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Original Research Article

Sublingual Misoprostol versus Intramuscular Oxytocin for Prevention of Post-Partum Haemorrhage: A Competitive Study

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Abstract

Introduction: After a caesarean section (CS) or a natural delivery, postpartum haemorrhage (PPH) is a serious obstetric emergency (NVD). A 500 mL or 1000 mL haemorrhage following vaginal or caesarean delivery, respectively, may be used to characterize it. Globally, PPH is a leading cause of maternal mortality and a common obstetric maternal complication.

Aim & Objectives: The purpose of this study is to evaluate the efficacy of sublingual misoprostol in comparison to the gold-standard dose of 10 IU of intramuscular oxytocin for active management of the third stage of labour.

Materials and Methods: After receiving approval from the institutional ethics committee, this prospective, randomized trial involving 100 pregnant women was carried out. After a vaginal delivery, patients were randomly assigned to receive either 10 IU of intramuscular oxytocin (Group O) or 600 µg of misoprostol sublingually (Group M). The major outcomes assessed were mean blood loss, primary postpartum hemorrhage (PPH) incidence, and hemoglobin level decline. The duration of the third stage of labour, adverse medication reactions, the need for further uterotonics, manual placenta removal, and, if necessary, surgical intervention for postpartum haemorrhage was all secondary outcomes that were monitored.

Results: In total, 100 term-pregnant women were studied, divided into two groups of 50 each. For sublingual misoprostol and intramuscular oxytocin groups, the mean blood loss was 320.59 ± 244.13 vs. 253.28 ± 171.75 ml; (P = 0.11); respectively. In misoprostol and oxytocin groups pre- and post-delivery hemoglobin levels were statistically significant (p=0.001), whereas those between misoprostol and oxytocin were not (p=0.42 and p=0.27). In both the groups average length of the third stage of labour (4.27 ± 1.77 vs. 5.51 ± 2.33 minutes) and the requirement for further uterotonics misoprostol and oxytocin (8.0% versus 2.0%; p = 0.36) were comparable and the difference was statistically insignificant (P = 0.19). In terms of the incidence of PPH, there weren't any differences between groups (20.0% vs. 14.0%, respectively; P=0.44). The primary adverse

effects in the current trial were shivering, fever, vomiting, diarrhea, and abdominal pain. Shivering and fever were the side effects that were observed more frequently in the misoprostol group, which is similar with earlier studies.

Conclusion: During Oxytocin labour induction, misoprostol administration during the 3rd stage of labour demonstrated a tendency towards significantly lowering postpartum hemorrhage and postpartum hemorrhage incidence. Similar to conventional injection oxytocin, sublingual misoprostol is as effective as in active management of the third stage of labour. Misoprostol at 600 µg through its activity and thermostability seems to be an appropriate substitute for injectable oxytocin.

Keywards: Oxytoxin, Misoprostol, Primary Postpartum Hemorrhage, Post Delivery Hemoglobin.

Introduction

After a cesarean delivery (LSCS) or a natural delivery (NVD), postpartum hemorrhage (PPH) is a serious obstetric emergency. It can be described as less than 500 mL of bleeding following vaginal birth or less than 1000 mL after CS birth [1,2]. One of the most typical obstetric maternal problems and one of the most typical causes of maternal death globally is PPH [3]. In the US, there are roughly 17 women killed directly during pregnancy for every 100,000 live births. Postpartum hemorrhage (PPH) is thought to be the cause of about 11% of these fatalities, according to national U.S. statistics [4].

PPH typically is among the top 3 contributors of maternal death in industrialized nations, after hypertension & embolism [5]. Several emerging nations exhibit maternal mortality rates that are higher than 240 /100,000 live births [6]. According to estimates from the World Health Organization, PPH caused more than 650,000 maternal fatalities between the years of 2003 and 2009, or 27% of all maternal deaths [7]. PPH continues to be among the most difficult problems an obstetrician faces, despite advancements in its care.

