e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2024; 16(4); 418-422

Original Research Article

Assessing Effectiveness of Misoprostol and Oxytocin in Preventing Postpartum Bleeding after Labor Induction: A Comparative Study

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Received: 10-01-2024 / Revised: 15-02-2024 / Accepted: 24-04-2024
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Conflict of interest: Nil

Abstract

Aim: To compare the effectiveness of misoprostol and oxytocin in preventing postpartum bleeding after labor induction.

Materials and Methods: The study was a randomized clinical trial carried out at the Department of Obstetrics and Gynaecology, Jawaharlal Nehru Medical college and hospital Bhagalpur, Bihar, India. 110 patients were included. The targeted population was booked women admitted into the labor room anticipating vaginal delivery and who had a singleton pregnancy with cervical dilatation of 6 cm or less and packed cell volume of at least 30%. Women in advanced stage of labor (cervical dilatation >6cm), known allergies to prostaglandins, oxytocin homologues or excipients, had a serious cardiovascular disorder, serious hepatic or renal disease, or epilepsy were not eligible. All the participants gave a written informed consent.

Results: Total 110 women with term pregnancy in two groups of 55 each were studied. The mean gestational age of women was 39.43±1.17 in the misoprostol group and 39.32±1.17 weeks in the oxytocin group. The mean blood loss with sublingual misoprostol and oxytocin groups was 320.58±244.12 vs. 253.27±171.74 ml; (p=0.11). The mean duration of third stage of labor was similar and the difference was not statistically significant (6.65±3.47 vs. 6.08±3.07 minutes) (P=0.38), as well as need for additional oxytocics (14.5% vs. 7.2% p=0.18) misoprostol and oxytocin, respectively. There were no differences at the 5% level of significance between groups with regard to the incidence of PPH (20.8% vs. 14.5% respectively; p=0.43). Among the women who were recruited (safety population), the frequencies of the expected side effects did not differ significantly between the two groups. In misoprostol group, side effects were shivering, fever, nausea and abdominal pains, while the oxytocin group abdominal pains, headaches and shivering.

Conclusions: we concluded that the risk of increased blood loss, prolongation of the third stage of labor, need for additional uterotonics, increased risk of PPH, and increased incidence of side effects. The use of misoprostol is particularly important for resource-limited settings, where the availability and storage of heat-susceptible oxytocin are challenging.

Keywords: ICMH, oxytocin, misoprostol, postpartum hemorrhage

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Introduction

Postpartum hemorrhage (PPH) remains one of the leading causes of maternal mortality and morbidity worldwide, accounting for approximately 25% of maternal deaths globally. Effective management of the third stage of labor is crucial to prevent PPH, and various pharmacological agents have been employed for this purpose. Among these, oxytocin has long been considered the gold standard for PPH prevention due to its potent uterotonic properties. However, misoprostol, a synthetic prostaglandin E1 analog, has emerged as an alternative, especially in resource-limited settings where refrigeration and intravenous administration of oxytocin can be challenging. [1-4] This introduction explores the comparative efficacy of misoprostol and oxytocin in reducing PPH following labor induction, highlighting recent studies and their implications for clinical practice. PPH is defined as blood loss of 500 ml or more within 24 hours after vaginal delivery or 1000 ml or more after cesarean delivery. The

