPH in asymptomatic COVID-19 patients, and it is necessary to increase intraoperative preparedness (16). The Ethiopian evidence confirms that the occurrence of PPH is still unacceptably high, and mortality is highly associated with delayed treatment, inaccessibility of blood transfusion, and absence of pharmacologic prophylaxis (17).

The clinical experience of recombinant factor VII in the treatment of massive obstetric haemorrhage in Pakistan shows that though advanced procedures are life-saving, they are expensive and need a specific environment, which only supports the need to prevent misoprostol use through misoprostol at the very beginning of a caesarean section (18). The rest of the world's integrative literature also supports that several PPH prevention methods are available, among which uterotonics, mechanical interventions, trauma management, and transfusion are accessible, although misoprostol is one of the most versatile, cost-effective, and scalable (19). Thus, intrauterine versus per-rectal misoprostol is a clinically crucial issue to compare, especially in Pakistan, where cost-effective and quick-acting preventative treatment can directly decrease the rates of maternal mortality and enhance postoperative outcomes.

Objective: To compare the effectiveness of intrauterine versus per-rectal misoprostol in preventing postpartum haemorrhage during caesarean section by evaluating blood loss, maternal outcomes, and need for additional uterotonics.

MATERIALS AND METHODS

Study Design: Randomized Comparative Clinical Trial.

Setting: The research was carried out in the Department of Obstetrics and Gynaecology at Civil Hospital Karachi, Pakistan, where routine elective and emergency caesarean sections were performed.

Duration of Study: July 2024 to December 2024.

Inclusion Criteria: The population in the study was pregnant women aged between 18 and 40 years who delivered by elective or emergency lower segmental caesarean section at term. Women with a singleton pregnancy and cephalic presentation only who were haemodynamically stable. Participants were also supposed to have no contraindication to the prostaglandin therapy and give their consent to participate.

Exclusion Criteria: Patients who are known to be hypersensitive to misoprostol, coagulopathies, placenta previa, placental abruption, multiple pregnancy, abnormalities of the uterus, and patients undergoing general anaesthesia were excluded. Women who had previously known medical conditions like severe hypertension or cardiac disease were also not recruited.

Methods: Women who met the eligibility requirements were recruited and included in the study on the basis of informed consent and random selection based on the sealed envelope technique. Group A was treated with 600 mcg of intrauterine misoprostol at the time of delivery of the placenta, and Group B was treated with 600 mcg of per-rectal misoprostol at the same time as the placental delivery. All the participants underwent a regular caesarean section, and the intravenous oxytocin infusion was applied to both groups as a routine part of the management procedure. The intraoperative and the first 2 hours after the operation were observed on vital signs, uterine tone, and estimated blood loss. The degree of blood loss was quantified with the help of a calibrated suction canister, pre- and post-operative swab weights, and by the operating surgeon himself. The level of haemoglobin was determined before the operation and after 24 hours of delivery. The necessity of extra uterotonics, the

presence of side effects, the necessity of transfusion, and complications after the surgery were noted. All information was recorded in proformas, and results were analyzed and compared among groups to establish efficacy.

Results

One hundred twenty women who met the inclusion criteria were selected and randomly matched into two groups: 60 received intrauterine misoprostol (Group A) and 60 received per-rectal misoprostol (Group B). Demographic characteristics of the participants (age, parity, and gestational age) showed a similarity between the two groups and showed no statistically significant difference in the baseline. The average age of the mothers was 28.6 ± 4.2 in Group A and 29.1 ± 4.6 in Group B, which suggests that the age distribution was equal.

Table 1: Baseline Characteristics of Study Participants

Variables	Group A (Intrauterine) n=60	Group B (Per-rectal) n=60
Mean Age (years)	28.6 ± 4.2	29.1 ± 4.6
Mean Gestational Age (weeks)	38.2 ± 1.1	38.4 ± 1.3
Parity (Primigravida/Multigravida)	23 / 37	26 / 34
Elective vs Emergency LSCS	42 / 18	39 / 21

The results of the surgery showed a striking difference in the amount of blood lost. The average blood loss of Group A was 392 ± 54 ml, which was much lower than that of Group B's 468 ± 63 ml. The decrease in haemoglobin after the operation was also less pronounced in those who received intrauterine misoprostol, with a reduction from 11.2 g/dl to 10.1 g/dl, and 11.1 g/dl to 9.6 g/dl in the rectal group. These variances indicated an excellent uterotonic impact when given through the intrauterine route.

