

# A comparative study of oxytocin, carboprost, methylergometrine and misoprostol in prevention of postpartum haemorrhage a prospective study

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## Abstract

**Background:** Post partum hemorrhage (PPH) is an important cause of maternal mortality accounting for nearly 15-20% of maternal deaths in India. Oxytocic drugs like oxytocin, ergot alkaloids, and various prostaglandins are being used for active management of third stage of labour. **Materials and Methods:** A prospective study was conducted in the Department of Obstetrics and Gynaecology of Al Ameen Medical College, Vijayapur, in 400 women. Patients were randomized into four groups of 100 each and were given oxytocic within 60 seconds of delivery anterior shoulder of the baby. Oxytocics used were 10 IU intramuscular oxytocin, 125 µg intramuscular carboprost, 0.2 mg intravenous methylergometrine, and 800 µg tablet misoprostol per rectally in groups A, B, C and D respectively. **Results:** Duration of third stage of labor recorded was minimum with carboprost with mean duration of 3.84±0.99 minutes and was maximum with methylergometrine with mean duration of 5.04±1.02 minutes. Amount of blood loss observed was minimum with carboprost (mean 131 ±72.037 ml) and maximum with Methylergometrine (mean 435±147.578 ml). Hemoglobin drop was also seen more with Methylergometrine with mean drop of 0.872±0.458 gm% and minimally with carboprost with mean drop of 0.236 ±0.221 gm%. **Conclusion:** It is concluded from this study that carboprost is the uterotonic of choice followed by oxytocin for active management of third stage of labor.

**Keywords:** Postpartum Hemorrhage, Active Management of Third Stage of Labor, Oxytocic Drugs, Third stage of labour.

## Introduction

The third stage of labour is the most crucial stage, begins with expulsion of baby and ends with expulsion of placenta and membranes. Its average duration is 15 min in both primigravida and multigravida [1]. Postpartum hemorrhage is one of the dreaded complications of third stage of labour. In India every 4 minutes a woman dies during childbirth [2]. Maternal mortality rate in India is 212 per 100000 live births. Among them 30% of deaths are due to postpartum hemorrhage (PPH) [3].

Reducing likelihood of postpartum haemorrhage by routine active management of third stage of labour could play an important role in reducing maternal mortality and morbidity in modern obstetrics. The

decrease in the problems associated with third stage of labour has been attributed to judicious use of different oxytocic preparations administered at time of delivery of anterior shoulder and a transition from expectant to active intervention [4-5]. Drugs conventionally used for prophylaxis against PPH includes oxytocin, methylergometrine, misoprostol and 15 methyl PGF<sub>2</sub>α (Carboprost) [6]. Recent studies have shown that there are still wide variations in practice around the world in the management of third stage of labour [7-8].

Prophylactic use of oxytocic agents after delivery of the infant has been shown to reduce the incidence of PPH by 40%. But it is associated with side effects ranging from nausea, vomiting, and hypertension to postpartum eclampsia, intracerebral haemorrhage, myocardial infarction, cardiac arrest and pulmonary oedema [2]. Carboprost tromethamine is a PGF<sub>2</sub> α analogue. It is

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### Original Research Article

given as a single intramuscular injection. It is free from side effects such as hypertension [9]. Postpartum haemorrhage is defined as any amount of bleeding following delivery which can lead to deterioration in the condition of woman.

It is difficult to delineate the risk factors for postpartum haemorrhage. So, all woman are considered at risk. Active management of third stage of labor has been universally recommended as not an option but a rule.

This includes administration of uterotonics, controlled cord traction and fundal massage the placenta will be delivered safely after the delivery of fetus and can prevent postpartum haemorrhage and maternal deaths.

