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Original Research Article

A comparative study of various oxytocics in management of third stage of labour

Neethika Raghuwanshi, Nikita Roy*

Department of Obstetrics and Gynecology, Government Medical College, Akola, Maharashtra, India

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***Correspondence:**
Dr. Nikita Roy,
E-mail: drroy1310@gmail.com

ABSTRACT

Background: Postpartum hemorrhage (PPH) is a leading cause of maternal mortality, with a global incidence of 2-11% following vaginal delivery. Active management of the third stage of labour (AMTSL) through prophylactic uterotonic administration is the cornerstone of PPH prevention. Comparative data on oxytocic agents from Indian tertiary care settings remain limited.
Methods: A prospective observational study was conducted at the Department of Obstetrics and Gynecology, Government Medical College, Akola, Maharashtra, from February 2024 to March 2026. A total of 224 women with uncomplicated term vaginal deliveries were allocated to five groups: Group A-Oxytocin 10 IU IM; group B-Misoprostol 600 µg sublingual; group C-Methylergometrine 0.2 mg IM; group D-Carboprost 250 µg IM; group E-Carbetocin 100 µg IV. Primary outcomes were duration of the third stage, haemoglobin (Hb) drop, and time to uterine tone. Secondary outcomes included side effects, blood transfusion requirement, and need for repeat dosing.
Results: Carbetocin demonstrated the shortest third stage (3.93 min), fastest uterine tone (1.86 min), lowest Hb drop (0.43 g/dL), no blood transfusions, lowest side effect rate (4.7%), and lowest repeat dose requirement (2.3%). Oxytocin and methylergometrine showed comparable efficacy. Misoprostol had the longest third stage (6.17 min), slowest uterine tone (8.47 min), and highest side effect rate (26.1%). Carboprost was effective but associated with a higher side effect burden (23.9%).
Conclusions: Carbetocin demonstrated superior efficacy and tolerability for AMTSL. Oxytocin remains the recommended first-line agent given its safety and cost profile. Misoprostol is viable in resource-limited settings despite its higher side effect rate.

Keywords: Postpartum haemorrhage, Oxytocin, Carbetocin, Misoprostol, Third stage of labour, Uterotonic agents

INTRODUCTION

The third stage of labour begins after fetal delivery and ends with placental expulsion. Despite its short duration, it carries significant risk of postpartum hemorrhage (PPH), which remains the leading cause of maternal mortality worldwide.[1]

Globally, PPH affects an estimated 2-11% of deliveries and accounts for nearly 30% of maternal deaths.[2,3] In India, the maternal mortality ratio is approximately 212 per 100,000 live births, with PPH contributing disproportionately to this burden.[3] The World Health Organization (WHO) strongly recommends the prophylactic administration of a uterotonic agent as the most critical intervention during the third stage of the labour.[4]

Multiple oxytocic agents are available for AMTSL, including oxytocin, methylergometrine, misoprostol, carboprost, and carbetocin, each with distinct pharmacological properties, routes of administration, and adverse effect profiles.[5,6] Oxytocin is currently endorsed as the gold-standard uterotonic, but alternatives are widely used, particularly in settings where cold-chain maintenance is challenging.[7]

This study aims to compare the efficacy, speed of action, dose requirements, route of administration, and adverse effect profiles of five commonly used oxytocic agents in the management of the third stage of labour at a tertiary care centre in Maharashtra, India.

METHODS

A prospective observational study was conducted at department of obstetrics and gynecology, government medical college, Akola, Maharashtra, India, from February 2024-March 2026. Ethical approval was obtained from the institutional ethics committee of government medical college, Akola. Written informed consent was obtained from all participants prior to enrolment.

Women with singleton term pregnancies (37-40 weeks of gestation) admitted for vaginal delivery were included. Multiple gestations, instrumental/ operative deliveries, antepartum haemorrhage, coagulation disorders, known contraindications to study drugs, and perineal/cervical lacerations at delivery were excluded. Evidence supports that AMTSL significantly reduces blood loss and PPH incidence compared to expectant management.[13] A total of 250 participants enrolled; 26 were subsequently excluded, yielding a final study population of 224 participants (Oxytocin n=45, misoprostol n=46, methylergometrine n=44, carboprost n=46 and carbetocin n=43).