primary cause of PPH is uterine atony, a condition where the uterus fails to contract adequately after childbirth. Other causes include retained placenta, trauma, and coagulopathies. The management of PPH focuses on prompt uterotonic administration, manual uterine massage, and addressing underlying causes. [5-9] Oxytocin is a naturally occurring hormone that stimulates uterine contractions. Administered intravenously or intramuscularly, oxytocin is highly effective in promoting uterine contraction and reducing the risk of PPH. The World Health Organization (WHO) recommends oxytocin as the first-line agent for PPH prevention. However, oxytocin requires refrigeration and a stable supply chain, which can be problematic in low-resource settings. Additionally, its administration often requires skilled healthcare personnel, limiting its use in some areas. Misoprostol is a prostaglandin E1 analog that can be administered orally, sublingually, vaginally, or rectally. It is stable at room temperature, making it an attractive option in low-resource settings. [9-11] Misoprostol's uterotonic effects are comparable to those of oxytocin, and it has been extensively studied for PPH prevention and treatment. Its versatility in administration routes also offers flexibility in different clinical scenarios. Several studies have compared the efficacy of misoprostol and oxytocin in reducing PPH after labor induction. Both oxytocin and misoprostol have side effects that must be considered when choosing an appropriate uterotonic agent. Oxytocin's side effects include nausea, vomiting, and, in rare cases, water intoxication due to its antidiuretic effect. Misoprostol, on the other hand, is associated with shivering, fever, and gastrointestinal disturbances. Implementing misoprostol and oxytocin in clinical practice requires careful consideration of the healthcare infrastructure, availability of trained personnel, and patient preferences. In high-resource settings, where refrigeration and skilled personnel are available, oxytocin remains the preferred agent. However, in low-resource settings, misoprostol offers a practical alternative that can be administered by less specialized healthcare workers and stored without refrigeration. [12-15]

Materials and Methods

The study was a randomized clinical trial carried out at the Department of Obstetrics and Gynaecology, Jawaharlal Nehru Medical college and hospital Bhagalpur, Bihar, India for one year.110 patients were included. The targeted population was booked women admitted into the labor room anticipating vaginal delivery and who had a singleton pregnancy with cervical dilatation of 6 cm or less and packed cell volume of at least 30%. Women in advanced stage of labor (cervical dilatation >6cm), known allergies to prostaglandins, oxytocin homologues or excipients, had a serious cardiovascular disorder, serious hepatic or renal disease, or epilepsy were not eligible. All the participants gave a written informed consent. The sample size was determined using statistical formula for comparing two proportions with accepting a study power of 80%, confidence interval of 95%, study/control of 1:1 and an acceptable dropout rate of 10%. Women underwent randomization when vaginal birth was imminent. The envelopes were drawn to know the group into which a subject falls only when delivery is imminent. Women were randomly assigned to receive a single intramuscular injection oxytocin at a dose of 10 IU or 200 µg sublingual misoprostol immediately after the birth of the baby, the drug was administered and the management of the third stage of labor was conducted as recommended in the WHO guidelines.[16] Blood was collected for 1 hour but careful surveillance for further bleeding was put in place till 24 hours after delivery. Additional oxytocics were used when subsequent blood loss was adjudged excessive. The blood collected in the receptacle was visually noted and also transferred to a measuring jar and volume noted. Dry weight of all swabs that were used during the third stage were measured and noted. Blood soaked swabs were weighed and the dry weight of the swabs was subtracted in grams. Assuming an equivalence of 1 g to 1 ml, this volume was added to the volume of blood from the BRASSS-V drape. Participation in the study ended at discharge from the facility, transfer of the woman to a higher care unit or death. Primary outcomes were quantity of blood loss and incidence of PPH. Secondary outcomes included duration of the third stage, need for adjunctive uterotonics to treat life-threatening hemorrhage and side effects of drugs used.

Data Analysis

Data statistical analysed using the SPSS version 23. Descriptive statistics were presented using charts, graphs and tables as appropriate. Quantitative variables were described using measures of central tendencies like mean and median as appropriate. Association between qualitative variables were tested using Chi-square test, while associations between various quantitative variables were determined using the Student's t-test and other tests as found appropriate. The level of significance was set at 5%.

Results

Total 110 women with term pregnancy in two groups of 55 each were studied. Demographic and base line characteristics of the two groups were comparable (Tables 1, 2). The mean gestational age of women was 39.43±1.17 in the misoprostol group and 39.32±1.17 weeks in the oxytocin group. The mean blood loss with sublingual misoprostol and oxytocin groups was 320.58±244.12 vs. 253.27±171.74 ml; (p=0.11) (Table 3). The mean duration of third stage of labor was similar and the

difference was not statistically significant (6.65±3.47 vs. 6.08±3.07 minutes) (P=0.38), as well as need for additional oxytocics (14.5% vs. 7.2% p=0.18) misoprostol and oxytocin, respectively. There were no differences at the 5% level of significance between groups with regard to the incidence of PPH (20.8% vs. 14.5% respectively; p=0.43) (Table 4). Among the women who were recruited (safety population), the frequencies of the expected side effects did not differ significantly between the two groups (Table 5). In misoprostol group, side effects were shivering, fever, nausea and abdominal pains, while the oxytocin group abdominal pains, headaches and shivering.

