



## Original Article

# Comparison of intramuscular methylergometrine, rectal misoprostol, and low-dose intravenous oxytocin in active management of the third stage of labor

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## ABSTRACT

**Objective:** Active management of the third stage of labor (AMTSL) is a critical intervention for the prevention of postpartum hemorrhage (PPH), which is still the most common cause of maternal morbidity and mortality worldwide. The objective of the study is to compare the effect of intramuscular methylergometrine, rectal misoprostol, and low-dose intravenous oxytocin in the AMTSL in terms of amount of blood loss and duration of the third stage of labor, cost-effectiveness, and side effect profile. **Materials and Methods:** Seventy-five pregnant patients admitted in the maternity ward for vaginal delivery from February 2017 to February 2018 received either intramuscular methylergometrine (0.2 mg) or rectal misoprostol (400 mcg) or low-dose intravenous oxytocin (5 units oxytocin in 100 mL normal saline) for AMTSL. Data were recorded in three groups: Group A (methylergometrine), Group B (misoprostol), and Group C (oxytocin) consisting of 25 cases each. **Results:** Mean blood loss was found to be least in methylergometrine group ( $246.87 \pm 65.44$  mL) as compared to misoprostol ( $346.13 \pm 58.35$  mL) and oxytocin ( $334.5 \pm 69.20$  mL) ( $P = 0.000$ ) Mean duration of the third stage of labor was also least in methylergometrine group ( $6.21 \pm 1.58$  min) ( $P = 0.0008$ ). **Conclusion:** Although methylergometrine was found to have higher incidence of side effects such as nausea, vomiting, headache, and raised blood pressure, it was found to be the most effective drug for minimizing blood loss in the third stage of labor. In remote places where healthcare facilities are limited and drugs cannot be administered by parenteral route, rectal misoprostol remains an alternative.

**KEYWORDS:** *Methylergometrine, Misoprostol, Oxytocin, Postpartum hemorrhage, Third stage of labor*

Received : 02-May-2018  
Revised : 06-Jun-2018  
Accepted : 24-Jul-2018

## INTRODUCTION

Postpartum hemorrhage (PPH) is one of the leading causes of maternal morbidity and mortality worldwide [1]. Active management of the third stage of labor (AMTSL) as recommended by the WHO is a critical intervention for the prevention of PPH and is composed of three components: (1) administration of a uterotonic, preferably oxytocin, immediately after birth of the baby; (2) controlled cord traction (CCT) to deliver the placenta; and (3) massage of the uterine fundus after the placenta is delivered. A unified consensus has been reached over the years that AMTSL with use of uterotonic drugs is more effective in reducing the duration of the third stage, incidence of retained placenta, amount of blood loss, and hence puerperal morbidity and mortality [2]. We conducted this study in context with Indian scenario where majority of the population is anemic, and

there is need to reconsider the choice of uterotonic drug with preference to the drug most effective in controlling blood loss.

## MATERIALS AND METHODS

A prospective hospital-based study was conducted in the Department of Obstetrics and Gynaecology of S.P. Medical College, Bikaner, between February 2017 and February 2018. Patients with full-term singleton pregnancy admitted in the maternity ward for vaginal delivery were enrolled in the study after taking written informed consent.

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**How to cite this article:** Jain R, Agrawal S, Verma K, Jain A, Baid M. Comparison of intramuscular methylergometrine, rectal misoprostol, and low-dose intravenous oxytocin in active management of the third stage of labor. Tzu Chi Med J 2019;31(3):158-62.

Access this article online	
<b>Quick Response Code:</b> 	<b>Website:</b> www.tcmjmed.com
	<b>DOI:</b> 10.4103/tcmj.tcmj_89_18

Patients who had hemoglobin <7 g/dL, previous history of PPH, pregnancy-induced hypertension, mal-presentations, coagulation abnormalities, antepartum hemorrhage, intrauterine demise, history of previous cesarean section, medical disorders such as diabetes, heart disease, stroke, peripheral vascular disorders, epilepsy, asthma, liver and kidney disorders, uterine rupture, or scar dehiscence were excluded from the study.

The third stage of labor was actively managed in these patients by either intramuscular methylergometrine (0.2 mg) (Group A) or rectal misoprostol (400 mcg) (Group B) or low-dose intravenous oxytocin (5 units in 100 mL normal saline) (Group C). For randomization, computer-generated random table was used. Data were recorded for a total of 75 cases with 25 cases in each group. The placenta was delivered by CCT (modified Brandt–Andrews method) and uterine massage was given in all cases.

