Randomized Controlled Trial of sublingual versus rectal Misoprostol in the prevention of primary postpartum hemorrhage

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Randomized Controlled Trial of sublingual versus rectal Misoprostol in the prevention of primary postpartum hemorrhage

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Abstract

Background: Over 25% of all maternal deaths, especially in low-income nations, are attributed to postpartum hemorrhage (PPH), in accordance with the World Health Organization (WHO). Most severe maternal morbidities, including extended hospital stays, the need for blood transfusions, and surgical operations that may result in the loss of reproductive function, are also caused by PPH.

Aim of work: To evaluate the efficaciousness of sublingual misoprostol (600 microns) vs the same amount given to patients as a rectum shortly after birth in reducing postpartum hemorrhage.

Patient and methods: Over the study's one year, the obstetrics and gynecology departments at El-Monira General Hospital and Al-Azhar University Hospitals will host a randomized prospective controlled clinical experiment. Two hundred women who gave birth vaginally or by C.S. were enrolled in this research and were split into 2 groups at random fashion divided into 100 patients of each group forming 2 subgroups representing V.D or C.S.

Results: The sublingual administration of misoprostol may present as a more favorable alternative due to its prompt absorption, extended duration of effect, and superior overall bioavailability when compared to the rectal route of administration.

Conclusion: The sublingual route of misoprostol administration is related to a lower frequency of PPH compared to rectal administration at the indicated dosage. Although the sublingual administration of misoprostol is linked with a higher occurrence of shivering and pyrexia, it was preferred by a greater number of women compared to the rectal route of administration.

Keywords: Sublingual; Rectal Misoprostol; Prevention; Primary Postpartum Hemorrhage

1. Introduction

WHO estimates that postpartum hemorrhage accounts for 25% of all pregnancy-related deaths worldwide, with low-income nations being the primary culprits. The bulk of severe maternal morbidities, including extended hospital stays, the requirement for blood transfusions, and surgical operations that may result in the loss of reproductive function, are also caused by PPH.

In the past, the term "postpartum hemorrhage" referred to an expected blood loss of over 500 ml following a vaginal delivery or over 1000 ml following a cesarean delivery. Today, however, this definition no longer applies. ACOG modified the definition of PPH in 2017 to consist of any woman who experiences blood loss in excess of 1000 mL and shows indicators of hypovolemia within twenty-four hours of giving birth.

Although this modification was made knowing that blood loss during vaginal birth is frequently overestimated, blood loss above 500 mL should be regarded as abnormal and may require intervention.
Bleeding that happens throughout the 1st day of birth is known as primary postpartum hemorrhage, and bleeding that happens between 24 hours and 12 weeks postpartum is known as secondary postpartum hemorrhage.6

Because of its potent uterine impact, misoprostol, an analog of PGE1, has been used to treat and prevent PPH; however, a consensus has not yet been reached regarding the best dosage or mode of administration.7

The efficiency of misoprostol, along with its ease of administration and storage, makes it a desirable option for use in resource-poor regions.8

In the majority of trials, misoprostol was administered either orally or rectally, and the dosages varied anywhere from 400 to 1000 ug.9

In 2019, the WHO Executive Guideline Steering Group (GSG) for Maternal and Perinatal Health recommendations gave top priority to updating the previous guidelines for distributing misoprostol to pregnant women in advance to prevent PPH in light of new research. Thus, the advice in this document takes precedence over the prior WHO recommendation found in the 2012 guideline, the WHO’s recommendations for the avoidance and management of PPH, with regard to PPH prevention.2

Misoprostol can cause a variety of adverse effects, including pyrexia, diarrhea, vomiting, and shivering. However, these symptoms are dose-related and self-limiting.10

Fascinatingly, misoprostol can be injected rectally, vaginally, orally, sublingually, or buccally. In order to prevent postpartum hemorrhage (PPH) after a cesarean delivery or spontaneous vaginal delivery, rectal misoprostol is commonly utilized. When compared to the rectal route of administration, sublingual misoprostol administration has a greater overall bioavailability, a longer duration of action, and a faster rate of absorption.11

This study compares the efficacy of misoprostol (600 micrograms) given sublingually to the same amount given per rectum to patients shortly after birth to reduce primary PPH.