### Aims and Objectives

1. To evaluate and compare the efficacy of oxytocin, carboprost, methylergometrine and misoprostol in the active management of third stage of labor and thereby prevention of PPH.
2. To compare the amount of blood loss in third stage.
3. To compare the duration of third stage.
4. To evaluate the side effects

### Methods

The present prospective study was conducted in the Department of Obstetrics and Gynaecology, Al Ameen Medical College, Vijayapur, over the period from 2017 to 2018 after taking approval from Institutional Ethical Committee. Four hundred patients were enrolled and these patients were distributed in four different groups randomly.

Informed consent and counselling of the patients was done. A detailed history of all the patients was taken including name, age, parity, socioeconomic status, and menstrual history, period of gestation (in weeks), obstetrical history including postpartum hemorrhage and history of any medical disorder. Complete general and systemic examination was done. Detailed systemic and obstetrical examination was done. Pelvic examination was done.

After detailed history and examination, patients were randomized into four groups of 100 each as follows:

**Group A-** Patients received 10 IU intramuscular oxytocin.

**Group B-** Patients received 125 µg intramuscular carboprost

**Group C-** Patients received 0.2 mg intravenous methylergometrine.

**Group D-** Patients received 800 µg tablet misoprostol per rectally.

Placebo control is not possible in this study because we can't deny a uterotonic to a patient after delivery.

**Inclusion Criteria:** Women with singleton pregnancy, Term gestation, without any high risk factors.

### Exclusion Criteria

1. Period of gestation <37weeks and >42week.
2. Fetal complications: IUFD, IUGR.
3. Maternal complications: PIH, Multiple pregnancy, Grand multipara, APH, malpresentations, patient with known blood coagulation disorder, patient with known allergy to prostaglandins, history of medical disorders—cardiac disease/renal disease, anemia (Hb<7gm%)

Active management of third stage of labor was done within one minute after the birth of the baby using one of the four oxytocic drugs as per the group of the patient.

Within a minute of delivery of baby, Brass-V drapes were immediately applied to measure the amount of blood loss. Placenta was delivered by controlled cord traction as soon as signs of placental separation appeared. Inspection of vulva for perineal tears and per speculum examination for cervical tear was carried out and if present patients were not taken into series. Repeat haemoglobin estimation was done on second postpartum day.

**Type of study:** Prospective study.

**Ethical Approval:** The study was approved by the institutional ethics committee.

**Sampling Method:** Randomisation done.

**Statistical Methods:** The statistical analysis was performed using students t-test and paired t-test for continuous variables. p-value of <0.05 was considered statistically significant. Data were calculated as means, standard deviation (SD), numbers and frequency (%). No scoring system and surgical procedure used.

The data were evaluated for the following

1. Duration of third stage of labor in all groups.
2. Amount of blood loss during third stage of labor.
3. Drop in mean hemoglobin levels in various groups.
4. Comparison of the side effects of various uterotonics.

## Results

Patients in all four groups were comparable with regards to their age, socioeconomic status, parity, booking status, BMI and number of episiotomies given (Table1).

Mean duration of third stage of labor was 4.72 minutes in group A, 5.04 minutes in group C and 4.93 minutes in group D. It was lowest in group B (3.84 minutes) which is statistically significant with p value of 0.002 (Table2) (Graph1).

Mean blood loss in various study groups A, B, C and D was 223.2, 131.8, 435 and 255.8ml respectively. Maximum blood loss was in patients given methylergometrine and minimal in patients given Carboprost with a p-value of <0.001 which is statistically significant (Table 2) (Graph 2).

Groups A, B and D showed comparable drop in haemoglobin 0.3, 0.2 and 0.4 gm%. The maximal drop was observed in group C up to 0.8 gm% with a significant p-value of 0.002 (Table2).

However 6 patients in group C had postpartum hemorrhage (statistically significant with p-value of 0.004) (Table 2).

Two patients out of six who had postpartum haemorrhage necessitating additional oxytocics and blood transfusion which is statistically significant with a p-value of 0.111 (Table 2).

Nausea and vomiting were found to be the commonest side effects in all groups followed by shivering and fever.

