

## A COMPARATIVE STUDY OF PER ORAL MISOPROSTOL VERSUS INTRAMUSCULAR OXYTOCIN FOR PREVENTION OF POSTPARTUM HEMORRHAGE

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### Abstract

**Background:** A comparative study of per oral misoprostol versus intramuscular oxytocin for prevention of Postpartum hemorrhage. **Materials and Methods:** The experiment had a total of 60 patients, who were randomly assigned to two groups: 30 patients in the Misoprostol group and 30 patients in the Oxytocin group. The study focused on women who were admitted to the labor room for vaginal birth and met the following criteria: they had a singleton pregnancy, their cervical dilatation was 6 cm or less, and their packed cell volume was at least 30%. Participants were randomly assigned to receive either: Misoprostol Group: 600 µg per oral misoprostol and Oxytocin Group: 10 IU intramuscular injection of oxytocin. Both medications were administered immediately after the birth of the baby, and the management of the third stage of labour followed WHO guidelines. **Result:** The average gestational age was similar in both groups, with the Misoprostol group having an average of 39.39±1.56 weeks and the Oxytocin group having an average of 39.29±1.65 weeks (p=0.14). The average arterial blood pressure was 82.99±5.37 mmHg in the group treated with Misoprostol and 80.89±4.75 mmHg in the group treated with Oxytocin (p=0.16). The intrapartum packed cell volume was 33.12±2.45% in the group that received Misoprostol and 31.99±2.32% in the group that received Oxytocin (p=0.32). In the Misoprostol group, the average blood loss was 319.45±22.54 ml, whereas in the Oxytocin group it was 249.87±12.59 ml (p=0.21). The average length of the third stage of labor was 6.71±1.11 minutes in the Misoprostol group and 5.99±1.04 minutes in the Oxytocin group (p=0.16). Regarding postpartum hemorrhage (PPH), 20% of patients in the Misoprostol group encountered PPH with a volume of 500 ml or more, whereas only 12% of patients in the Oxytocin group saw the same. As a result, 80% of patients in the Misoprostol group did not have postpartum hemorrhage (less than 500 ml) in comparison to 88% in the Oxytocin group. In terms of the need for extra oxytocics, 10% of patients in the Misoprostol group necessitated further oxytocics, while only 4% of patients in the Oxytocin group required them. **Conclusion:** We concluded that both Misoprostol and Oxytocin are successful in decreasing postpartum hemorrhage, Oxytocin seems to be more beneficial. It results in less average blood loss, a shorter period of the third stage of labor, and a decreased need for more oxytocics. Misoprostol continues to be a viable substitute, particularly in situations when Oxytocin is not accessible, despite its increased occurrence of specific adverse effects such as shivering and fever.

## INTRODUCTION

Postpartum hemorrhage (PPH) is a major contributor to maternal mortality and morbidity, responsible for around 27% of maternal deaths worldwide. The most recent WHO definitions of PPH (2012) reflect the 1990 definition. For vaginal births, PPH is defined as

blood loss >500mL and severe PPH is defined as loss of >1000 mL. In cases of cesarean birth, the standard for PPH is raised to 1000 mL in some guidelines.<sup>[1]</sup> It is crucial to promptly and effectively treat PPH to avoid serious consequences and mortality. The active management of the third stage of labor (AMTSL) is a crucial approach to avoid postpartum hemorrhage

(PPH). It includes the use of uterotonic medicines, controlled cord traction, and uterine massage.<sup>[2,3]</sup>

Active management of the third stage of labor (AMTSL) is a preventive approach for postpartum hemorrhage (PPH) that involves specific measures to assist in the delivery of the placenta and avoid uterine atony. AMTSL is associated with a nearly 60% reduction in PPH occurrence. Universal use of AMTSL will prevent 27% of deaths from PPH.<sup>[4]</sup> Although there has been a decrease in total maternal mortality, PPH remains the primary cause of maternal fatalities. Maternal Mortality Ratio of India has declined from 384 in 2000 to 103 in 2020 whereas Global Maternal Mortality Ratio has declined from 339 in 2000 to 223 in 2020. It is observed that MMR in India has declined to 97/100,000 live births in 2018 – 2020 from 130/100,000 live births in 2014 – 2016. Worldwide drop in MMR between 2000-2020 is 34%. The Sustainable Development Goals has set new target of reducing the global maternal mortality ratio to less than 70 per 100,000 live births by the year 2030.<sup>[5]</sup> Uterine atony is responsible for more than 70% of cases of primary postpartum hemorrhage (PPH). Research has focused on determining the most optimal uterotonic agent for actively managing the third stage of labor. Postpartum hemorrhage (PPH) is the primary cause of maternal mortality globally. Each year, about 14 million women experience PPH resulting in about 70,000 maternal deaths globally.<sup>[6]</sup> Postpartum hemorrhage (PPH) affects 5% of all births and is a significant contributor to maternal mortality.<sup>[7,8]</sup>