2. Patients and methods

The obstetrics and gynecology departments at Al-Azhar University Hospitals and El-Monira General Hospital will host this randomized prospective controlled clinical trial for a year, from June 2022 to June 2023. Two hundred women who gave birth vaginally or by C.S. were enrolled in this research and were randomly split into two groups.

Group I (100 cases): Divided into 50 patients (post-C.S) and another 50 patients (post-vaginal delivery) received a dose of 600 ug misoprostol sublingually immediately after delivery.

Group II (100 cases): Divided into 50 patients (post-C.S) and another 50 patients (post-vaginal delivery) received 600 ugs of misoprostol per rectum.

The blood loss was measured as follows.

The following factors were used to quantify blood loss: AFV (ml) (C), weight differential of linen towels (g) (B) [weight of soaked linen towels (g) - weight of dried linen towels (g)], and volume of the suction bottle's contents (ml) (A). Blood loss during surgery (ml), therefore, equals (A+B)-C. It was noted how long the third stage of labor lasted, as well as the requirement for extra uterotonic medicines and blood transfusions. Following 24 hours, blood was drawn for hemoglobin estimation, and hospital records were examined to look for any instances of extra uterotonic usage or other issues such as blood transfusions.

Quantification of maternal blood loss is a team effort

Make a list of dry weights along with instructions on how to calculate blood loss for delivery goods that might get saturated in blood.

Start measuring blood loss as soon as the baby is delivered (before the placenta is delivered), and note how much fluid is gathered in a calibrated under-the-buttocks drape.

Remember that amniotic fluid, urine, and feces make up the majority of the fluid collected prior to placenta delivery. Subtract the amount of irrigation, if any, from the total volume of fluid collected.

Note the complete amount of liquid gathered in the drape beneath the buttocks.

To calculate the actual blood loss more precisely, reduce the preplacental volume of fluid from the post-placenta fluid volume. Remember that the majority of the fluid that is collected after the placenta is born is blood.

To calculate the total amount of blood loss or quantify blood loss, add the liquid volume caught in the drapes to the blood volume determined by weighing soaked items.

Weigh every item saturated in blood and every clot to find the total volume. One gram of weight equals one milliliter of blood loss volume.

The WET Object, Gram Weight-DRY equation, is utilized to determine the blood loss of an item saturated in blood. The milliliters of blood contained within an item are its gram weight.

Despite the fact that a milliliter is a unit of volume and a gram is a unit of mass, there is a straightforward 1-to-1 conversion between the two.12

The side effects of the misoprostol were assessed.

Fate of patients:
Primary outcome measures were specified prior to commencing
the study: blood transfusion, hemoglobin level
day 1 after delivery <6g/dl, measured blood loss ≥500 ml in 1 hour after enrollment, mean measured blood loss in 1 hour after enrollment, and side effects (pyrexia 38.5°C or greater, severe or moderate shivering one hour after enrolment).

Secondary outcome measures were blood loss greater than 1000 ml in an hour following enrollment, a blood transfusion, a hemoglobin level below 8 g/dl one day after delivery, extra uterotonics administered following enrollment, placenta removal by hand, removal of retained materials from conception, hysterectomy, and maternal death.

Inclusion criteria: Cephalic presentation, estimated fetal weight (EFW) within the average range (<4kg), singleton pregnancies, gestational age 37-41 weeks, primigravidae and multigravidas, and reactive non-stress test.

Exclusion criteria: multi-fetal pregnancy, previous uterine surgery, fetal macrosomia>4kg, and known hypersensitivity to misoprostol.