The blood loss during the third stage of labor was measured in a blood collecting bag (BRASSS-V-DRAPE). Blood clots were weighed separately considering 1 g equal to 1 mL of blood. Blood-soaked swabs were weighed, the known dry weight subtracted, and the calculated volume was added to the volume of blood in the measuring bag to get the total blood loss. Duration of the third stage of labor for each case was also noted. Maternal hemoglobin and hematocrit were repeated 24 h after the delivery, and the fall in hemoglobin and hematocrit was taken as an objective measure of blood loss. The occurrence of side effects such as nausea, vomiting, headache, shivering, fever, and diarrhea was noted for the next 24 h.

## RESULTS

One patient each in Group A, Group B, and Group C had blood loss >500 mL and was labeled as PPH. They were managed according to the guidelines and excluded from our study. Final data consisted of 24 cases each in Group A (methylergometrine), Group B (misoprostol), and Group C (oxytocin).

Demographic profile of the patients is shown in Table 1, and duration of the three stages of labor, episiotomy, baby weight, and mean blood loss in the third stage of labor are shown in Table 2.

Figure 1 shows flowchart depicting group distribution of the patients and Figure 2 shows the distribution of cases according to duration and blood loss in the third stage of labor and side effects.

Mean duration of the third stage of labor in Group A (methylergometrine) was  $6.21 \pm 1.58$  min, Group B (misoprostol) was  $7.79 \pm 1.35$  min, and Group C (oxytocin) was  $7.46 \pm 1.41$  min. *P* value was found to be 0.0008. Mean blood loss during the third stage of labor in Group A (methylergometrine) was  $246.87 \pm 65.44$  mL, Group B (misoprostol) was  $346.13 \pm 58.35$  mL, and Group C (oxytocin) was  $334.5 \pm 69.20$  mL. *P* value was found to be 0.000.

Fall in the hemoglobin and hematocrit level was also found to be least in methylergometrine group but was not statistically significant [Table 3].

**Table 1: Demographic profile of the patients**

	Group A (methylergometrine) (%)	Group B (misoprostol) (%)	Group C (oxytocin) (%)	<i>P</i>
Mean age (years)	23.03±3.02	24.32±3.40	25.08±4.05	
Residence				
Rural	8 (33)	10 (42)	11 (46)	
Urban	16 (67)	14 (48)	13 (54)	
Parity				
Primigravida	9 (38)	13 (54)	11 (46)	
Multipara	15 (62)	11 (46)	13 (54)	
Socioeconomic class (modified Kuppuswamy scale)				
I. Upper	1	1	2	
II. Upper middle	5	4	9	
III. Lower middle	9 (38)	10 (42)	9 (38)	
IV. Upper lower	7 (29)	8 (33)	1 (4)	
V. Lower	2	1	3	
Mean BMI (kg/m <sup>2</sup> )	24.43±1.43	25.14±2.2	24.39±1.99	0.311
Booked	15 (63)	16 (67)	15 (63)	
Unbooked	6 (25)	8 (33)	9 (37)	

BMI: Body mass index

Twenty-nine percent of cases in Group A, 8% cases in Group B, and 8% cases in Group C complained of nausea and vomiting. 8% cases in Group A, 8% cases in Group B, and 12.5% cases in Group C complained headache. 8% cases in Group A, 12.5% cases in Group B, and 8% cases in Group C developed pyrexia. 12.5% cases in Group B complained of diarrhea in the postoperative period.

Cost per dose was found to be Indian National Rupees (INR) 47.5 in methylergometrine group, INR 10.7 in misoprostol group, and INR 71.72 in oxytocin group [Table 4].

## DISCUSSION

Hemorrhage along with hypertension and infection forms a part of the “deadly triad,” contributing to maternal morbidity and mortality worldwide [1]. An estimated 500,000 women die from pregnancy-related causes every year with up to a quarter of deaths occurring due to hemorrhage, especially in the developing countries. It is axiomatic that PPH occurs unpredictably and no parturient is immune from it. PPH is a significant contributor to maternal morbidity, to long-term disability, as well as to other severe conditions generally associated with more substantial blood loss, including shock and organ dysfunction. Blood loss up to 500 mL following vaginal delivery is generally considered as physiologically normal [3].

The effect of blood loss is more important than the amount of blood loss; therefore, defining PPH as any amount of blood loss accompanied by signs and symptoms of hypovolemia regardless of the route of delivery is clinically more significant as opposed to the traditional definition [4].

