

METHODS FOR COMPARING THE EFFECTIVENESS OF MISOPROSTOL WITH OXYTOCIN AGAINST OXYTOCIN ALONE IN AVOIDING POSTPARTUM BLEEDING

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Abstract

Background: Postpartum hemorrhage is the most common kind of uterine bleeding (PPH). This study aimed to compare the effectiveness of misoprostol in conjunction with oxytocin alone in reducing postpartum hemorrhage. **Materials and Methods:** Using simple randomization, 150 patients from the labour ward of the Department of Obstetrics and Gynecology at Indore Medical College were assigned to either test group A or test group B. In group A, women received the standard drug treatment of 10 IU of oxytocin intramuscularly along with the other components of AMTSL (Active management of the third stage of labour) criteria. In group B, women received the standard drug treatment of 10 IU of oxytocin intramuscularly along with 600 gm of misoprostol administered orally during active management of the third stage of labour. **Result:** In group A, the average maternal weight was 66.29 kg, whereas, in group B, it was 69.84 kg. The average birth weight in group A was 2.83 kg, whereas it was 2.91 kg in group B. In group A, the average blood loss was 448.3 mL, whereas it was only 306.1 mL in group B. A significant difference ($P < 0.05$) was observed. 27 individuals in group A and 8 individuals in group B needed a blood transfusion. A significant difference ($P < 0.05$) was observed. 36 participants in Group A and 7 patients in Group B required additional uterine-stimulating medications. The change was statistically significant ($P < 0.05$). **Conclusion:** The results of this study a single dosage of 600 mg of sublingual misoprostol was more successful in reducing blood loss during active management of the third stage of labour when combined with the normal ten units of intramuscular oxytocin.

INTRODUCTION

The two kinds of obstetric hemorrhage are antepartum hemorrhage (APH) and postpartum hemorrhage (PPH). APH is mostly caused by placental abruption and placental Previa. Postpartum hemorrhage is the most common kind of uterine bleeding (PPH).^[1] According to the World Health Organization, it caused around a quarter of all maternal deaths worldwide in 2015.^[2] In the event of a normal vaginal delivery, blood loss of more than 500 ml is classified as postpartum hemorrhage (PPH), whereas blood loss of greater than 1000 ml is classified as post-caesarean section. The two

categories of PPH are primary and secondary. Primary PPH occurs within 24 hours after delivery, but secondary PPH, or late PPH, develops between 24 hours and 6 weeks postpartum. Some countries define PPH as a lower blood loss threshold, while others use a greater one.^[3]

It seems that misoprostol is a uterotonic agent. It is a prostaglandin E1 analog that was manufactured synthetically. This procedure often terminates pregnancies throughout the first and second trimesters. In addition, it is used in the induction of labour. The effects of uterotonics are highly powerful. It is handy since it may be administered orally and sublingually. In contrast to oxytocin,

which must be kept refrigerated and can only be supplied intravenously, this hormone may be held at ambient temperature for lengthy periods without losing its effectiveness. Shortly after delivery, both vaginal and surgical deliveries include the injection of uterotonic medicines, with oxytocin serving as the gold standard.^[4] The objective of this study was to compare the effectiveness of misoprostol with oxytocin against oxytocin alone in avoiding postpartum hemorrhage.

MATERIALS AND METHODS

Patients were recruited from the department of Obstetrics & Gynecology at Indore Medical College's labour ward. Before any research-related procedures, written informed consent was obtained in the relevant regional language from patients who indicated a wish to participate. Patients who lacked formal schooling had their left thumb imprints taken after a detailed explanation of the study and with the birth partner present to serve as an impartial witness. The demographic information of patients was collected. Patients who satisfied the inclusion and exclusion criteria of the research were recruited and randomly allocated to the A or B testing groups. In group A, women received the standard drug treatment of 10 IU of oxytocin intramuscularly,

along with the other components of AMTSL (Active management of the third stage of labour) criteria. In group B, women received the standard drug treatment of 10 IU of oxytocin intramuscularly, along with 600 g of misoprostol administered orally during active management of the third stage of labour. The acquired data was statistically analyzed. The significance threshold utilized was 0.05.

RESULTS

According to [Table 1], the average Group A mother weighed 66.29 kilograms, whereas the average Group B mother weighed 69.84 kilograms. The average birth weight in group A was 2.83 Kg, whereas it was 2.91 Kg in group B. In group A, the average blood loss was 448.3 ml, whereas it was only 306.1 ml in group B. A significant difference (P 0.05) was observed.

[Table 2] shows that need for blood transfusion was seen in 27 in group A and 8 in group B. The difference was significant (P< 0.05).

According to [Table 3], 7 individuals in Group B and 66 patients in Group A needed additional stereogenic medications. A significant difference (P <0.05) was observed.