Intervention[s]: All cases subjected to the following before therapy:
Detailed medical history includes maternal name and age, gestational age, parity, residence, socioeconomic status, special habits, and any medical problems. Obstetric history: first day of last menstrual period, history of previous pregnancy& history of previous PPH and family history of similar conditions.

General physical examination, including Crucial information, includes blood pressure, pulse, and body temperature; pallor or jaundice; heart and chest examinations; the detection of blisters or swelling of the skin to rule out the presence of blood diseases or coagulation defects; and the calculation of BMI.

Abdominal & vaginal examination: represented by uterine tenderness and abdominal pain, the scar of previous laparotomies, fundal level and gestational age, and fetal viability.
Ultrasound examination by the 2-5 MHz abdominal probe.
Laboratory investigations (CBC, RBS, Rh-factor) and a 600 ug dose of misoprostol were given to 2 divided groups of patients.

Statistical Analysis
After being gathered, edited, coded, and entered, the data were added to IBM SPSS, a statistical tool for social science, version 20. The quantitative results were given as mean, standard deviations, and limits when their distribution was found to be parametric, whereas qualitative information was presented as numbers and percentages.

When comparing two groups with qualitative data, the Chi-square test or the Fisher exact test was utilized in place of the Chi-square test if any cell’s predicted count was less than five. Two independent groups with quantitative data and parametric distribution were compared utilizing the independent t-test. The confidence interval was 95%, and the margin of error was 5%. A p-value of <0.05 denotes significance (S), P>0.05 indicates non-significant (N.S.), and P<0.001 indicates highly significant (H.S.).

3. Results
Table 1: Socio-demographic characteristics of the participants versus route of treatment

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Route of administration</th>
<th>Test value</th>
<th>P-value</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 30</td>
<td>Group I: 52 (52.0%)</td>
<td>1.325</td>
<td>0.251</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>Group II: 54 (54.0%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 30</td>
<td>Group I: 48 (48.0%)</td>
<td>2.694</td>
<td>0.102</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>Group II: 46 (46.0%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>Group I: 28.35 ± 5.26</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Group II: 29.23 ± 5.55</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range Gestational age</td>
<td>Group I: 20–45</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parity</td>
<td>Group I: 22 (22.0%)</td>
<td>0.113</td>
<td>0.737</td>
<td>NS</td>
</tr>
<tr>
<td>Primipara</td>
<td>Group II: 24 (24.0%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multipara</td>
<td>Group I: 78 (78.0%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Group II: 76 (76.0%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Employment status</td>
<td>Group I: 16 (16.0%)</td>
<td>2.485</td>
<td>0.115</td>
<td>NS</td>
</tr>
<tr>
<td>Employed</td>
<td>Group II: 25 (25.0%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unemployed</td>
<td>Group I: 84 (84.0%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Education Primary</td>
<td>Group I: 36 (36.0%)</td>
<td>0.324</td>
<td>0.851</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>Group II: 33 (33.0%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secondary Tertiary</td>
<td>Group I: 53 (53.0%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Group II: 57 (57.0%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The average age in Group I was 28.35 ± 5.26, and the average age in Group II was 29.23 ± 5.55. Of the individuals in Group I, 52.0% were over 30 and 48.0% were under 30, while in Group II, 54.0% were over 30 and 46.0% were under 30. Regarding age, there was no significant variation among Group I and Group II. Also, Group I had an average gestational age of 37.84 ± 1.27, while Group II had an average gestational age of 37.56 ± 1.1. Regarding gestational age, there was no
significant distinction amongst Group I & II. In Group I, there were 22.0% Primipara, 78.0% Multipara, and in Group II, there was 24.0% Primipara and 76.0% Multipara. Regarding parity, there was no significant variation among Group I and Group II. Tilt 16.0% of Group I’s participants were employed; and 84.0% were unemployed; in contrast, 25.0% of Group II’s participants were employed, and 75.0% were unemployed. Regarding employment status, there was no significant variance between Group I and Group II. Comparing the educational attainment, 33.0% were primary, 57.0% were secondary, and 10.0% were tertiary in Group II, whereas 36.0% were primary, 53.0% were secondary, and 11.0% were tertiary in Group I. Regarding schooling, there was no significant variance among Group I and Group II.