Hence, the keys to reducing its impact are prevention, early recognition, and prompt suitable management. PPH has not yet been given a single, all-encompassing definition. The diagnosis has frequently been made using an estimated loss of blood of >500 ml after a vaginal delivery and 1000 ml after a caesarean delivery [8]. A 10% decrease in hemoglobin levels (between antepartum and postpartum) is another way to define PPH [9]. The placenta separates during 3rd stage of labour mostly due to the myometrium contracting, which also results in hemostasis when the blood vessels constrict [10]. About 80% or more of instances with primary PPH, uterine atony is the underlying etiology [11,12].

Studies have indicated that effective management of 3rd stage of labour reduces overall blood loss and does not raise the likelihood of placental adhesion [13,14]. Labor induction is carried out with the synthetic prostaglandin E1 derivative misoprostol. It increases uterine contractions, a key method for regulating PPH [15]. It is affordable, stable at room temperature, and has little negative effects. Contrarily, oxytocin causes uterine contractions by acting on particular receptors found in the myometrium.

When oxytocin is used to induce labour in the early stages of labour, it may exhaust its receptors, making it less efficient when used to regulate PPH. The Oxytocin Receptor is a member of a group of receptors that can become less sensitive when stimulation to it's own complementary hormone grows in quantity or time. During prolonged or repetitive stimulation, the receptor is hypothesized to become desensitized [16].

Although oxytocin is preferred, its need for cool storage makes it often impractical to administer it in environments with limited resources [17]. The WHO has recently developed carbetocin ambient room temperature stable (RTS) to address the issue of oxytocin storage and transportation in a cold chain, but it also requires trained workers for parenteral drug administration and sterile consumables like oxytocin [18].

Aims and Objectives

Comparison of the effectiveness of injectable oxytocin and sublingual misoprostol for preventing postpartum hemorrhage under the specified parameters:

1. Blood loss.
2. Fall in hemoglobin.
3. Duration of third stage.
4. Side effects.

Materials and Methods

This prospective, randomized trial was conducted on 100 women who were in term pregnancy after receiving approval from the institutional ethics committee and written informed consent.

Inclusion criteria: The target population consisted of labouring women who had been scheduled for vaginal birth, had a singleton pregnancy, a cervical dilatation of ≤ 6 cm, and at least 30% packed cell volume.

Exclusion criteria: Women who were in an advanced stage of labour (cervical dilatation >6 cm), had reported hypersensitivity to prostaglandins, oxytocin homologues, or excipients, had a significant cardiovascular issue, a serious liver or kidney condition, or had epilepsy were ineligible.

Sample size calculation: A statistical method for comparing different proportions was used to calculate the sample size, considering 80% study power of , 95% confidence interval, study/control ratio of 1:1, and 10% allowable dropout rate.

As a vaginal delivery was about to occur, women were randomly assigned. The subjects' groups were determined by drawing envelopes, but only as delivery was about to occur. Following the baby's birth, women were randomized to receive either a single 10 IU intramuscular injection of oxytocin (Group O) or 600 μg of sublingual misoprostol (Group M); the medication was given, and the third stage of labour was managed in accordance with WHO recommendations [9]. It was documented how long it took from the delivery of the fetus to the placenta.

The BRASSS-V Drape, a plastic drape used to collect blood, was placed under the buttocks prior to delivery; however, the calibrated blood collection container was not opened until after the baby was delivered, the cord was clamped and severed, and the amniotic fluid had been drained. Blood was taken for an hour, but careful monitoring for more bleeding continued for 24 hours following birth. When it was determined that the ensuing blood loss was too much, more uterotonics were administered.

The amount of blood collected inside the container was measured and visually noted before being moved to a measuring jar. All of the swabs used in 3rd stage were weighed and noted for their dry weight. Swabs that had been dipped in blood were weighed, and their dry weight was deducted in gram. This quantity subsequently added to the amount of blood out from BRASSS-V drape using the equivalent of 1 g = 1 ml as a guide. When a lady was discharged from the facility, transferred to a higher care unit, or passed away, participation in the study came to an end.