Participants were allocated to five groups using a computer-generated randomization sequence. Within one minute of fetal delivery, participants received: Group A-Oxytocin 10 IU intramuscularly (IM); group B-Misoprostol 600 µg sublingually (SL); group C-Methylergometrine 0.2 mg IM; group D-Carboprost 250 µg IM; group E-Carbetocin 100 µg intravenously (IV). Calibrated brass-V drapes were applied immediately after delivery for quantitative blood loss measurement. Placental delivery was accomplished by controlled cord traction once signs of separation appeared. Primary outcomes were: mean duration of the third stage of labour, mean Hb drop (baseline vs. 12 hours post-delivery), and mean time to achieve adequate uterine tone (minutes from drug administration). Secondary outcomes were: incidence of side effects, blood transfusion requirement, and need for repeat uterotonic dosing. Statistical analysis used SPSS version 21.0. Continuous variables were compared with one-way ANOVA and categorical variables with chi-square test; $p<0.05$ was considered statistically significant.

RESULTS

Of 250 enrolled women, 26 were excluded after randomization (perineal tears, incomplete data, or withdrawal of consent), leaving 224 participants for analysis. The groups were comparable at baseline in mean age (range 25.58-26.35 years) and gestational age (range 38.15-39.43 weeks); there were no statistically significant differences in baseline characteristics ($p>0.05$).

Duration of third stage of labour

Carbetocin demonstrated the shortest mean third stage duration (3.93 min), followed by methylergometrine (4.51 min), oxytocin (4.78 min), carboprost (5.20 min), and misoprostol (6.17 min). Differences across groups were statistically significant ($p<0.001$) (Table 1).

Hb drop and blood transfusion

Mean Hb drop was lowest in the carbetocin group (0.43 g/dL), followed by oxytocin (0.60 g/dL), methylergometrine (0.60 g/dL), carboprost (0.62 g/dL), and misoprostol (0.89 g/dL). Blood transfusion was required in 4 patients (8.7%) in the misoprostol group, 3 patients (6.5%) in the carboprost group, 2 each in the oxytocin and methylergometrine groups, and none in the carbetocin group (Table 2).

Time to achieve uterine tone

Carbetocin produced the fastest adequate uterine contraction at a mean of 1.86 minutes. Oxytocin (2.49 min) and methylergometrine (3.01 min) followed, while carboprost took 5.08 min and misoprostol took the longest at 8.47 min.

Side effects and repeat dosing

Side effects were absent in all oxytocin recipients. The highest rate was observed with misoprostol (26.1%), predominantly shivering, pyrexia, and nausea. Carboprost was associated with flushing, diarrhoea, and shivering in 23.9% of patients. Methylergometrine caused hypertension, nausea, or vomiting in 18.2%. Carbetocin had the lowest side effect profile (4.7%). Repeat uterotonic dosing was least required with carbetocin (2.3%) and most common with misoprostol (19.6%). Results are summarised in Table 2 and drug profiles in Table 3.

Table 1: Baseline characteristics and primary outcomes across study groups.

Parameters	Oxytocin, (n=45)	Misoprostol, (n=46)	Methergine, (n=44)	Carboprost, (n=46)	Carbetocin, (n=43)
Mean age (in years)	25.58	25.87	26.07	26.35	26.19
Mean gestational age (in weeks)	38.91	38.15	39.43	38.89	38.98
Mean 3rd stage duration (min)	4.78	6.17	4.51	5.20	3.93*
Mean Hb drop (g/dL)	0.60	0.89	0.60	0.62	0.43*
Time to uterine tone (min)	2.49	8.47	3.01	5.08	1.86*

*Carbetocin group showed best performance for all three primary outcomes. GA=gestational age; Hb=haemoglobin.