Table 2: Clinical and obstetric characteristics of the participants.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Route of administration</th>
<th>0.010</th>
<th>0.024</th>
<th>S</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of PPH</td>
<td>Group I Sublingual n (%)</td>
<td>98 (98.0%)</td>
<td>100 (100.0%)</td>
<td>2.020*</td>
</tr>
<tr>
<td>Antepartum PCV (%)</td>
<td>Group II Rectal n (%)</td>
<td>2 (2.0%)</td>
<td>0 (0.0%)</td>
<td>0.569</td>
</tr>
<tr>
<td>≥33</td>
<td></td>
<td>74 (74.0%)</td>
<td>76 (76.0%)</td>
<td>-0.569*</td>
</tr>
<tr>
<td>&lt; 33</td>
<td></td>
<td>26 (26.0%)</td>
<td>24 (24.0%)</td>
<td>34.56±3.25</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>Duration of pregnancy (weeks) ≤40</td>
<td>96 (96.0%)</td>
<td>98 (98.0%)</td>
<td>0.031*</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>Duration of active phase of labour (hours) &lt; 3</td>
<td>4 (4.0%)</td>
<td>6 (6.0%)</td>
<td>1.154*</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>Duration of active phase of labour (hours) ≥12</td>
<td>94 (94.0%)</td>
<td>90 (90.0%)</td>
<td>4 (4.0%)</td>
</tr>
</tbody>
</table>

Table 2 shows that, In Group I; 98.0% of them were No History of PPH and 2.0% were History of PPH, while the Group II; All Patient were History of PPH, the average Antepartum PCV (%) in Group I were; 34.56 ± 3.25, while average Antepartum PCV (%) in Group II were 34.82 ± 3.21, In Group I; 74.0% of them were Antepartum PCV (%) ≥33 and 26.0% were Antepartum PCV (%) < 33, while the Group II; 76.0% of them were Antepartum PCV (%) ≥33 and 24.0% were Antepartum PCV (%) < 33, the average Duration of pregnancy (weeks) in Group I were; 38.30 ± 1.19, while average Duration of pregnancy (weeks) in Group II were 38.39 ± 1.02, In Group I; 96.0% of them were Duration of pregnancy (weeks) ≤40 and 4.0% were Duration of pregnancy (weeks) > 40, while the Group II; 98.0% of them were Duration of pregnancy (weeks) ≤40 and 2.0% were Duration of pregnancy (weeks) > 40, In Group I; 4.0% of them were Duration of active phase of labour (hours) < 3, 94.0% were Duration of active phase of labour (hours) 3-12 and 2.0% were Duration of active phase of labour (hours) > 12, while the Group II; 6.0% of them were Duration of active phase of labour (hours) < 3, 90.0% were Duration of active phase of labour (hours) 3-12 and 4.0% were Duration of active phase of labour (hours) > 12, In Group I; 100.0% of them were CCT and 100.0% were Uterine massage, while the Group II; 98.0% of them were CCT and 96.0% were Uterine massage.