Primary outcomes:

- Quantity of blood loss and incidence of PPH.
- Fall in hemoglobin level from pre delivery and 24hrs after delivery.

Secondary outcomes:

- Duration of the third stage.

- Need for adjunctive uterotonics to treat life-threatening hemorrhage.
- Side effects of drugs used.
- Manual removal of placenta, operative intervention if any for post-partum hemorrhage.

Statistical Analysis

Statistical data analysis was performed using SPSS version 20. In the appropriate cases, tables, charts, and graphs were used to display descriptive statistics. When appropriate, measurements of central trends such as mean and median were used to describe quantitative variables.

The Student's t-test and other relevant tests were used to determine relationships between different quantitative variables, while associations between qualitative and quantitative factors were tested using the Chi-square test. 5% was chosen as the degree of significance.

Results

In total, 100 term-pregnant women were studied, assigned to two groups of 50 each. The two groups' demographic and fundamental traits were similar. **[Tables 1]**

Table 1: Demographic and baseline characteristics

Variables		Group M (n=50) (Mean ± SD)	Group O (n=50) (Mean ± SD)	p-value
Age (years)		25.74 ± 3.651	26.10 ± 3.401	0.612 (NS)
Gestational age (weeks)		38.52 ± 0.94	38.68 ± 1.01	0.410 (NS)
Parity (n %)	Primigravidae	50	50	0.690 (NS)
	Multigravidae	54	46	
Gestational age (weeks)		39.44 ± 1.18	39.33 ± 1.18	0.671 (NS)
Mean arterial pressure		83.54 ± 10.43	81.58 ± 9.58	0.331 (NS)
Intrapartum packed cell volume		32.93 ± 2.98	32.18 ± 3.14	0.941 (NS)

NS- Not Significant

For misoprostol & oxytocin groups, the mean loss of blood was 320.59 ± 244.13 vs. 253.28 ± 171.75 ml; (p = 0.11); respectively. After birth, there was no statistically significant difference in the mean hemoglobin (p = 0.27).

Both the requirement for supplementary uterotonics (8.0% versus 2.0%; P = 0.36) and the average length of the third stage of labour were comparable and also the discrepancy was statistically insignificant (4.97 ± 1.77 vs. 5.51 ± 2.33 minutes) (P = 0.19).

In terms of the incidence of PPH, there were no differences between groups (20.0% vs. 14.0%, respectively; P=0.431). **[Table 2]**

Table 2: Comparison of different parameters between the two groups

Variables		Group M (n=50) (Mean ± SD)	Group O (n=50) (Mean ± SD)	p-value
Blood loss (ml)		320.59 ± 244.13	253.28 ± 171.75	0.11
Hb (gm/dl)	Before delivery	10.82 ± 1.74	10.55 ± 1.55	0.42
	After delivery	8.99 ± 0.96	8.79 ± 0.82	0.27
Duration of third stage (min)		4.27 ± 1.77	5.51 ± 2.33	0.19
PPH (≥ 500 ml)		20%	14%	0.44
Additional uterotonics required		8%	2%	0.36

Fever was the most common adverse effect compared to the oxytocin group in the misoprostol group (8% vs 0), and the discrepancy was significant statistically (p=0.041).