Most of these fatalities happen within a time frame of 4 hours after childbirth, suggesting that they are a result of the third stage of labor. Although oxytocin is often preferred, it may not be practical to use in economically disadvantaged areas due to the need for refrigeration. The Oxytocin receptor is one of a group of receptors that may become less sensitive when exposed to increasing amounts or longer durations of its corresponding hormone. It is believed that the receptor becomes desensitized during prolonged or repetitive activation. Although oxytocin is often preferred, it may not be practical to use in economically disadvantaged areas due to the need for refrigeration.<sup>[9]</sup> Oxytocin and other injectable uterotonics are often limited to metropolitan areas. The ease of managing and storing misoprostol, together with its proven efficacy, makes it a favorable choice for usage in resource-limited regions. The latest Cochrane database review on misoprostol for the third stage of labor acknowledged the lack of published studies on the use of lower doses of misoprostol for actively managing the third stage of labor. It recommended more study on the use of low-dose misoprostol.<sup>[10]</sup>

Oxytocin, a synthetic version of a hormone found naturally in the body, is commonly considered to be the most effective uterotonic for preventing postpartum hemorrhage (PPH) because of its strong uterotonic capabilities and safe characteristics. Nevertheless, the need for cold storage and the

necessity for intravenous or intramuscular delivery of the vaccine present difficulties in low-resource areas where these facilities may not be easily accessible.<sup>[11,12]</sup>

Misoprostol, a homologue of prostaglandin E1, offers a preferred alternative to oxytocin, particularly in settings with low resources. It is an economical and thermally stable substance that may be taken orally, sublingually, or rectally, making it a flexible choice for preventing and managing postpartum hemorrhage (PPH). Although misoprostol has some benefits, it is also linked to adverse effects such as shivering, fever, and gastrointestinal problems. These side effects might potentially affect its acceptability and use.<sup>[13-15]</sup>

## MATERIALS AND METHODS

This research was a randomized clinical trial done at the Department of Gynaecology & Obstetrics from January 2022-December 2022 at the clinical centres attached to HIMS, Dehradun. The experiment had a total of 60 patients, who were randomly assigned to two groups: 30 patients in the Misoprostol group and 30 patients in the Oxytocin group. The study focused on women who were admitted to the labor room for vaginal birth and met the following inclusion criteria: low-risk pregnant women between 34 weeks to 40 weeks, who had a singleton pregnancy with cephalic presentation. their cervical dilatation was 6 cm or less, and their packed cell volume was at least 30% and who were willing to participate in the study. The exclusion criteria included advanced labor (cervical dilatation >6 cm), multifetal pregnancy and noncephalic presentation and with polyhydramnios and placenta previa or abruption and macrosomia, documented allergies to prostaglandins, oxytocin homologues or excipients, severe cardiovascular problems, hypertensive disorders, severe hepatic or renal illness, asthma or anemia, epilepsy or coagulation disorders and patients undergone instrumental delivery or traumatic PPH and a history of uterine surgery or previous cesarean sections. Prior to their participation, all individuals were required to submit written informed permission. Randomization was conducted at the time of impending vaginal birth, guaranteeing that the allocation to treatment groups was fair and kept hidden until the crucial moment of delivery.

Participants were randomly assigned to receive either:

Misoprostol Group: 600 µg per oral misoprostol

Oxytocin Group: 10 IU intramuscular injection of oxytocin

Both medications were administered immediately after the birth of the baby, and the management of the third stage of labor followed WHO guidelines.