Table 3: Primary and secondary outcome measures by route of administration.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Route of administration</th>
<th>Test value</th>
<th>P-value</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Out come</td>
<td>Group I Sublingual n (%)</td>
<td>94 (94.0%)</td>
<td>84 (84.0%)</td>
<td>5.107</td>
</tr>
<tr>
<td>Blood loss ≥500 ml</td>
<td>Yes</td>
<td>6 (6.0%)</td>
<td>16 (16.0%)</td>
<td>5.980</td>
</tr>
<tr>
<td>≥10% change in PCV</td>
<td>No</td>
<td>92 (92.0%)</td>
<td>80 (80.0%)</td>
<td>8.811</td>
</tr>
<tr>
<td>Secondary Out come</td>
<td>Yes</td>
<td>8 (8.0%)</td>
<td>20 (20.0%)</td>
<td>7.117</td>
</tr>
<tr>
<td>Blood loss after delivery (ml)</td>
<td>1 h</td>
<td>Means±SD</td>
<td>169.97±37.15</td>
<td>198.70±47.07</td>
</tr>
<tr>
<td></td>
<td>200-430</td>
<td>Range</td>
<td>100-250</td>
<td>120-275</td>
</tr>
<tr>
<td></td>
<td>24 h</td>
<td>Means±SD</td>
<td>253.53±62.34</td>
<td>318.19±76.32</td>
</tr>
<tr>
<td></td>
<td>250-520</td>
<td>Range</td>
<td>158-368</td>
<td>200-430</td>
</tr>
<tr>
<td>Pattern of PCV changes pre- and postpartum</td>
<td>Pre-PCV</td>
<td>Means±SD</td>
<td>35.46±2.73</td>
<td>35.49±2.72</td>
</tr>
</tbody>
</table>
In Group I; 6.0% of them were Blood loss ≥ 500 ml and 8.0% were ≥ 10% change in PCV, while the Group II; 16.0% of them were Blood loss ≥ 500 ml and 20.0% were ≥ 10% change in PCV, also the average Blood loss after 1 h in Group I were; 169.97 ± 37.15, while average Blood loss after 1 h in Group II were 198.70 ± 47.07the average Blood loss after 4 h in Group I were; 253.53 ± 62.34while average Blood loss after 4 h in Group II were 329.78 ± 60.02, the average Blood loss after 24 h in Group I were 392.21 ± 76.32, the average Blood loss after 24 h in Group II were 318.19 ± 70.66, while average Blood loss after 4 h in Group I were; 31.65 ± 3.01, while average Pre-PCV in Group I were; 35.46 ± 2.73, while average Pre-PCV in Group II were 35.49 ± 2.72and the average Post-PCV in Group I were; 31.65 ± 3.01, while average Post-PCV in Group II were 31.43 ± 2.91, so, There was highly statistically significant difference between Group I and Group II regarding Blood loss after delivery (ml), and there was no statistically significant difference between Group I and Group II regarding Pattern of PCV changes pre- and postpartum. In Group I; 10.0% of them were Need for additional uterotonic, 2.0% were Vaginal bleeding ≥ 1000 ml and 2.0% were Need for blood transfusion, while the Group II; 20.0% of them were Need for additional uterotonic, 2.0% were Vaginal bleeding ≥ 1000 ml and 4.0% were Need for blood transfusion, In Group I; 88.0% of them were Satisfied, 58.0% were Shivering, 2.0% were Headache, 2.0% were Diarrhoea, 12.0% were Fever, 10.0% were Pyrexia and 1.0% were Death, while the Group II; 72.0% of them were Satisfied, 16.0% were Shivering, 2.0% were Headache, 2.0% were Diarrhoea, 4.0% were Fever, 0% were Pyrexia and 1.0% were Death, There was highly statistically significant difference between Group I and Group II regarding Satisfied and Shivering, and there was statistically significant difference between Group I and Group II regarding Fever and Pyrexia, and there was no statistically significant difference between Group I and Group II regarding Headache, Diarrhea and Death.

4. Discussion

In the present investigation, no significant variations were identified between the two groups concerning age, parity, and duration of pregnancy in weeks.

This agreed with Gohar et al. There was no significant variance observed in demographic characteristics, such as age, parity, and gestational age, between the two groups. In this trial, the researchers aimed to evaluate the effectiveness of administering 400 μg of rectal misoprostol with an intravenous infusion of 30 IU of oxytocin as part of the standard active management approach for PPH. Additional data have been reported that need to be more consistent with the outcomes of our investigation. A trial by Vodouhe et al. examined the effects of 600 g of sublingual misoprostol and 20 units of intravenous oxytocin given at the time of umbilical cord ligation. There was not a significant distinction in average blood loss among the misoprostol & oxytocin groups. The present study observed a substantial and statistically significant rise in the loss of blood after delivery (measured in milliliters) among participants in Group I in contrast to those in Group II at 1 hour, 4 hours, and 24 hours postpartum.

