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

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Abstract

Introduction: Postpartum Hemorrhage, or PPH, is one of the most common causes of maternal mortality and morbidity, mostly in the developing world. Misoprostol is a dry prostaglandin E1 analog that is commonly used for the preve ntion of PPH. However, the practical route of administration during cesarean sections is still debatable.

Objectives: To comparatively determine whether intrauterine and per-rectal misoprostol are more effective and safer for the prevention of PPH during cesarean sections.

Materials and Methods: The quantitative study designed in this research was a randomized controlled trial conducted at Khyber Teaching Hospital Peshawar, Pakistan with 200 samples, where only females with planned cesarean sections were selected. To facilitate the procedure, participants was given 600 mcg of misoprostol through intrauterine or per-rectal approach. The amount of blood loss, the hemoglobin concentrations, and the side effects were evaluated.

Results: Compared to the control group, intrauterine misoprostol was associated with less intraoperative blood loss (450 ± 50 mL vs. 500 ± 70 mL; $p = 0.01$) and lower decrease in hemoglobin (1.2 ± 0.4 g/dL vs. 1.6 ± 0.5 g/dL; $p < 0.001$). Complications were reported to be less in the intrauterine group than in the extra amniotic group (18% compared to 32%; $p = 0.02$).

Conclusion: Intrauterine misoprostol is more effective and safe than the per-rectal one for the prevention of PPH, especially during a cesarean section.

Keywords: Postpartum hemorrhage, misoprostol, intrauterine, per-rectal, cesarean section.

INTRODUCTION

PPH has been recognized as one of the most important causes of maternal mortality, including in developing countries. This prevalence can make milestones the best measure of care while delivering babies, particularly through cesarean sections. This study also showed that misoprostol was effective and safe compared with oxytocin when used as a selective uterotonic agent to control PPH. This particular type of storage facility entails some drive and advantages, including administration convenience and cost, as well as the ability to maintain constant temperatures at room temperatures (1). The purpose of this paper is to evaluate the effectiveness and differences between the intrauterine and the per-rectal administration of misoprostol during cesarean sections for the prevention of PPH within the confines of a health facility. The classical cesarean section is believed to cause an increase in the risk of PPH due to uterine atony, surgical interventions, or other reasons. The impact of misoprostol as a measure for controlling blood loss in the different routes of administration observed has been thought sufficient to some extent. Shah et al. (2021) determined that rectal misoprostol provides preventive measures for PPH with similar efficacy as intravenous oxytocin (1). Likewise, Awoleke et al. (2020) also mentioned the benefits of misoprostol, especially for rural health facilities, since the equipment and supplies used need to be stored properly (2). These discoveries have channeled further studies into the mechanisms of administration routes for the purposes of optimizing these findings.

The accessibility of misoprostol through other administration routes differs a lot depending on the pharmacokinetics and its therapeutic impact. The administration through the per-rectal route provides rapid absorption and maintains the requisite plasma level of the drug, which makes it more desirable in many cases (3). Intrauterine treatment, on the other hand, acts directly in the uterine area, and hence there are fewer likelihoods of the woman developing side effects such as rigors and pyrexia. Junardi and Awaloei (2023) state that the route of administration must be selected for each patient. For instance, the efficacy of misoprostol, besides its complications, may vary according to the route of administration (4). Such variations necessitate enhanced comparative data when handling clinical practice. In many of the studies conducted, the efficacy and safety of the use of misoprostol has been evaluated in various settings. Akter et al. also revealed that misoprostol can be successfully given to prevent PPH, and it reportedly had fewer side effects (5). Therefore, Mishra et al. (2021) advocated for enhanced established selective sequential administration to improve its efficacy with fewer side effects (6). However, there is little information on its use in the cesarean section, especially with regard to the intrauterine and per-rectal approaches, which warrants further studies to establish the standard prescriptions for this method.

Consequently, the decisions to implement the PPH prevention methods have to be made depending on their efficacy, economic feasibility, and accessibility due to resource constraints. Matloob et al. (2021) described that such drugs include Misoprostol, which meets these criteria by comparing it with tranexamic acid, pointing out that it was cheaper in preventing PPH (7). Moreover, Ginnane et al. (2024) performed a systematic review focusing on the cost difference between Misoprostol and other uterotonics, stressing its effectiveness in LMICs (8). These economic considerations are well recognized, especially in Pakistan, due to the limited availability of health resources. Particularly, the existence of previous uterine surgeries complicates preventive measures for PPH, as women with such a history have increased levels of uterine scar tissue weakness. Mohamed Aboul Fotouh et al. (2024) pointed out the increased PPH incidences in such cases and also called for special measures to address them, especially in this higher-risk group (9). Due to these measures, Misoprostol has the potential to fix these challenges to meet various administrations and appears to be vital in the clinical aspects.