Blood loss was carefully monitored and measured. Blood was collected using the BRASSS-V drape for one hour post-delivery, with further surveillance for bleeding up to 24 hours. Blood collected in the receptacle was visually inspected and transferred to a

measuring jar for volume recording. Additionally, dry weights of all swabs used during the third stage were noted. Blood-soaked swabs were weighed, and the dry weight was subtracted from the total to calculate the blood loss, assuming 1 g of weight equals 1 ml of blood.

**Primary Outcomes:** Quantity of blood loss and incidence of postpartum hemorrhage (PPH). **Secondary Outcomes:** Duration of the third stage of labor, need for additional uterotonics to treat life-threatening hemorrhage, and side effects of the administered drugs.

Data on blood loss were collected and recorded up to 24 hours post-delivery. Participants were monitored until discharge, transfer to a higher care unit, or death. The total blood loss was calculated by combining the volume from the BRASS-V drape and the adjusted weight of blood-soaked swabs.

#### Statistical Analysis

Data statistical analysed using the SPSS version 25. Data analysis focused on comparing the primary and secondary outcomes between the Misoprostol and Oxytocin groups. The effectiveness of each treatment in reducing postpartum hemorrhage and other complications was evaluated using appropriate statistical methods.

## RESULTS

The trial had a total of 60 patients, with an even distribution between the Misoprostol and Oxytocin groups. The age distribution across the groups did not show any statistically significant difference ( $p=0.22$ ). between the Misoprostol group, 33.33% of patients were between the age range of 20-30 years, 60% were between the ages of 30-40 years, and 6.67% were older than 40 years. In the Oxytocin group, 53.33% of the participants were between the ages of 20 to 30, 43.34% were between the ages of 30 to 40, and 3.33% were above the age of 40.

The parity distribution similarly exhibited no statistically significant change ( $p=0.21$ ). Among the patients in the Misoprostol group, 20% had never given birth, 30% had one kid, 40% had two children, 6.67% had three children, and 3.33% had four children. Within the Oxytocin group, 43.33% of individuals had never given birth, 23.33% had one kid, 30% had two children, 3.33% had three children, and 6.67% had four children.

The distribution of blood types was comparable across the groups ( $p=0.11$ ). Among the participants

in the Misoprostol group, 50% had blood type O-positive, 30% had blood type A-positive, 16.67% had blood type B-positive, and 3.33% had blood type O-negative. All patients in the Misoprostol group had blood types other than B-negative or A-negative. Within the Oxytocin group, 56.67% had blood type O-positive, 13.34% had blood type A-positive, 20% had blood type B-positive, 3.33% had blood type O-negative, 3.33% had blood type B-negative, and 3.33% had blood type A-negative.

The average gestational age was similar in both groups, with the Misoprostol group having an average of  $39.39 \pm 1.56$  weeks and the Oxytocin group having an average of  $39.29 \pm 1.65$  weeks ( $p=0.14$ ). The average arterial blood pressure was  $82.99 \pm 5.37$  mmHg in the group treated with Misoprostol and  $80.89 \pm 4.75$  mmHg in the group treated with Oxytocin ( $p=0.16$ ). The intrapartum packed cell volume was  $33.12 \pm 2.45\%$  in the group that received Misoprostol and  $31.99 \pm 2.32\%$  in the group that received Oxytocin ( $p=0.32$ ) [Table 2].

In the Misoprostol group, the average blood loss was  $319.45 \pm 22.54$  ml, whereas in the Oxytocin group it was  $249.87 \pm 12.59$  ml ( $p=0.21$ ). The average length of the third stage of labor was  $6.71 \pm 1.11$  minutes in the Misoprostol group and  $5.99 \pm 1.04$  minutes in the Oxytocin group ( $p=0.16$ ) [Table 3].

Regarding postpartum hemorrhage (PPH), 20% of patients in the Misoprostol group encountered PPH with a volume of 500 ml or more, whereas only 10% of patients in the Oxytocin group saw the same. As a result, 83.33% of patients in the Misoprostol group did not have postpartum hemorrhage (less than 500 ml) in comparison to 86.67% in the Oxytocin group. In terms of the need for extra oxytocics, 16.67% of patients in the Misoprostol group necessitated further oxytocics, while only 3.33% of patients in the Oxytocin group required them. In contrast, only 90% of patients in the Misoprostol group needed extra oxytocics, whereas 93.33% of patients in the Oxytocin group required them. [Table 4].