Table 1: Distribution of patients

Parameters	Group A (Oxytocin)	Group B (Oxytocin+ Misoprostol)	P value
Mean weight (Kgs)	66.29	69.84	0.05
Baby mean weight (Kgs)	2.83	2.91	0.12
Blood loss (ml)	448.33	306.1	0.04

Table 2: Need for blood loss transfusion in both group

Group	Need for blood transfusion				P value
	Yes	%	No	%	
Group A	27	36	48	64	0.001
Group B	8	10.7	67	89.3	

Table 3: Need for additional stereogenic agents

Group	Need for additional stereogenic agents				P value
	Yes	%	No	%	
Group A	36	48	39	52	<0.001
Group B	7	9.3	68	90.7	

DISCUSSION

Postpartum hemorrhage is identified when blood loss is greater than 500 ml after a vaginal delivery and greater than 1000 ml following a cesarean section. Poor maternal health (PPH) is the major cause of maternal mortality and morbidity in developing and low-income countries. Even though several methods and suggestions have been developed for its prevention, the incidence of PPH continues to climb.^[5]

To reduce the incidence of PPH in pregnant women, the RCOG (Royal College of Obstetricians and Gynecologists) and the World Health Organization (WHO) advocate adhering to the AMTSL guidelines (Active Management of Third Stage of Labor). In

addition to early cord clamping and uterine massage, the use of uterotonic drugs is an AMTSL requirement.^[6]

Oxytocin is often recommended as the first-line uterotonic medication for the treatment and prevention of PPH in clinical settings. And the negative effects are less severe. For intramuscular and intravenous administration of oxytocin, qualified medical personnel is required.^[7] Ultimately, the efficacy of oxytocin is dependent on changes in the formulation's pH when exposed to heat, rendering it unstable at ambient temperature and demanding specific storage conditions, including a temperature range of 20 °C–80 °C and cold chain maintenance until delivery. There is a

buccal formulation of Des amino oxytocin, although it comes at a relatively high cost.^[8]

Misoprostol, a prostaglandin analog, may be administered orally, sublingually, rectally, vaginally, or buccally without the requirement for medical expertise. Misoprostol is inexpensive, easily available, and does not need specific storage conditions (such as refrigeration) to be preserved. This material is susceptible to becoming hydrated and wet when exposed to moisture.^[9] The objective of this study was to compare the effectiveness of misoprostol with oxytocin against oxytocin alone in avoiding postpartum hemorrhage.

The typical mother in group A weighed 66.29 kilograms, whereas the average mother in group B weighed 69.84 kg. The average birth weight in group A was 2.83 kgs, whereas it was 2.91 Kg in group B. In group A, the average blood loss was 448.3 mL, whereas it was only 306.1 mL in group B. Chaudhuri P. et al,^[10] examined women with risk factors for postpartum hemorrhage to see if the use of misoprostol in combination with oxytocin was more beneficial than using oxytocin alone in reducing blood loss after vaginal delivery (PPH). Following a vaginal delivery, some subjects received sublingual oxytocin (10 units) and others received sublingual misoprostol (400 g). The primary objectives were 1-hour postpartum blood loss and the incidence of PPH. A treatment-intention analysis was conducted. 144 individuals were divided equally between the two groups. At 1 hour postpartum, misoprostol-treated women had significantly less blood loss than placebo-treated women (225.8 ± 156.7 mL vs. 302.4 ± 230.3 mL; $P < 0.001$). Misoprostol significantly decreased the incidence of moderate PPH (500-999 mL) compared to placebo (5 [3.5%] vs. 15 [10.4%] individuals; $p < 0.03$).

27 participants in Group A and 8 participants in Group B required a blood transfusion, respectively. Widmer et al,^[11] compared the effectiveness of misoprostol in conjunction with traditional uterotonics to that of conventional uterotonics alone in the treatment of postpartum hemorrhage. Women were randomly randomized to receive 600 micrograms of misoprostol sublingually or a placebo, along with normal injectable uterotonics. The distribution of the therapy packets, which were sealed and numbered in the order of registration, helped conceal the allocation procedure. The treatment assignment was kept secret from both doctors and patients. Blood loss of 500 mL or more within 60 minutes after randomization was deemed the primary outcome. For a total of 1422 women, misoprostol (705 women) and placebo (717 women) were administered. Similar proportions of women in the misoprostol and placebo groups had 500 mL or more of blood loss within 60 minutes (100 [14%] and 100 [14%] respectively; relative risk 1.02, 95% confidence interval [CI]: 0.75 to 1.33). In the first 60 minutes, shivering (455/704 [65%] vs 230/717 [32%]; 2.01, 1.79-2.27) and body temperature of 38

degrees C or greater (303/704 [43%] vs 107/717 [15%]; 2.88, 2.37-2.50) were more prevalent in women using misoprostol than in those receiving placebo.