In 2012, the results of a large WHO-directed, multicenter clinical trial were published and showed that the most important

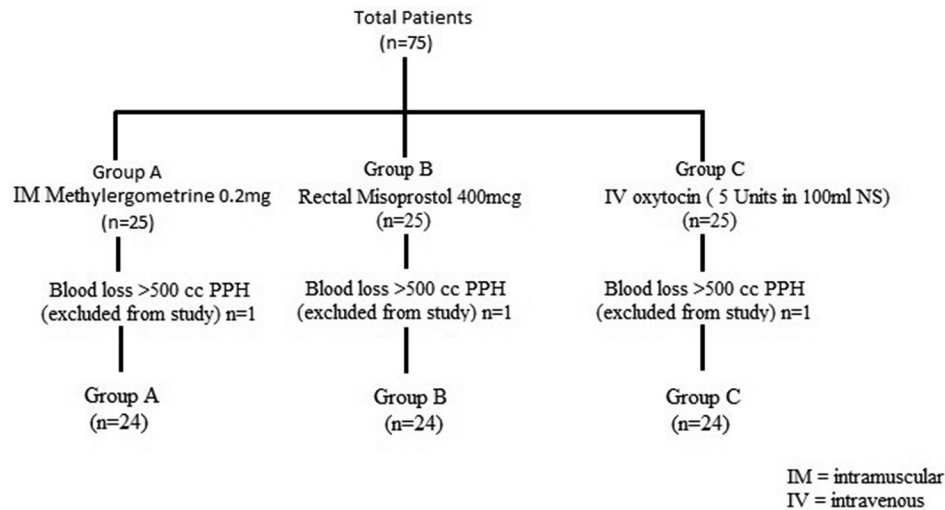


Figure 1: Flowchart showing group distribution of the patients

Table 2: Distribution according to duration of the three stages of labor, episiotomy, baby weight, and mean blood loss in the third stage of labor

	Group A (methylergometrine)	Group B (misoprostol)	Group C (oxytocin)	P
Duration				
First stage of labor (h)	6.25±1.98	5.23±1.6	6.27±1.51	0.0008
Second stage of labor (min)	41.25±18.57	32.87±12.12	42.5±16.4	
Third stage of labor (min)	6.21±1.58	7.79±1.35	7.46±1.41	
Right mediolateral episiotomy (%)				
Yes	15 (63)	16 (75)	15 (63)	0.569
No	9 (37)	8 (25)	9 (37)	
Mean baby weight (kg)	2.82±0.43	2.85±0.52	2.91±0.39	0.778
Mean blood loss in third stage (mL)	246.87±65.44	346.13±58.35	334.5±69.20	0.000

Table 3: Distribution of cases according to predelivery hemoglobin and hematocrit and fall in hemoglobin and hematocrit (24 h after delivery)

	Mean			P
	Group A	Group B	Group C	
Predelivery Hb (g/dL)	8.88±1.17	8.85±1.4	8.72±1.4	0.912
Predelivery Hct (%)	31.1±3.03	30.6±2.3	30.1±3.23	0.539
Fall in Hb (g/dL)	0.93±0.47	1.05±0.64	1.02±0.52	0.766
Fall in Hct (%)	1.33±0.9	1.48±1.14	1.47±0.99	0.694

Hct: Hematocrit, Hb: Hemoglobin

component was the administration of an uterotonic agent [5]. The most commonly used uterotonic drugs in the management of third stage of labor include ergot alkaloids, prostaglandins, and oxytocin.

McDonald *et al.* [6] (2004) addressed prophylactic ergometrine–oxytocin versus oxytocin for the third stage of labor in their meta-analysis. Their review indicated that the use of ergometrine–oxytocin as a part of the routine AMTSL appears to be associated with a small but statistically significant reduction in the risk of PPH when compared to oxytocin for blood loss of 500 mL or more. No statistically significant difference was observed between the groups for blood loss of 1000 mL or more.

Satwe *et al.* [7] conducted a study to assess effect of injection oxytocin versus injection methylergometrine in AMTSL. The study concluded that intramuscular oxytocin and intravenous methylergometrine are equally effective in reducing the third-stage blood loss. This reduction in blood loss reduced the incidence of postpartum anemia, infection, and hence maternal mortality and morbidity.

In our study, methylergometrine was found to be most effective drug with mean blood loss of 246.87 ± 65.44 mL as compared to misoprostol 346.13 ± 58.35 mL and oxytocin 334.5 ± 69.20 mL (*P* = 0.000 which is highly significant). Mean duration of the third stage of labor was also least in methylergometrine group (6.21 ± 1.58 min) (*P* = 0.0008). Methylergometrine was found to be associated with higher incidence of nausea, vomiting (29%), headache (8%), and raised blood pressure. Headache was more commonly noted in oxytocin group (12.5%). Pyrexia (12.5%) and diarrhea (12.5%) were most commonly reported in misoprostol group.