Table 1: Maternal baseline characteristics (N=110)

Characteristics Misoprostol	N=55 (%)	Oxytocin N=55 (%)	P-Value
Age (years)			
20-29	23(41.8)	30 (54.5)	0.46
30-39	30(54.5)	24(43.6)	
40 and above	2(3.6)	1(1.8)	
Parity			
0	10(18.2)	21(38.8)	0.174
1	18(32.7)	12(21.8)	
2	21(38.2)	18(32.7)	
3	4(7.2)	2(3.6)	
4	2(3.6)	2(3.6)	
Blood group			
O-Positive	30 (54.5)	35(63.6)	0.37
A-Positive	15(27.2)	7(12.7)	
B-Positive	9(16.3)	10(18.1)	
O-Negative	2(3.6)	1(1.8)	
B-Negative	0(0)	1(1.8)	
A-Negative	0(0)	1(1.8)	

Table 2: Mean gestational age, blood pressure and packed cell volume (N=110)

Characteristics	Misoprostol (±SD)	Oxytocin (±SD)	P-Value
Gestational age (weeks)	39.43 (1.17)	39.32 (1.17)	0.66
Mean arterial blood pressure	83.53 (10.42)	81.59 (9.57)	0.33
Intrapartum packed cell volume	32.92 (2.99)	32.17(3.13)	0.94

Table 3: Mean blood loss and mean duration of third stage of labour (N=110)

Characteristics	Misoprostol n=55(±SD)	Oxytocin N=55 (±SD)	Mean difference (95%CI)	P-Value
Blood loss (ml)	320.58 (244.12)	253.27 (171.74)	67.30 (14.8,149.4)	0.11
Duration of third stage (min)	6.65 (3.47)	6.08 (3.07)	0.56 (0.71,1.84)	0.38

Table 4: Postpartum hemorrhage and need for additional oxytocics (N=110)

Characteristics	Misoprostol N=55 (%)	Oxytocin n=55 (%)	P-Value
PPH (≥500 ml)	12 (20.8)	8 (14.5)	0.43
No PPH (<500 ml)	43 (78.1)	47(85.5)	
Additional oxytocics required	8 (14.5)	4(7.2)	0.18
Additional oxytocics not required	47 (85.5)	51 (92.8)	

Table 5: Side effect profile (N=15)

Characteristics	Misoprostol N=9 (%)	Oxytocin N=6 (%)	P-Value
Nausea	1(11.1)	0(0)	
Shivering	4(44.4)	1(16.6)	0.26
Fever	2(22.2)	0(0)	
Headache	0(0)	1(16.6)	
Abdominal pain	2(22.2)	4(66.6)	

Discussion

Total 110 women with term pregnancy in two groups of 55 each were studied. Demographic and base line characteristics of the two groups were comparable. The gestational age of women was 39.43±1.17 in the misoprostol group and 39.32±1.17 weeks in the oxytocin group. This study