PPH remains one of the leading causes of maternal morbidity and mortality but has become a progressive problem in many countries, including Pakistan. Tiruneh et al. (2022) described the burden of PPH in Ethiopia and similar contexts, stating that such is also seen in many other low-income countries (10). Misoprostol is a low-cost tool and, when used as part of routine antenatal and postnatal care, can greatly contribute to reducing the morbidity and mortality resulting from PPH. Hathila et al. (2020) also conducted a survey of the drugs that are needed to prevent PPH, and the investigations

demonstrated that there was an improvement in the utilization of misoprostol due to its availability in tertiary care hospitals (11). Literature that described details of the comparative analysis of the outcomes of misoprostol given through different routes was useful in its practical application. Khan et al. (2020) compared misoprostol and dinoprostone for induction of labor, where the management of the routes influenced the clinical effect. Similarly, Abd El-Wahab et al. (2020) sought to assess the effects of carbetocin along with rectal nectin misoprostol where investigation revealed that the latter was effective in managing PPH through blood loss occurring in the third stage of labor (13). Further researches are required for the better implementation of misoprostol in the outcome of cesarean section.

Additionally, Najeeb et al. (2022), in sublingual and per rectal misoprostol vs. Oxytocin meta-analysis, reported that, although both are comparable regarding success rate, misoprostol has benefits such as no significant side effects, is comfortable to use, and relatively cheaper (14). In the same regard, Gohar et al. (2020) postulated that sublingual misoprostol in the prevention of PPH is effective and suitable (15). Although this background creates an impression of proper administration and usage of misoprostol, the change resulting from intrauterine and per-rectal administration during the cesarean sections is slightly blurred. This study aims to address this issue by evaluating the two routes in a methodologically sound approach that targets, among other things, the efficiency, security, and practicability of the two approaches in clinical operations. Thus, it seeks to contribute to the improvement of the preferred protocols for the prevention of PPH in CS to further improve maternal health in Pakistan and other countries.

Objective: To assess the effectiveness, side effects, and feasibility of using intrauterine and per-rectal misoprostol in the prevention of postpartum hemorrhage in actual operating cesarean sections in a clinical area in Pakistan.

MATERIALS AND METHODS

Study Design: This study is a randomized controlled trial investigating the effectiveness and side effect profiles of intrauterine and per-rectal misoprostol in the prevention of PPH after CS.

Study setting: The research took place at Khyber Teaching Hospital Peshawar, Pakistan, which is an extensive health-providing teaching hospital with well-developed obstetrics and maternity units.

Duration of the study: The study took place for 6 months starting from January, 2024 to June, 2024.

Inclusion Criteria:

The participants in this study were pregnant women attending the study hospital for elective and or emergency cesarean sections. Inclusion criteria included women who were 18 to 40 years of age, had a singleton pregnancy at term, were defined as 37 to 42 weeks of gestation, and did not have a history of coagulopathy or known hypersensitivity to prostaglandins. This included all women who remained of stable and comparable hemodynamic status pre-operatively and had no contra-indications to either regional or general anesthesia. All participants in the study voluntarily agreed to take part and signed consent forms to show that they understood the nature and design of the study.

Exclusion Criteria

Patients who might have had either multiple gestation pregnancies, uterine anomalies, or placental disorders like placenta previa or placental abruption were also excluded from the study. The study eliminated those individuals with severe anemia, cardiovascular diseases, and conditions affecting the liver and kidneys to reduce bias. Further, the respondents who had taken over-the-counter uterotonics within 24 hours prior to us or those who did not consent to participate in the study were excluded. Such exclusion minimizes the risks of participating individuals and the credibility of the study findings.

Methods

Participants were randomly assigned into two groups: one offers intrauterine misoprostol (600 mcg), and the other offers per rectal misoprostol (600 mcg) after the delivery of the baby through cesarean section. For random assignment, the participants were assigned an identification number generated by a computer program. The parturient and control groups both received oxytocin intravenous infusion 10 IU as a part of general practice. A quantitative assessment of blood loss was done by using suction equipment and weighing any material that was soaked in blood. Hemoglobin levels of patients were taken before surgery and within the next 24 hours to determine the degree of change.

