

# COMPARISON OF SUBLINGUAL MISOPROSTOL VERSUS INTRAVENOUS OXYTOCIN FOR REDUCING MEAN BLOOD LOSS AFTER VAGINAL DELIVERY

#### KHAN MA, PARVEEN M, SADIQ S, UMAIR RM, KAINAT S

Department of Gynecology, Nishtar Medical University & Hospital Multan-Pakistan \*Correspondence author email address: drkash226@gmail.com

(Received, 14<sup>th</sup> July 2022, Revised 29<sup>th</sup> November 2022, Published 13<sup>th</sup> December 2022)

**Abstract:** Postpartum hemorrhage (PPH) is significantly associated with maternal morbidity and mortality, and many maternal deaths are preventable. Uterine atony is managed through uterotonic agents like prostaglandin F2 alpha (PGF2a), misoprostol, ergometrine and oxytocin and uterine rubbing. This prospective study was designed to compare the role of sublingual misoprostol and IV oxytocin in preventing blood loss after vaginal deliveries. This study was conducted at the Department of Obstetrics & Gynecology, Nishtar Hospital Multan, from 15 February 2021 to 14 August 2021. The study was conducted on 60 patients, 30 in both groups, who were selected through consecutive nonprobability sampling. Subjects were divided into Group A and Group B. 600  $\mu$ g misoprostol (3 doses of 200  $\mu$ g) was administered to Group A. 5 IU oxytocin was administered to Group B, with 3.3 IU/min at the beginning with the interval of 20 minutes until regular contractions are achieved. A maximum of 30mU/min oxytocin was infused. Mean blood loss was measured and recorded in proforma. The mean age of the subjects was 29.21 ± 6.07 years. The mean age of Group A was 29.40 ± 5.85 years, while that of Group B was 29.21 ± 6.32 years. Mean PPH blood loss in Group A, and B was 118.97 ± 20.26 ml and 154.13 ± 15.21 ml (P = 0.0001). The mean postpartum blood loss was higher by intravenous oxytocin than by sublingual misoprostol.

Keywords: Postpartum hemorrhage, maternal morbidity, oxytocin, misoprostol

#### Introduction

Postpartum hemorrhage (PPH) is significantly associated with maternal morbidity and mortality, and many maternal deaths are preventable. Timely recognition and accurate assessment of risk factors and blood loss is a significant challenge(Bláha and Bartošová, 2022). The prevalence of postpartum hemorrhage is 1 to 5% in developed and developing countries (Boltman-Binkowski, 2018). WHO has defined postpartum hemorrhage as blood loss > 500milliliters after vaginal delivery and blood loss > 1000 ml after caesarian delivery (Alejandra et al., 2021). Various factors lead to the high mortality rate of PPH (Lohano et al., 2016). A stepwise approach and exclusion of genital tract trauma and retained products are required to manage blood loss. Uterine atony is managed through uterotonic agents like prostaglandin F2 alpha (PGF2a), misoprostol, ergometrine and oxytocin and uterine rubbing. Different studies show that labor induction and augmentation using oxytocin are associated with an increased risk of PPH (Diaz et al., 2018). There is limited evidence that labor induction through prostaglandin postpartum bleeding is the same as in spontaneous vaginal delivery (Diaz et al., 2018). It is crucial to identify third-stage blood loss early for

prompt treatment. Practitioners usually do visual estimation for assessing blood loss, which is prone to error. A specialized collection bag provides a more accurate blood loss estimate than a visual estimation (Hancock et al., 2019). Uterotonic agents are used for controlling blood loss after delivery. Oxytocin infusion followed by methylergometrine and carboprost tromethamine are administrated at intervals of 15 to 20 minutes (Shaheen and Khalil, 2019). Oxytocin is standard for the management of PPH. It limits post-delivery bleeding by stimulating uterine contractions (Shaheen and Khalil, 2019). An alternative to oxytocin is misoprostol, a synthetic prostaglandin that acts uterotonic agent. It has added advantages, can be administered orally and sublingually and has a long shelf life, greater bioavailability and rapid onset of action (Ottun et al., 2022). A comparative study conducted on oxytocin and misoprostol showed that mean blood loss with sublingual misoprostol was 200± 126ml, while with oxytocin was 361±135ml (Aziz et al., 2014). This study is conducted to ascertain the role of sublingual misoprostol and IV oxytocin in preventing blood loss after vaginal deliveries.