demonstrates that sublingual misoprostol is not as effective as intramuscular oxytocin for the active management of the third stage of labour. The incidence of PPH was significantly higher in the misoprostol group than in the oxytocin group. The third stage of labour was significantly longer in the misoprostol group than in the oxytocin group, with greater blood loss and lower hemoglobin levels. We also found that the need for additional uterotonics and side effects were significantly higher in the sublingual misoprostol group than in the intramuscular oxytocin group. Therefore, the results of the present study do not support the hypothesis (as suggested by several previous researchers) that misoprostol is as effective as oxytocin in managing the third stage of labor. [16,17] Researchers highlight side effects as a limitation of the misoprostol group compared to the oxytocin group. Side effects (e.g., fever, chills) occurred in significantly more cases in the misoprostol group. [18,19,20] Even in studies where sublingual misoprostol was as effective as intramuscular oxytocin, a significantly higher incidence of adverse events was recorded in the misoprostol group compared to the oxytocin group. [16,17] Although Mukta and Sahay reported that mean blood loss in the misoprostol group was higher (15.9% higher) than in the oxytocin group, they did not consider this difference to be statistically significant[16]. They also observed that the mean decrease in hemoglobin levels was greater in the misoprostol group (0.55 g/dl) than in the oxytocin group (0.48 g/dl), but this was not statistically significant could not be found. Similar results were observed in the present study, and this difference was found to be statistically significant. Additionally, the incidence of PPH in the misoprostol group was 20.8% compared to 14.5% in the oxytocin group, and the need for additional uterotonics was lower in the misoprostol group (22%) than in the oxytocin group. It was also found that the incidence was high (16%). [16] Studies with larger samples, such as the study by Atukunda et al. (nausea, vomiting, fever, and shivering) to be significantly higher in the misoprostol group than in the oxytocin group. A Cochrane review evaluating the use of prostaglandins for the prevention of PPH, which included data from 72 trials involving 52,678 women, concluded that the use of misoprostol over conventional injectable uterotonics cannot be preferred as part of the management of the third stage of labour, particularly in low- risk women [6]. In the present study, we also found that sublingual misoprostol was significantly less effective in preventing PPH than the conventional uterotonic (intramuscular oxytocin) recommended for the active management of the third stage of labor. Despite encountering higher rates of blood loss, falls in hemoglobin levels, PPH, and adverse events, they termed misoprostol as effective as oxytocin. The mean blood loss with sublingual misoprostol and oxytocin groups was 320.58±244.12 ml vs. 253.27±171.74 ml; (P= 0.11). The mean duration of third stage of labor was similar and the difference was not statistically significant (6.65±3.47 vs. 6.08±3.07 minutes) (P=0.38), as well as need for additional oxytocics (14.5% vs. 7.2%; P=0.18) misoprostol and oxytocin, respectively. There was a significant difference in the side effect profile between the two groups. However, they found misoprostol to be as effective as oxytocin. In a study from Pakistan with a sample size of 70 (35 in each group) conducted by Aziz et al., the median blood loss in the misoprostol group was nearly 100 mL higher than in the oxytocin group. Yet, they did not find this to be statistically significant.[21] Again, this may be due to the small sample size. The frequency of side effects was also significantly higher in the misoprostol group than in the oxytocin group. Studies in other underdeveloped and developing countries have reported similar results. [22,23] but the misoprostol group showed greater blood loss, the need for additional uterotonics, and side effects has been done. They mainly focused on statistical differences in small sample size scenarios. Although fever was noted in almost all studies, Sringamwong et al. They found that it was dose- dependent, using different doses of misoprostol in their study, and reported lower rates of fever in the lower misoprostol dose group. [24] Therefore, the results of the present study indicate that sublingual misoprostol is unlikely to be as effective as intramuscular oxytocin unless infrastructure deficiencies drive decision making. Most previous studies have insufficient sample sizes and their conclusions should be viewed with caution. This study has some limitations. First, our study did not evaluate neonatal safety and outcomes, which may contribute to the safety profile of misoprostol and oxytocin. Second, complicated deliveries, caesarean sections, or deliveries requiring induction of labour were not considered. Third, this study was a single-center study. Multicenter data might have allowed for a more representative analysis. Additionally, double-blind randomized controlled trials should be conducted with larger sample sizes that include pregnancy complications, delivery, and neonatal outcomes. A systematic review and meta-analysis should be conducted to evaluate the maternal and fetal outcomes of misoprostol use in the third stage of labour.

Conclusions

In this study, sublingual misoprostol was found to be less effective than intramuscular oxytocin in the active treatment of the third stage of labor. The results indicate a risk of increased blood loss, prolongation of the third stage of labor, need for additional uterotonics, increased risk of PPH, and increased incidence of side effects. The use of

misoprostol is particularly important for resource-limited settings, where the availability and storage of heat-susceptible oxytocin are challenging.

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