These medical recordings were taken for several days and included checking the vital signs at least once every 4 hours in order to observe any signs of distress or fever, shivering, or gastrointestinal manifestations. The main dependent variable was the quantity of blood loss that the patients incurred during and post-procedure. Secondary variables consisted of extra doses of uterotonic agents, transfusion requirements, and side effects. Quantitative data were analyzed via statistical software, and the significance level was set at $p < 0.05$. This study received approval regarding its ethical consideration before it was conducted.

RESULTS

A total of 200 women were enrolled and randomly assigned into two groups: 100 received intrauterine misoprostol, while 100 received per-rectal misoprostol. Maternal age, gestational age, and preoperative hemoglobin values were similar between the groups, which validates the comparability of the study groups. The mean intraoperative blood loss was significantly lower in the intrauterine group (mean ± SD: The caloric water intake was also significantly different between the two groups, with the mammography group consuming less (mean ± SD: 450 ± 50 mL) than the per-rectal group (mean ± SD: 500 ± 70 mL; $p = 0.01$). The decrease in mean values of hemoglobin concentrations 24 hours after surgery was also significantly smaller in the intrauterine group (1.2 ± 0.4 g/dL than in the per-rectal group (1.6 ± 0.5 g/dL; $p < 0.001$).

Group	Intraoperative Blood Loss (mL)	Postoperative Hemoglobin Decrease (g/dL)
Intrauterine Misoprostol	450 ± 50	1.2 ± 0.4
Per-Rectal Misoprostol	500 ± 70	1.6 ± 0.5
p-value	0.01	<0.001

Use of Additional Uterotonics

In the intrauterine group, 76% of the patients needed additional uterus contraction stimulating agents compared to 90% of the per-rectal group ($p = 0.04$). The percentage of women who received an additional uterotonic was highest among those who received intravenous oxytocin. Intrauterine procedure required blood transfusion in 6% of patients while per-rectal in 10% of patients, compared between the two groups there was no significant difference in blood transfusion requirement ($p = 0.28$).

Outcome	Intrauterine Group (%)	Per-Rectal Group (%)	p-value
Additional Uterotonics	12	20	0.04
Blood Transfusion	6	10	0.28

Adverse Effects

There was a higher rate of side effects among the per-rectal group, with fever, shivering, and diarrhea being observed in 32% of the patients while only 18% in the intrauterine group $p = 0.02$. Among the side effects, trembling was reported most commonly in both groups. There were no cases of severe complications like uterine rupture or thromboembolic events in the group.

Adverse Effect	Intrauterine Group (%)	Per-Rectal Group (%)	p-value
Fever	8	15	0.08
Shivering	10	14	0.20
Diarrhea	0	3	0.09
Any Adverse Effect	18	32	0.02

Thus, the intrauterine route of misoprostol seems to offer more benefit in terms of decreased postoperative blood loss and hemoglobin drop and fewer side effects compared to the per-rectal route. Both the intrauterine and oral administration of misoprostol were proven to be effective in the prevention of postpartum hemorrhage, though the intrauterine use of misoprostol showed better safety and clinical results, speaking more on the administration of misoprostol during cesarean sections.

DISCUSSION

However, postpartum hemorrhage (PPH) continues to be a major cause of maternal morbidity and mortality, especially in the developing world. Preventive measures are vital in the reduction of maternal mortality, particularly in the peri partum period, especially during cesarean section, where the possibility of PPH is already higher. This research aimed to establish the effectiveness, safety, and feasibility of using intrauterine and per-rectal misoprostol methods. The study also established that using intrauterine misoprostol was safer in the operating room since it had less intraoperative blood loss and postoperative hemoglobin drop than per-rectal misoprostol. The mean blood loss in the intrauterine group was lower, and this was supported by other studies that pointed out that intrauterine misoprostol is localized and does not cause general systemic effects (1, 4). This route enables rapid uptake and immediate effect to be exerted on the uterus with little systemic exposure and thus improves the contractile force of the uterus. On the other hand, oral administration, though as effective as per-rectal, showed a slightly slower response rate due to the difference in adsorption as established by Awoleke et al. (2).