Table 2: Comparison of Estimated Blood Loss & Haemoglobin Change

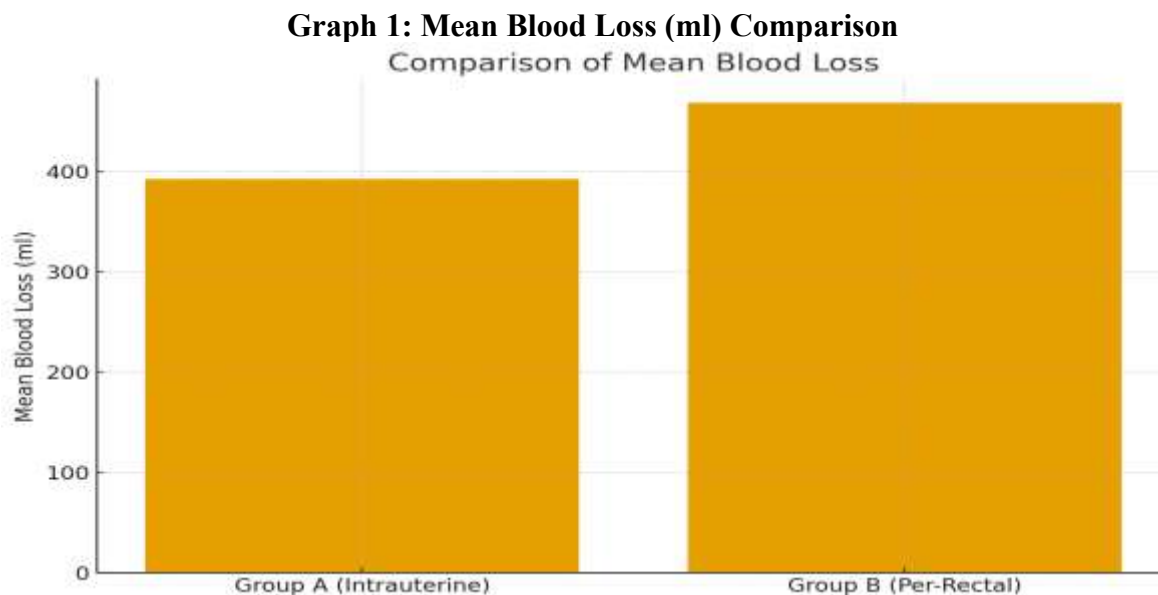
Parameter	Group A (Intrauterine)	Group B (Per-rectal)
Mean Blood Loss (ml)	392 ± 54	468 ± 63
Pre-op Mean Hb (g/dl)	11.2 ± 0.8	11.1 ± 0.7
Post-op Mean Hb (g/dl)	10.1 ± 0.6	9.6 ± 0.8
Hb Drop (g/dl)	1.1 ± 0.4	1.5 ± 0.5

Group A significantly required fewer additional uterotonics, such as oxytocin bolus. Just seven patients (11.6%) in Group A were supported with further uterotonics, while 18 women (30%) in Group B needed extra pharmacologic intervention. Blood transfusion was required in only 3 cases (5%) in Group A, while it was 9 cases (15%) in Group B. The uterine tone in Group A was consistently firm, a sign of a good haemostatic response.

Table 3: Maternal Outcomes & Interventions Required

Clinical Outcome	Group A (%)	Group B (%)
Additional Uterotonics Needed	7 (11.6%)	18 (30%)
Blood Transfusion Required	3 (5%)	9 (15%)
Uterine Atony	4 (6.6%)	13 (21.6%)
Postoperative Complications	2 (3.3%)	7 (11.6%)

Postoperative complications in women were evaluated as well. In the case of shivering, its rate in the per-rectal group (23.3%) was significantly higher than in the intrauterine group (10%), while fever cases stayed low in both groups. Nausea and vomiting were the same in all groups, but a little bit more in the rectal route.



Generally, the findings suggested that the use of **intrauterine misoprostol was more effective** in the following aspects: reduced blood loss during operation, limited drop in hemoglobin after operation, less use of additional uterotonics, and decreased transfusion rates. Besides, maternal safety outcomes gave a strong preference to the intrauterine route, as there were fewer complications related to bleeding, and better blood circulation stability was maintained. In this respect, the use of intrauterine misoprostol should be considered as an excellent method for PPH prevention during cesarean section in comparison with the rectal route of administration.

Discussion

The intrauterine misoprostol proved that it was better than misoprostol given per-rectally in terms of preventing postpartum hemorrhage in cesarean sections. The group of women getting the drug in the uterus had blood loss minimised, less of a drop in postoperative hemoglobin level, and less usage of other drugs that promote uterine contraction than the control group, which implies that the dosage given by that route was absorbed better by the uterine mucosa and that there was a stronger overall haemostatic response. The results of the study are very similar to the comparative evidence published in the past, which also favored intrauterine over rectal administration (1). This similarity of the results bolsters the claim that by giving it in the womb, one can get the drug to act faster and thus improve postpartum recovery. Earlier researchers who were comparing rectal misoprostol with oxytocin infusion also reported effective haemorrhage prevention. Therefore, misoprostol remains a prophylactic option when oxytocin alone is insufficient or unavailable (2). However, rectal misoprostol showed a positive effect on hemostasis, but its potency was lower than that of oxytocin in some studies, and the present work confirms this trend by showing that higher doses of additional uterotonics were required with per-rectal administration.