**Table-1: Biosocial characteristics of the study subjects.**

	Group A	Group B	Group C	Group D	p-value
Mean age (years)	22.96	22.16	22.84	23.16	0.051
Booking (%)					
Booked	52	48	44	52	
Unbooked	48	52	56	48	0.931
Socioeconomic status (%)					
Upper	0	0	0	4	
Upper middle	36	32	36	44	0.921
Lower middle	44	40	40	36	
Upper lower	12	24	20	12	
Lower	8	4	4	4	
Parity (%)					
P1	64	72	76	56	0.803
P3	8	8	12	20	
BMI (%)					
<18.50	8	8	0	0	
18.50-24.99	84	84	100	96	
25.00-29.99	8	4	0	0	0.286
30.00-34.99	0	4	0	0	
35.00-39.99	0	0	0	4	
>40	0	0	0	0	
Episiotomy (%)					
Given	80	72	84	64	0.369
Not given	20	28	16	36	

**Table-2: Post-delivery data in four groups.**

	<b>Group A Oxytocin</b>	<b>Group B Carboprost</b>	<b>Group C Methylegometrine</b>	<b>Group D Misoprostol</b>	<b>p- value</b>
Duration of third stage of labor (minutes)	4.72	3.84	5.04	4.93	0.002
Amount of blood loss (ml)	223.2	131.8	435	255.8	<0.0001
Drop in hemoglobin (gm%)	0.372	0.236	0.872	0.44	<0.0001
Number of patients having blood loss > 500 ml	0	0	6	0	0.0004
Number of patients requiring blood transfusion	0	0	2	0	0.111

## Discussion

Postpartum hemorrhage is one of the most important cause for maternal deaths throughout the world. Active management of third stage of labor and the use of prophylactic oxytocics has reduced its incidence in many countries. The primary aim in the management of postpartum hemorrhage should be its prevention. The active management of the third stage with routine prophylactic administration of oxytocics at the time of delivery of the anterior shoulder of the fetus has been shown to reduce the risk of postpartum hemorrhage by about 40% [5,10].

Recent studies show that there are still wide variations in practice around the world in the management of third stage of labour. Methyl ergometrine is a conventional oxytocic used extensively but is associated with unpleasant side effects like hypertension. Intramuscular oxytocin used alone has been found effective in preventing postpartum hemorrhage with fewer side effects and is recommended by world health organization but most of the times additional uterotonics are required [8,11]. Various drugs and routes of administration have been tested with varying success. Oxytocin is probably the most commonly used oxytocic and has been well known in midwifery for a long time. Though commonly used it is not the potent drug and many a times requires additional drugs and blood loss is more compared with other drugs [11].

The production of PGF<sub>2</sub> $\alpha$  in the decidual tissue was found to be more when obtained during labour indicating the increase in the synthesis and release of PGF<sub>2</sub> $\alpha$  into the circulation. PGF<sub>2</sub> $\alpha$  is a powerful uterotonic agent with a physiological role in human parturition both in the delivery of the foetus and control of post partum bleeding. The discovery of prostaglandins and its analogues as an oxytocics has improved prospect in modern era in control of PPH due to its significant influence on uterine tone resulting in minimizing blood loss which outweighs its cost. The side effects are also subtle [12-13]. Hence this study was conducted at Al Ameen medical college to evaluate the four uterotonic drugs. This study has shown that that carboprost is the uterotonic of choice followed by oxytocin for active management of third stage of labor.