The analysis of side effects showed that among the patients in the Misoprostol group, 16.7% reported nausea, 50.0% experienced shivering, 16.67% experienced fever, and 16.67% suffered stomach pain. There were no complaints of headache. Within the Oxytocin group, shivering was reported by 25.0% of patients, headaches by 25.0%, and stomach discomfort by 50.0%. No instances of nausea or fever were reported. The information is shown in [Table 5].

**Table 1: Demographic parameter.**

Parameter	Misoprostol		Oxytocin		P-Value
Age (years)	Number =30	Percentage	Number =30	Percentage	0.22
20-30	10	33.33	16	53.33	
30-40	18	60	13	43.34	
Above 40	2	6.67	1	3.33	
Parity					0.21
0	6	20	13	43.33	
1	9	30	7	23.33	
2	12	40	9	30	
3	2	6.67	1	3.33	

4	1	3.33	2	6.67	
Blood group					0.11
O-Positive	15	50	17	56.67	
A-Positive	9	30	4	13.34	
B-Positive	5	16.67	6	20	
O-Negative	1	3.33	1	3.33	
B-Negative	0	0	1	3.33	
A-Negative	0	0	1	3.33	

**Table 2: Mean gestational age, blood pressure and packed cell volume**

Characteristics	Misoprostol	Oxytocin	1
Gestational age (weeks)	39.39±1.56	39.29±1.65	0.14
Mean arterial blood pressure	82.99±5.37	80.89±4.75	0.16
Intrapartum packed cell volume	33.12±2.45	31.99±2.32	0.32

**Table 3: Mean blood loss and mean duration of third stage of labour**

Characteristics	Misoprostol	Oxytocin	P-Value
Blood loss (ml)	319.45±22.54	249.87±12.59	0.21
Duration of third stage (min)	6.71±1.11	5.99±1.04	0.16

**Table 4: Postpartum hemorrhage and need for additional oxytocic's**

Characteristics	Misoprostol		Oxytocin	
	Number	Percentage	Number	Percentage
PPH (≥500 ml)	6	20	3	10
No PPH (<500 ml)	25	83.33	26	86.67
Additional oxytocics required	5	16.67	1	3.33
Additional oxytocics not required	27	90	28	93.33

**Table 5: Side effect profile**

Side Effect	Misoprostol (N=6)	Percentage	Oxytocin (N=4)	Percentage
Nausea	1	16.7	0	0
Shivering	3	50	1	25
Fever	1	16.7	0	0
Headache	0	0	1	25
Abdominal pain	1	16.7	2	50

## DISCUSSION

The objective of this research was to assess and contrast the effectiveness and safety of Misoprostol and Oxytocin in the reduction of postpartum hemorrhage (PPH) during labor induction. There were no notable disparities in the age distribution, parity, and blood group distribution between the Misoprostol and Oxytocin groups. This finding aligns with previous research that has sought to reduce the influence of extraneous factors by ensuring that the comparison groups had identical initial characteristics.<sup>[16]</sup> The clinical data, including gestational age, mean arterial blood pressure, and intrapartum packed cell volume, were similar in both groups. The resemblance in these indicators indicates that the groups were medically comparable at the beginning of the intervention, therefore confirming the credibility of the results on the therapies themselves.

This research provides evidence that per oral misoprostol is less effective than injectable oxytocin for actively managing the third stage of labor. The occurrence of postpartum hemorrhage (PPH) was much greater in the misoprostol group compared to the oxytocin group. In the misoprostol group, the duration of the third stage of labour was much longer compared to the oxytocin group. Additionally, there was a higher amount of blood loss and lower levels of hemoglobin. Furthermore, our research revealed a substantial increase in the need for supplementary