Although shivering was more frequent in the misoprostol group (14% vs. 6% in the oxytocin group), the variation was statistically insignificant (p=0.182)In the misoprostol group, only 2% of the women experienced vomiting, comparing to 8% in the oxytocin group, however this difference was insignificant statistically (p=0.169In the misoprostol group, 2% of the patients experienced diarrhea, compared to no one in the group O (p=0.315) While no cases of abdominal pain were recorded in the misoprostol group, 6% of the oxytocin group experienced abdominal pain (p = 0.079, NS). **[Table 3]**

Table 3: Comparison of side-effects between the two groups

Side-effects	Group M (%)	Group O (%)	p-value
Nil	74	80	0.48
Shivering	14	06	0.18
Fever	08	00	0.04
Vomiting	02	08	0.17
Diarrhea	02	00	0.32
Pain abdomen	00	06	0.08

Discussion

The effects of oral misoprostol start working quickly, however there are certain side effects (fever, shivering) that depend on the dosage [18]. This is mostly because it has a shorter duration and reaches a sharp peak than that of other routes [19, 20]. However, compared to the oral route, rectal methods have a delayed onset of action, a lower peak, a prolonged duration of action, and fewer negative effects. In our study, a total of 100 term pregnant women were examined in two subgroups of 50 each.

For both misoprostol and oxytocin groups, the mean blood loss was 320.59 ± 244.13 vs. 253.28 171.75 ml; (P = 0.11); respectively. Because to its low cost, convenience in storage, and durability at room temperature, misoprostol is considered to be a more viable choice in low-resource situations. In this randomized comparison trial, we discovered that the active management of the third stage of labour with equivalent mean blood loss was achieved with 600 µg misoprostol sublingually and 10 IU oxytocin intramuscularly following vaginal birth. Despite the fact that oxytocin reduced total blood loss, which suggests improved efficacy, the disparity was not significant statistically. This result is consistent with earlier research on larger doses of misoprostol conducted in Nigeria by Afolabi *et al*. [18] and Oboro & Tabowei [19].

Similar to oxytocin, a similar percentage of individuals in the misoprostol group reported PPH. Comparable amounts of extra uterotonics were required by the two groups to treat PPH. The results of this study are in agreement with those of Afolabi *et al*. [18], Oboro and Tabowei [19], and Chaudhuri *et al*. [20]. The implementation of BRASSS-V drapes further provided a more accurate assessment of postpartum blood loss, perhaps reducing cases that might have been incorrectly classified as PPH cases [21].

When compared to women who had intravenous Oxytocin postoperatively, misoprostol was roughly substantially more successful at reducing the drop in hemoglobin levels in women whose labour was triggered by the hormone. Clinically speaking, this drop in hemoglobin levels is significant because it lowers the total amount of iron a patient will need to replenish the blood she lost after giving birth [22].

By improving adherence to the recommended iron therapy, this will provide the doctor and the patient with an additional benefit. Also confirming the idea of Oxytocin receptor desensitization, the outcome measures of EBL and mean reduction in hemoglobin levels were similarly higher in the Oxytocin group with a tendency towards significance [23]. We used a 10% Hb drop as the outcome measure because it is objective and unaffected by personal bias, even if it is influenced by many other factors besides the blood lost throughout delivery, such as hemoconcentration in situations when the plasma volume is constrained.

Visual assessment of blood loss is employed in daily practice and helps the obstetrician to intervene early to control any excessive blood loss. Although though real loss of blood is an objective measurement that is less prone to human error, using it for diagnosis takes time and is not practical [18,22,23], and most obstetricians were not in favour of it.

The primary adverse effects in the current trial were shivering, fever, vomiting, diarrhea, and abdominal pain. Shivering and fever were the side effects that were observed more frequently in the misoprostol group, which is similar with earlier studies. [11,25,26]

Parenteral uterotonics are still mostly used in hospitals and are only accessible for the management of 3rd stage of labour in urban areas. Parenteral uterotonics are rarely used in developing nations since most births take place outside of hospitals, and even when they do; maintaining cold chain for oxytocin is extremely difficult.

Conclusion

During Oxytocin labour induction, misoprostol administration during the 3rd stage of labour demonstrated a tendency towards significantly lowering postpartum hemorrhage and postpartum hemorrhage incidence. Similar to conventional injection oxytocin, sublingual misoprostol is as effective as in active management of the third stage of labour. Misoprostol at 600 µg through its activity and thermostability seems to be an appropriate substitute for injectable oxytocin.

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