**Table-3: Mean duration of third stage**

<b>Study</b>	<b>Methyl ergometrine</b>	<b>Carboprost</b>	<b>Oxytocin</b>	<b>Misoprostol</b>
Singh nisha etal [20]	5.52 minutes	6.10 minutes	-	
Anjaneyu etal [13]	6.1 minutes	3.5 minutes	--	
Bhattacharya et al [4]	8.08 minutes	4.8 minutes	-	
B. Rajupuroshotam etal [19]	3.6 minutes	2.63 minutes	-	
Present study	5.04 minutes	3.84 minutes	4.72 minutes	4.93 minutes

There are few studies where carboprost has been compared with methyl ergometrine and found that the mean duration of third of labour with carboprost was comparable to our study [14,15]. As compared to other studies and in accordance with it, the present study showed decrease in mean duration of third stage of labor in carboprost group was 3.84 minutes compared to oxytocin 4.72 minutes. Therefore carboprost can be effective in reducing the duration of third stage of labour.

**Table-4: Comparison of estimated blood loss in ml.**

Study	Methyl ergometrine	Carboprost	Oxytocin	Misoprostol
Reddy et al [14]	202 ml	127ml	-	
B. Rajupuroshotam [19]	169ml	111ml	-	
Present study	435ml	131.8ml	223.2ml	255.8ml

Various studies have shown that the mean blood loss with carboprost 125µg was less compared to methyl ergometrine. Few studies compared carboprost with syntometrine, which did not show any difference in mean blood loss in both the group [14]. In the present study mean blood loss in third stage in carboprost was 131.8 ml and oxytocin was 223.2 ml. (p value of 0.0001) which was highly significant [11]. None of them developed PPH in carboprost group but 6 women had PPH in methylergometrine group. This was comparable with other studies as shown in the table. Hence carboprost is effective in reducing blood loss and carboprost has sustained impact on tone of uterus. Hemoglobin was 0.3 in oxytocin and 0.23 carboprost, 0.87gm% in methylergometrine group, 0.44gm% in misoprostol group which was statistically significant (p value of 0.0001). Two required blood transfusion in methylergometrine group and none in other 3 groups.

In group A, minor side effects in the form of shivering, vomiting and headache were observed. Our findings are not consistent with that of Gohil J et al (2011) as the incidence of these minor side effects was much lower in their study [21].

In group B Diarrhea and vomiting were most commonly observed along with chills in only 12%. This is comparable to the study of Chua S et al (1995) where they found a significant increase in the incidence of diarrhea with prostidin [24].

In group C in addition to shivering and nausea, side effects like hypertension was also observed in 24% of patients, study being consistent with that of Gohil J et al (2011) as patients exhibited hypertension in their study also [21].

In group D, minor side effects, like shivering and fever, were present in 48% and 56% of patients. Our study is consistent with the study of El Refaey et al (1997), Hofmeyer G J et al (1998), F Amant et al (1999), Hazem El- Rafaey et al (2000) in which their patients also exhibited fever and shivering [22,23,25].

The only Drawback in using carboprost is its storage in cold chain at 2- 4 celsius while oxytocin can be stored at room temperature.

## Conclusion

Carboprost when used prophylactically results in minimal blood loss with fewer side effects. This small dose 125µg is well tolerated by the patients. An added advantage is it can be used in patients with hypertension and cardiovascular disease. In India where anemia highly prevalent, the risk of PPH is very high.

Intramuscular carboprost, a potent uterotonic is a desirable drug as it is well tolerated in small doses and significantly reduces the risk of PPH by limiting duration of 3<sup>rd</sup> stage of labour & by reducing the blood loss Our study emphasizes that carboprost is better alternative to intramuscular oxytocin in active management of third stage of labour.

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**Contribution by Co-Authors:** Our corresponding author and second author are senior professor and experienced in this field, hence their guidance helped us in selecting the type of study in various discussions of cases and getting maximum number of study material and patients.

## What this study adds to existing knowledge:

1. Our study proves that carboprost is most effective and well tolerated uterotonic in prevention of PPH.
2. Lesser requirement of additional uterotonics and blood transfusion.

## Declarations

**Funding:** Nil, **Conflict of interest:** Nil

**Permission from IRB:** Yes

**Ethical approval:** The study was approved by the institutional ethics committee.

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