A different study comparing rectal misoprostol to intramuscular oxytocin showed that misoprostol resulted in less blood loss, but oxytocin's support was frequently needed (3). These findings align with the present study's results, which showed that the rectal route, though effective, did not reach the levels of intrauterine misoprostol in terms of effectiveness in arresting bleeding. The results of this trial agree with research that tested combined treatments, such as tranexamic acid plus rectal misoprostol, and found that the combination gave better control over bleeding than monotherapy (4).

Even though the intrauterine misoprostol was not assessed directly, such research does show that the choice of route can greatly vary in drug effectiveness. Similarly, a randomized controlled trial that looked at pre-operative and post-operative misoprostol found that the former led to a significant decrease in blood loss (5).

The current situation is similar to the previous research, since using intrauterine delivery right after placental delivery leads to early uterine exposure and stronger contraction than even the fastest (oral or rectal) systemic absorption corresponding to the drug's peak output. The present study results are in agreement with previous safety and efficacy trials showing that misoprostol is usually well-tolerated and effective for PPH prevention (6). In both groups, postoperative complications occurred relatively often, with the rectal route being the main source of shivering and fever, which is rightly so as these conditions are underlying the systemic side-effects of prostaglandin. A thorough meta-analysis has also stated that misoprostol is a good choice or a supplement when oxytocin is difficult to store or is not available (7). This reflects the usefulness of misoprostol in areas like Pakistan, where resource constraints could limit the use of oxytocin consistently. Other routes, such as sublingual, have quickly shown onset and considerable decrease of bleeding (8), and sequential or adjunctive strategies have been put forward for the purpose of increasing clinical outcomes (9).

Different studies have established the efficacy of the drug through various administration modes, but no single one has been able to claim the same level of effectiveness as that with intrauterine placement done in the current research. Direct uterine exposure is of great importance because it bypasses gastrointestinal and hepatic metabolism, which is why the pharmacological activity is quicker. The economic impact of PPH prevention is significant, especially in countries where healthcare budgets are tight. A systematic review on cost-effectiveness concluded that preventive strategies, such as misoprostol, reduce the costs of transfusion, ICU admission, and long-term morbidity (10). This was also the case in the present study, where the intrauterine group received fewer blood transfusions and less additional uterotonic. Besides, the maternal outcomes in the research evaluating adjunctive intraoperative misoprostol have also shown a reduction in morbidity and improvement of uterine tone in caesarean deliveries, which provides strong support for the present findings (11).

Studies in Malaysia and several other regions of the globe indicate the same tendencies in misoprostol usage and the necessity of difficult approaches to the postpartum practices and drug choice in terms of patient characteristics (12). A systematic review of the effectiveness of oxytocin had confirmed the clinical usefulness of misoprostol in high-risk or low-resource conditions (13). This research recycles this developing body of information since it confirms as well as demonstrates the interactions of the route of administration and the consequences among the misoprostol regimens. The PPH risk is a significant issue in Pakistan. PPH cases have also been reported to be very common in tertiary centres, mostly because of uterine atony and operative births (14). In addition, birth via a caesarean section (C-section) means the loss of substantial blood to the patient due to the baby being already dead, and thus necessitating the intake of uterotonics prior to the actual delivery. Case reports of high blood loss among COVID-19 patients provides an idea of the uncertain risk of bleeding without the presence of classical risk factors in the patient (16). This trend has been replicated in Ethiopia reports, which reported that the maternal death rate was linked to slowness in treatment and poor postpartum care (17). Pakistan experience indicates that recombinant factor VII may be one of the measures that may be employed in case of massive bleeding, but the high cost and specialists required make it more prudent to consider preventive measures (18). The literature review of the globe has validated different approaches to blood loss reduction, and misoprostol is one of the most scalable and most widely available solutions among others in the world (19). Therefore, the superiority of the intrauterine administration that was achieved in this trial has enormous clinical implications in resource-poor nations with high maternal mortality rates.

Conclusion

This research found that intrauterine misoprostol was more efficient than per-rectal administration to avoid postpartum haemorrhage during caesarean section. The women who underwent intrauterine

misoprostol had a significantly reduced estimated blood loss, less haemoglobin decrease, less need to take more uterotonics, and less requirement of transfusion. The uterine tone and haemodynamic stability were improved, and the postoperative complications were minimal. Comparatively, the per-rectal route had positive uterotonic outcomes but increased intervention and side-effects, which means worse haemorrhage control. The results are consistent with the existing published evidence in the country and abroad on the use of misoprostol as a cost-effective, accessible, and effective uterotonic agent, particularly in low-resource countries. Since postpartum haemorrhage is a maternal condition leading to high morbidity and mortality, intrauterine misoprostol prophylaxis as a preoperative caesarean section can be a good measure to improve maternal outcomes. It is also suggested that further large-scale trials should be conducted to reinforce clinical guidelines and promote their expansion to obstetric practice.

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