Overall, 36 individuals in Group A and 7 patients in Group B required additional stereogenic medications. Patted et al,^[12] investigated the adverse effects of 600 micrograms of oral misoprostol delivered to the mother and the newborn to avoid postpartum hemorrhage (PPH). During the third stage of labour, women in rural India who gave birth at home or in subcenters were randomly allocated to receive misoprostol or a placebo. At two and twenty-four hours postpartum, women were evaluated for shivering, fever, nausea, vomiting, and diarrhea. During the first 24 hours of a newborn's existence, diarrhea, vomiting, and fever were evaluated. Symptomlessness, mild symptoms, and severe symptoms were noted. Misoprostol-treated women were more likely to have to shiver (52% vs. 17%, $p < 0.001$) and fever (4.2% vs. 1.1%, $p < 0.001$) at 2 hours postpartum. The misoprostol group experienced significantly more incidences of chills (4.6% vs. 1.4%, $p 0.001$) and fever (1.4% vs. 0.4%, $p 0.03$) after 24 hours than the placebo group. There were no differences between the two groups in terms of nausea, vomiting, or diarrhea. The incidence of vomiting, diarrhea, and five among newborns did not alter.

Strength and Limitations of the Present Study

There are a few limitations of the study. In the present study, only 18-40 years of age submerge participated in the research. Hence, in the future, we would like to include an increase in the number of participants to reach a concrete conclusion. The Present study gave a single dose of 600 mg of sublingual misoprostol decreased blood loss more than the standard dose of ten units of intramuscular oxytocin alone.

CONCLUSION

When added to the standard dose of ten units of intramuscular oxytocin, a single dose of 600 mg of sublingual misoprostol decreased blood loss more than the standard dose of ten units of intramuscular oxytocin alone.

REFERENCES

1. Bellad MB, Tara D, Ganachari MS, Mallapur MD, Goudar SS, Kodkany BS, et al. Prevention of postpartum haemorrhage with sublingual misoprostol or oxytocin: a double-blind randomised controlled trial. *BJOG*. 2012;119(8):975-82. doi: 10.1111/j.1471-0528.2012.03341.x.
2. Fawole AO, Sotiloye OS, Hunyinbo KI, Umezulike AC, Okunlola MA, Adekanle DA, et al. A double-blind, randomized, placebo-controlled trial of misoprostol and routine uterotonics for the prevention of postpartum hemorrhage. *Int J Gynaecol Obstet*. 2011;112(2):107-11. doi: 10.1016/j.ijgo.2010.08.023.
3. Raghavan S, Abbas D, Winikoff B. Misoprostol for prevention and treatment of postpartum hemorrhage: what do

- we know? What is next? *Int J Gynaecol Obstet.* 2012;119 Suppl 1:S35-8. doi: 10.1016/j.ijgo.2012.03.013.
4. Kumar N. Postpartum hemorrhage; a major killer of woman: a review of the current scenario. *Obstet Gynecol Int J.* 2016;4(4):00116.
 5. Rani PR, Begum J. Recent Advances in the Management of Major Postpartum Haemorrhage - A Review. *J Clin Diagn Res.* 2017;11(2):QE01-QE05. doi: 10.7860/JCDR/2017/22659.9463.
 6. Priya GP, Veena P, Chaturvedula L, Subitha L. A randomized controlled trial of sublingual misoprostol and intramuscular oxytocin for prevention of postpartum hemorrhage. *Arch Gynecol Obstet.* 2015;292(6):1231-7. doi: 10.1007/s00404-015-3763-5.
 7. Zuberi NF, Durocher J, Sikander R, Baber N, Blum J, Walraven G. Misoprostol in addition to routine treatment of postpartum hemorrhage: a hospital-based randomized-controlled trial in Karachi, Pakistan. *BMC Pregnancy Childbirth.* 2008;8:40. doi: 10.1186/1471-2393-8-40.
 8. Vimala N, Mittal S, Kumar S. Sublingual misoprostol versus oxytocin infusion to reduce blood loss at cesarean section. *Int J Gynaecol Obstet.* 2006;92(2):106-10. doi: 10.1016/j.ijgo.2005.10.008.
 9. Alam A, Shyam P, Goswami S. A comparative study of the efficacy of oxytocin, methylergometrine, and misoprostol in the prevention of post-partum hemorrhage. *Int J Reprod Contracept Obstet Gynecol.* 2017;6(5):1960-4.
 10. Chaudhuri P, Majumdar A. A randomized trial of sublingual misoprostol to augment routine third-stage management among women at risk of postpartum hemorrhage. *Int J Gynaecol Obstet.* 2016;132(2):191-5. doi: 10.1016/j.ijgo.2015.06.064.
 11. Widmer M, Blum J, Hofmeyr GJ, Carroli G, Abdel-Aleem H, Lumbiganon P, et al. Misoprostol as an adjunct to standard uterotonics for treatment of post-partum haemorrhage: a multicentre, double-blind randomised trial. *Lancet.* 2010;375(9728):1808-13. doi: 10.1016/S0140-6736(10)60348-0.
 12. Patted SS, Goudar SS, Naik VA, Bellad MB, Edlavitch SA, Kodkany BS, et al. Side effects of oral misoprostol for the prevention of postpartum hemorrhage: results of a community-based randomised controlled trial in rural India. *J Matern Fetal Neonatal Med.* 2009;22(1):24-8. doi: 10.1080/14767050802452309.