Gohil and Tripathi [8] conducted a study to compare the efficacy of misoprostol 400 µg per rectally, injection oxytocin 10 IU intramuscular, injection methylergometrine 0.2 mg intravenously, and injection ergometrine–oxytocin (0.5 mg ergometrine + 5 IU oxytocin) intramuscular in the management of the third stage of labor. They also concluded that

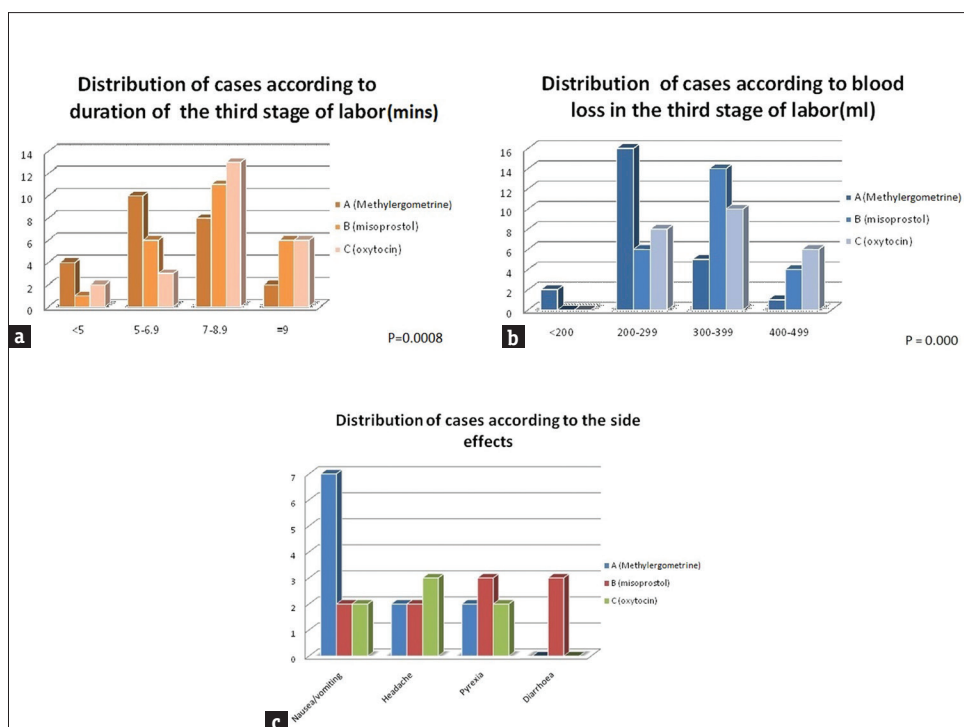


Figure 2: Distribution of cases according to (a) duration and (b) blood loss in the third stage of labor and (c) side effects

Table 4: Cost of each dose using methylergometrine, misoprostol, and oxytocin

	INR		
	Group A (methylergometrine 0.02 mg)	Group B (misoprostol 400 mcg)	Group C (oxytocin 5 units in 100 mL NS)
Drug (per dose)	14.5	9.5	18.72
Gloves	25 (sterile)	1 (examination gloves)	25 (sterile)
Syringes	0.5	-	0.5
Cold chain maintenance (approximate per vial)	5	-	5
Aseptic precautions (approximate)	2.5	-	2.5
Others	-	-	20 (NS 100 mL, drip set)
Total cost	47.5	10.5	71.72

INR: Indian national rupees, NS: Normal saline

Methylergometrine has the best uterotonic drug profile among the drugs. Misoprostol was found to cause a higher blood loss compared to other drugs and hence should be used only in low-resource setting where other drugs are not available.

Methylergometrine and oxytocin should be maintained in cold storage to preserve their efficacy and shelf life. They require syringes and needles for intramuscular and intravenous administration. Hence, rectal misoprostol is a more cost-effective drug as it can be easily stored at room temperature and does not require parenteral administration. Another advantage of rectal misoprostol is easy administration that can be done by health care workers and it does not require any specialized training.

**CONCLUSION**

As methylergometrine is found to be the most effective drug in reducing blood loss in the third stage of labor, its use needs to be reemphasized in the anemic population.

However, further multicentric trials are needed to substantiate our finding. In remote places where health care facilities are limited and drugs cannot be administered by parenteral route, rectal misoprostol remains an alternative and is also the more cost-effective.

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.

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