[Citation: Khan, M.A., Parveen, M., Sadiq, S., Umair, R.M., Kainat, S. (2022). Comparison of sublingual misoprostol versus intravenous oxytocin for reducing mean blood loss after vaginal delivery. *Biol. Clin. Sci. Res. J.*, **2022**: 153. doi: https://doi.org/10.54112/bcsrj.v2022i1.153]



# Methodology

The prospective study was performed at the Department of Obstetrics & Gynecology, Nishtar Hospital Multan, from 15 February 2021 to 14 August 2021. The study was conducted on 60 patients, 30 in both groups, who were selected through consecutive nonprobability sampling(calculated by Epi - info software of CDC). The study included patients aged between 20 to 30 years, gestational age of more than 36 weeks, nulliparous and multiparous and those in third-stage labor if vaginal deliveries. Those with a history of severe pregnancy-induced hypertension, deranged liver function, asthma and previous c-section were excluded. Informed consent of the patients was taken. The ethical board of the hospital approved the study. Subjects were divided into Group A and Group B. 600 µg misoprostol (3 doses of 200 µg) was administered to Group A. 5 IU oxytocin was administered to Group B, with 3.3 IU/min at the beginning with the interval of 20 minutes until regular contractions are achieved. A maximum of 30mU/min oxytocin was infused. Mean blood loss was measured and recorded in proforma. SPSS

version 20 was used for data analysis. Mean and standard deviation was calculated for quantitative variables like age, BMI and blood loss. For qualitative variables like obesity, socioeconomic status and age groups, frequency and percentage were calculated. An Independent sample t-test was used to compare blood loss in both groups. For quantitative variables, a post-stratification t-test was done. P value < 0.05 was considered statistically significant.

### Results

The mean age of the subjects was  $29.21 \pm 6.07$  years. The mean age of Group A was  $29.40 \pm 5.85$  years, while that of Group B was  $29.21 \pm 6.32$  years. 35 (58.33%) patients aged between 20-30 years. The mean gestational age in Group A and B was  $39.03 \pm 1.45$  weeks and  $39.03 \pm 1.45$  weeks, respectively. The mean BMI in Group A and B was  $27.10 \pm 1.81$  kg/m2 and  $27.0 \pm 1.70$  kg/m2, respectively. Mean PPH blood loss in Group A, and B was  $118.97 \pm 20.26$  ml and  $154.13 \pm 15.21$  ml (P = 0.0001) (Table I). Tables II and III show the stratification of mean PPH according to gestational age and parity.

Table I. Mean	nostnartum	blood loss	in hoth grouns
I able I. Micall	μυδιμαι ιαπ	DIUUU 1055	m both groups

	Group A	Group B
Mean	118.97	154.13
Standard Deviation	20.26	15.21

\*P-value = 0.0001, which is statistically significant.

GA (weeks)	Group A (n=30)		Group B (n=30)		p-value
	Blood Loss (ml)		Blood Loss (ml)		
	Mean	SD	Mean	SD	
37-39	120.41	18.46	150.29	14.41	0.0001
40-42	117.08	23.07	159.15	15.30	0.0001

# Table II: Stratification of mean postpartum blood loss according to gestational age

Table III: Stratification of mean postpartum blood loss according to parity

Parity	Group A (n=30)		Group B (n=30)		p-value
	Blood Loss (ml)		Blood Loss (ml)		
	Mean	SD	Mean	SD	
Primiparous	122.0	16.79	169.20	5.22	0.0001
Multiparous	118.36	21.14	151.12	14.77	0.0001

### Discussion

According to WHO, PPH is the leading cause of maternal morbidity and mortality (Morfaw et al., 2021). Mean blood loss is highest in emergency hysterectomy (3500 mL), followed by cesarean section (1000 mL) and vaginal delivery (500 mL of blood) (Koch and Rattmann, 2019). The use of oxytocin significantly reduces the risk of PPH

(Bilgin and Kömürcü, 2019). Oxytocin is the drug of choice

for preventing uterine inertia in the c- section. Still, it is not ideal for preventing PPH, particularly in patients with prolonged labor, cardiac disease and preeclampsia (Maged et al., 2022). Oxytocin has antidiuretic, antiplatelet and negative inotropic effects and increases the heart rate (Rabie et al., 2018). In the current study, the mean PPH blood loss