This disagreed with Awoleke et al. The study demonstrated that the sublingual Group...
had significantly reduced mean blood loss after the first, fourth, and twenty-fourth hour, as well as a significantly lower mean percentage change in hematocrit values compared to the rectal Group. This phenomenon may be attributed to its expedited onset of action, extended duration of effect, and enhanced serum absorption in comparison to rectal administration Adanikin et al., 14

In this research, it was observed that 10.0% of participants in Group I required additional uterotonics, but in Group II, this proportion was 20.0%. There wasn’t any significant disparity observed between Group I & Group II in terms of the requirement for supplementary uterotonics, the occurrence of vaginal bleeding equal to or above 1000 ml, and the necessity for blood transfusion.

This study found a significant increase in acceptance of the route of administration and shivering in Group I compared to Group II. Additionally, there was a significant increase in fever and pyrexia in Group I compared to Group II. However, there were no significant distinctions among Group I and Group II in terms of headache, diarrhea, and death.

This is not in line with Awoleke et al. The individual or Group responsible for reporting the most frequently observed adverse reactions associated with the medication was able to identify shivering and pyrexia as the most common side effects. Furthermore, it was determined that both of these side effects were much more prevalent following sublingual administration of the medicine.11

Multiple studies have provided evidence of the therapeutic superiority of misoprostol compared to oxytocin in reducing the occurrence and volume of postpartum hemorrhage (PPH). Hence, the concurrent administration of both medications is anticipated to yield a more favorable outcome. This assertion was substantiated by a single study that conducted a comparison between the administration of a combination dosage of 600-μg oral misoprostol and 20 IU intramuscular oxytocin and the individual administration of either misoprostol or oxytocin alone during cesarean birth. The findings of this study indicated that the combined Group exhibited the lowest mean quantity of blood loss.15

Several randomized, placebo-controlled studies have also looked into this phenomenon. After receiving standard uterotonics, eligible women in these studies were randomly randomized to receive either 400 mg of misoprostol (672 women) or a placebo (673 women) sublingually. Researchers discovered that when misoprostol was given alongside standard uterotonics, maternal outcomes improved. There was less blood loss after delivery, and women needed less oxytocin and hysterectomy. However, it should be noted that these observed differences did not reach statistical significance.16

The findings of this study provide empirical evidence in favor of the premise that the concurrent administration of both medicines is anticipated to yield reduced amounts of bleeding after cesarean section.

A study was conducted to investigate the matter, in which a total of 366 patients who were scheduled for elective cesarean delivery were randomly assigned to two groups. The 1st Group received sublingual misoprostol 400 µg (n = 179), while the second Group received a placebo tablet (n = 187) following intubation. The researchers observed that the Apgar scores at one and five minutes, as well as the neonatal cardiovascular condition, exhibited similar characteristics in both groups.17

Nevertheless, the findings of this study revealed a correlation between the administration of misoprostol and elevated incidences of pyrexia and chills in comparison to the placebo group. This disparity was particularly pronounced in the sublingual route of administration, aligning with previous research conducted in this area. However, the aforementioned adverse effects manifested within a time frame of three hours subsequent to the administration of the medication and resolved on their own without necessitating any form of symptomatic intervention.18

5. Conclusion

When misoprostol is delivered rectally, as opposed to sublingually, an increased risk of PPH is linked to the prescribed dosage. So, the sublingual route of administration of misoprostol is more effective in reducing the risk of PPH, and More women accepted the sublingual route than the rectally administered misoprostol despite the sublingual route’s higher rate of shivering and pyrexia.

5.1 Recommendations

Sublingual administration of misoprostol is recommended because it is more favorable for patients and more convenient than rectal administration..

Disclosure

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Funding

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Conflicts of interest

There are no conflicts of interest.

References