uterotonics and a greater occurrence of adverse effects in the per oral misoprostol group compared to the intramuscular oxytocin group. Consequently, the findings of this study contradict the idea (proposed by several prior researchers) that misoprostol is equally beneficial to oxytocin in the management of the third stage of labor.<sup>[17,18]</sup> Researchers emphasize the adverse effects as a drawback of the misoprostol group in comparison to the oxytocin group. There was a notable increase in the occurrence of side symptoms, such as fever and chills, in the group who received misoprostol.<sup>[19-21]</sup> Although per oral misoprostol was shown to be as effective as injectable oxytocin in some trials, the misoprostol group had a considerably greater number of adverse events compared to the oxytocin group.<sup>[12,13]</sup> While Mukta and Sahay observed that the average blood loss in the misoprostol group was 15.9% more than in the oxytocin group, they did not deem this disparity to have statistical significance.<sup>[12]</sup> Additionally, they noted that the average reduction in hemoglobin levels was higher in the misoprostol group (0.55 g/dl) compared to the oxytocin group (0.48 g/dl), although this difference did not reach statistical significance.

The average blood loss was greater in the Misoprostol group (319.45±22.54 ml) compared to the Oxytocin group (249.87±12.59 ml), although this difference did not have statistical significance (p=0.21). In the same vein, the average length of the third stage of labor was greater in the Misoprostol

group (6.71±1.11 minutes) compared to the Oxytocin group (5.99±1.04 minutes), although this difference did not reach statistical significance (p=0.16). The findings align with the results of Hofmeyr et al. indicating that Misoprostol was linked to a slightly greater average blood loss in comparison to Oxytocin.<sup>[22]</sup> Regarding postpartum hemorrhage (PPH), the Misoprostol group had a 20% incidence of PPH (≥500 ml), whereas the Oxytocin group had a 10% incidence. As a result, 83.33% of patients in the Misoprostol group did not have postpartum hemorrhage (less than 500 ml) in comparison to 86.67% in the Oxytocin group. In terms of the need for extra oxytocics, 16.67% of patients in the Misoprostol group necessitated more oxytocics, while only 3.33% in the Oxytocin group necessitated them. In contrast, only 90% of patients in the Misoprostol group needed extra oxytocics, whereas 93.33% of patients in the Oxytocin group required them. Although the difference was not statistically significant, it is consistent with the findings of the meta-analysis conducted by Gülmezoglu et al., which indicated that Oxytocin is marginally more efficacious in reducing postpartum hemorrhage (PPH) compared to Misoprostol.<sup>[8]</sup> Additionally, the need for additional oxytocics was higher in the Misoprostol group (16.67%) compared to the Oxytocin group (3.33%), indicating a trend towards better efficacy with Oxytocin in controlling blood loss.

The research done by Atukunda et al. and other investigations with bigger samples have consistently shown that oxytocin provides very moderate advantages compared to misoprostol.<sup>[20]</sup> In the aforementioned research, the incidence of postpartum hemorrhage (PPH) was much greater in the misoprostol group as compared to the oxytocin group. Nevertheless, the analysis revealed no statistically significant difference between the two groups. The need for supplementary uterotonic, length of the third stage of labor, and hemoglobin alterations were comparable in both groups.

The analysis of side effects showed that among the patients in the Misoprostol group, 16.7% had nausea, 50.0% experienced shivering, 16.67% experienced fever, and 16.67% experienced stomach discomfort. However, no cases of headache were reported. Within the Oxytocin group, shivering was reported by 25.0% of patients, headaches by 25.0%, and stomach discomfort by 50.0%. No instances of nausea or fever were reported. Blum et al. shown that Oxytocin typically leads to less blood loss and fewer adverse effects in comparison to Misoprostol, despite the effectiveness of both medicines.<sup>[12]</sup> Jafari et al. and Mousa et al. have also discovered that Oxytocin is linked to a decreased occurrence of severe postpartum hemorrhage (PPH) and a reduced need for extra uterotonic.<sup>[23]</sup>

## CONCLUSION

We concluded that both Misoprostol and Oxytocin are successful in decreasing postpartum hemorrhage, Oxytocin seems to be more beneficial. It results in less average blood loss, a shorter period of the third stage of labor, and a decreased need for more oxytocics. Misoprostol continues to be a viable substitute, particularly in situations when Oxytocin is not accessible, despite its increased occurrence of specific adverse effects such as shivering and fever. It is encouraged to conduct further research with bigger sample sizes and different groups in order to have a better understanding of these results and improve techniques for managing PPH.

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