[Citation: Khan, M.A., Parveen, M., Sadiq, S., Umair, R.M., Kainat, S. (2022). Comparison of sublingual misoprostol versus intravenous oxytocin for reducing mean blood loss after vaginal delivery. *Biol. Clin. Sci. Res. J.*, **2022**: 153. doi: https://doi.org/10.54112/bcsrj.v2022i1.153]

in Group A and B was  $118.97 \pm 20.26$  ml and 154.13 $\pm$  15.21 ml, respectively. Another study reported mean blood loss with misoprostol was 326.85±164.81mL and with oxytocin was 302.95±165.23mL (Rasri, 2018). A study reported that mean blood loss in the misoprostol group  $(490.65 \pm 158.80 \text{ mL})$  was significantly lower than in the oxytocin group( $602.07 \pm 298.59$  mL) (Othman et al., 2016). The need for additional therapy in the misoprostol group was 16.8%, and in the oxytocin group, 23.4%. The adverse effects incidence was higher in the misoprostol group than in the oxytocin group. In another randomized control study, women were divided into the misoprostol group (600 µg misoprostol sublingually) and oxytocin group (10 IU oxytocin intramuscularly), the occurrence of PPH in the misoprostol and oxytocin group was 28.7% and 17.5% respectively (Atukunda et al., 2014). Another study compared mean blood loss with oxytocin IM and sublingual misoprostol and found that it was higher in the oxytocin group  $(365 \pm 135 \text{ ml})$  as compared to the misoprostol group (193  $\pm$  125 ml) (Zeng et al., 2022). Hemoglobin loss of greater than 10% was observed in 45.7% and 9.8% of women in oxytocin and misoprostol, respectively. The adverse effects of the misoprostol group were higher than the oxytocin group. Another study showed that the hematocrit difference and mean blood loss were higher in the misoprostol group than in the oxytocin group (Naeem et al., 2021). A study found that the frequency of PPH was greater in misoprostol induction than in oxytocin labor induction (Valiani et al., 2018).

Our study has some limitations, including a small sample size and a short study period.

# Conclusion

The mean postpartum blood loss was higher by intravenous oxytocin than by sublingual misoprostol. Therefore, sublingual misoprostol should be the drug of choice for vaginal deliveries as it significantly reduces the risk of PPH, thus reducing maternal morbidity and mortality.

# **Conflict of interest**

The authors declared the absence of a conflict of interest.

# References

- Alejandra, G. C. L., Angel, R. Z. M., and Lisbeth, K. G. J. (2021). Postpartum Hemorrhage: Risk Factors and Preventive Strategies. *Journal of Gynecology and Obstetrics*9, 200-205.
- Atukunda, E. C., Siedner, M. J., Obua, C., Mugyenyi, G. R., Twagirumukiza, M., and

Agaba, A. G. (2014). Sublingual misoprostol versus intramuscular oxytocin for prevention of postpartum hemorrhage in Uganda: a double-blind randomized non-inferiority trial. *PLoS medicine***11**, e1001752.