The requirement for extra uterotonics was also lower in the intrauterine group, which indicates its efficacy. This is in line with the finding of Akter et al. (5), who noted that intrauterine misoprostol reduces supplementary preventive measures against uterine atony. However, the need for blood transfusion was not significantly different between the groups, but the intrauterine misoprostol seemed to have a better tendency to prevent severe PPH. Mishra et al. (6) stressed that blood transfusions should be reduced because they are expensive, and their usage is associated with certain complications like transfusion reactions or infections. Side effects as a loss-making factor should be taken into consideration when assessing the feasibility of any PPH prevention approach. In this study, the adverse effects, such as fever, shivering, and diarrhea, were more prevalent in the per-rectal group than in the other groups. This supports the opinion of Junardi and Awaloei (4), who said that rectal absorption of misoprostol causes dose-related side effects. On the other hand, the action of intrauterine misoprostol is localized, making systemic exposure significantly less dangerous. These side effects are usually mild and resolving, but more frequent in the per-rectal group might have an impact on patient acceptance.

Economic factors are another important factor that guides the choice of a PPH prevention strategy. The low storage temperature of Misoprostol also makes it cheaper and affordable, especially in developing countries, as argued by Ginnane et al. (8). Nevertheless, the route of administration might make a difference in the costs, especially in the need to add other drugs or address side effects. However, intrauterine Misoprostol eliminates the costly chance of requiring supplementary intervention and adverse effects. These findings are important in understanding the variation of stroke severity according to sample sources given limited health resources in countries like Pakistan. The effectiveness of PPH prevention strategies can contribute positively towards the downturn of

healthcare complications such as increased complications, prolonged hospital stay, and the high utilization of intensive care. In addition, Mohamed Aboul Fotouh et al. (9) pointed out that primary prevention programs should target special high-risk groups like women who have had prior uterine operations. Based on this study, intrauterine Misoprostol was found to be very useful in a variety of situations.

A literature review has shown that comparative analysis of different routes of administration of misoprostol has been helpful in the use of the drug in clinical practice. For instance, Khan et al. (12) showed that route choice indeed influences performance in labor induction and same goes for PPH prevention. Likewise, Najeeb et al. (14) and Gohar et al. (15) noted equivalent effectiveness of sublingual and rectal misoprostol with oxytocin stressing on the multirole of misoprostol. However, as mentioned in intrauterine administration, where the effects are localized, and the side effects are negligible, intrauterine administration has apparent advantages while performing Caesarean sections. However, there are several limitations to the findings. The study was carried out at a single tertiary care hospital, hence the findings may not be generalizable to other areas, especially rural areas with compromised healthcare facilities. Furthermore, to reduce confounding factors, the study used randomization yet did not collect data on delayed postpartum complications or patient satisfaction. Future studies should fill these gaps, particularly in terms of the subject's ethnic diversity and the assessment of post-intervention effects.

The results of this study have potential clinical application and policy implications. Intramniestic misoprostol should be one of the first lines of thought to be used for PPH prophylaxis during cesarean section, particularly in developing countries. Due to its higher efficacy and safety, together with the cost issues, it is appropriate to include this medication in standard obstetric protocols. However, the administration route should still be decided on a case-by-case basis depending on the patient's tolerance, risk, and clinical situation. Finally, the study of intrauterine misoprostol vs per rectal misoprostol also shows the possibility of the intrauterine approach being safer and more effective in preventing postpartum hemorrhage, especially in cases of cesarean sections. These findings add to the current literature on the use of misoprostol in obstetrics and stress the need for context-sensitive interventions that aim to enhance maternal care. Future research, meta-analyses of multicenter studies with long-term follow-up results of misoprostol, and cost analysis to determine the cost-effectiveness of this therapy in various clinical settings need to be done in order to provide better guidelines for misoprostol treatment.

CONCLUSION

In conclusion, this thesis showed that misoprostol administered intra-uterine was more effective and carried less risk than per-rectal administration in the control of postpartum hemorrhage in women who had undergone cesarean sections. The intrauterine administration method led to a marked decrease in intraoperative blood loss and a postoperative hemoglobin drop and also yielded low side effect rates such as fever and shivering episodes. Further, there was a decreased requirement for additional uterotonic agents in the intrauterine group, which shows that they are more effective in the management of uterine atony. These studies have shown the possibility of using intrauterine misoprostol as one of the best choices in preventing PPH, particularly in developing countries where factors such as cost and practicability are important. Even though both routes of administration had similar efficacy, intrauterine misoprostol has the advantages of fewer systemic side effects and more targeted action during cesarean deliveries. Subsequent research should concentrate on effectiveness over the long term and the possibility of scaling up intrauterine misoprostol in various healthcare organizations to reduce maternal mortality rates all over the world.

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