- Aziz, S., Kazi, S., Haq, G., and Soomro, N. (2014). Oral misoprostol versus oxytocin in the management of third stage of labour. *J Pak Med Assoc*64, 428-432.
- Bilgin, Z., and Kömürcü, N. (2019). Comparison of the effects and side effects of misoprostol and oxytocin in the postpartum period: A systematic review. *Taiwanese Journal of Obstetrics and Gynecology***58**, 748-756.
- Bláha, J., and Bartošová, T. (2022). Epidemiology and Definition of PPH Worldwide. *Best Practice & Research Clinical Anaesthesiology*.
- Boltman-Binkowski, H. (2018). A systematic review of best practices in the acute management of postpartum haemorrhage in primary maternity care settings.
- Diaz, V., Abalos, E., and Carroli, G. (2018). Methods for blood loss estimation after vaginal birth. *Cochrane Database of Systematic Reviews*.
- Hancock, A., Weeks, A. D., and Tina, L. D. (2019). Assessing blood loss in clinical practice. Best Practice & Research Clinical Obstetrics & Gynaecology61, 28-40.
- Koch, D. M., and Rattmann, Y. D. (2019). Use of misoprostol in the treatment of postpartum hemorrhage: a pharmacoepidemiological approach. *Einstein (São Paulo)*18.
- Lohano, R., Haq, G., Kazi, S., and Sheikh, S. (2016). Intrauterine balloon tamponade for the control of postpartum haemorrhage. *J Pak Med Assoc*66, 22-6.
- Maged, A. M., Wali, A. A., Metwally, A. A., and Salah, N. (2022). The efficacy of misoprostol in reducing intraoperative blood loss in women undergoing elective cesarean section. A systematic review and meta-analysis. *Journal of Obstetrics and Gynaecology Research***48**, 2038-2070.
- Morfaw, F., Miregwa, B., Bi, A., Mbuagbaw, L., Anderson, L. N., and Thabane, L. (2021). Comparing and combining evidence of treatment effects in randomized and nonrandomized studies on the use of misoprostol to prevent postpartum hemorrhage. *Journal of Evidence-Based Medicine*14, 198-207.
- Naeem, M., Latif, M., Nawaz, F., Latif, M., and Aftab, S. (2021). Compare the Sublingual and Per Rectal Routes of Misoprostol Administration in Third Stage of Labor in Terms of Average Blood Loss. Drug

<sup>[</sup>Citation: Khan, M.A., Parveen, M., Sadiq, S., Umair, R.M., Kainat, S. (2022). Comparison of sublingual misoprostol versus intravenous oxytocin for reducing mean blood loss after vaginal delivery. *Biol. Clin. Sci. Res. J.*, **2022**: 153. doi: https://doi.org/10.54112/bcsrj.v2022i1.153]

*Resistant TB and Bone Marrow Stem Cells***32**, 105.

- Othman, E. R., Fayez, M. F., Abd El Aal, D. E. M., Mohamed, H. S. E.-D., Abbas, A. M., and Ali, M. K. (2016). Sublingual misoprostol versus intravenous oxytocin in reducing bleeding during and after cesarean delivery: a randomized clinical trial. *Taiwanese Journal* of Obstetrics and Gynecology**55**, 791-795.
- Ottun, T. A., Adewunmi, A. A., Rabiu, A. K., Olumodeji, A. M., Oladipo, O. M., and Olalere, H. F. (2022). Misoprostol and oxytocin versus oxytocin alone in the active management of the third stage of labour: a randomised, double-blind, placebo-controlled trial. *Journal of Obstetrics and Gynaecology***42**, 1048-1053.
- Rabie, N. Z., Ounpraseuth, S., Hughes, D., Lang, P., Wiegel, M., and Magann, E. F. (2018). Association of the Length of the Third Stage of Labor and Blood Loss Following Vaginal Delivery. *Southern medical journal***111**, 178-182.
- Rasri, W. (2018). Intrauterine misoprostol plus intravenous oxytocin for reduction of blood loss in cesarean delivery. *Thai Journal of Obstetrics and Gynaecology*, 237-245.
- Shaheen, N., and Khalil, S. (2019). Safety and efficacy of 600 ug sublingual Misoprostol versus 10 U intramuscular Oxytocin for management of third stage of labor. *Rawal Medical Journal*44, 137-137.
- Valiani, M., Allameh, Z., Bahadoran, P., and Amani, E. (2018). A Study on the Combined Effect of Vaginal Misoprostol and Venous Oxytocin on Induction of Labor, Bishop Score, and Duration of Labor. *Journal of Isfahan Medical School***36**, 954-963.
- Zeng, Y., Zhang, Y., Zhen, M., Lao, L., Ma, Y., Liu, L., Fan, D., and Ai, W. (2022). Side-effects of oxytocin in postpartum hemorrhage: a systematic review and meta-analysis. *American journal of translational research***14**, 1934.



**Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or

other third-party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a of this licence. copy visit http://creativecommons.org/licen ses/by/4.0/. © The Author(s) 2022

[Citation: Khan, M.A., Parveen, M., Sadiq, S., Umair, R.M., Kainat, S. (2022). Comparison of sublingual misoprostol versus intravenous oxytocin for reducing mean blood loss after vaginal delivery. *Biol. Clin. Sci. Res. J.*, **2022**: 153. doi: https://doi.org/10.54112/bcsrj.v2022i1.153]