Table 2: Secondary outcomes-side effects, blood transfusion, and repeat dosing.

Outcome	Oxytocin	Misoprostol	Methergine	Carboprost	Carbetocin
Side effects	0 (0.0%)	12 (26.1%)	8 (18.2%)	11 (23.9%)	2 (4.7%)
Blood transfusion	2 (4.4%)	4 (8.7%)	2 (4.5%)	3 (6.5%)	0 (0.0%)
Repeat dose required	6 (13.3%)	9 (19.6%)	4 (9.1%)	6 (13.0%)	1 (2.3%)

*Side effects with misoprostol: shivering, pyrexia, nausea. Methylergometrine: hypertension, nausea, vomiting. Carboprost: flushing, diarrhoea, shivering. Carbetocin: mild flushing.

Table 3: Drug profiles-dose, route, and clinical performance summary.

Drugs	Dose	Route	N	3rd stage duration (min)	Time to uterine tone (min)
Oxytocin	10 IU	IM	45	4.78	2.49
Misoprostol	600 µg	SL	46	6.17	8.47
Methylergometrine	0.2 mg	IM	44	4.51	3.01
Carboprost	250 µg	IM	46	5.20	5.08
Carbetocin	100 µg	IV	43	3.93	1.86

*IM=intramuscular; SL=sublingual; IV=intravenous.

DISCUSSION

This prospective observational study comparing five oxytocic agents in 224 women undergoing vaginal delivery at a tertiary centre in Maharashtra provides valuable comparative data on their efficacy, tolerability, and clinical utility in AMTSL.

Carbetocin emerged as the superior agent across all measured outcomes. Its single intravenous dose produced the fastest uterine tone, shortest third stage, lowest Hb drop, no requirement for blood transfusion, and the fewest side effects and repeat doses. These findings are consistent with published systematic reviews demonstrating carbetocin's superiority over oxytocin in reducing additional uterotonic requirement and haemorrhage-related morbidity.[8,9] The prolonged uterotonic action of carbetocin-attributed to its longer half-life and sustained oxytocin-receptor binding-accounts for the lower repeat dosing observed in the present study.

Oxytocin performed consistently well, with rapid onset, no side effects, and efficacy comparable to methylergometrine in third stage duration and Hb drop. This corroborates WHO guidelines recommending oxytocin as the first-choice agent for AMTSL.[4] Methylergometrine was effective in shortening the third stage but carried a notable hypertensive and emetogenic side effect burden (18.2%), limiting its use in patients with hypertensive disorders of pregnancy.

Misoprostol, despite advantages of oral availability, thermostability, and low cost, demonstrated the longest third stage, slowest uterine tone, highest Hb drop, and highest side effect rate (26.1%) in our study. These findings are consistent with published comparative trials reporting higher rates of shivering and pyrexia with sublingual misoprostol versus injectable oxytocics.[10,11,14] These characteristics are attributed to its relatively slow and variable pharmacokinetics. Nonetheless, it remains a valuable alternative in low-resource settings where injectable uterotonics or cold-chain storage are unavailable.

Carboprost provided intermediate efficacy but was associated with the second-highest side effect burden (23.9%), principally flushing, diarrhoea, and shivering, consistent with tertiary-care comparative studies.[12,15] The higher acquisition cost of carbetocin may limit its routine use in resource-constrained environments, though its single-dose administration and superior haemostatic profile present long-term clinical and the logistic advantages.

This study is limited by its single-centre, non-blinded, observational design and moderate sample size. Multicentre randomised controlled trials with cost-effectiveness analyses are recommended to further guide national policy on uterotonic selection.

CONCLUSION

Among the five oxytocic agents evaluated in this study, carbetocin demonstrated the best overall performance with the shortest third stage duration, fastest uterine tone, lowest Hb drop, no blood transfusions required, and minimal side effects. Oxytocin remains the recommended first-line uterotonic for AMTSL based on its efficacy, safety, and cost-effectiveness. Misoprostol is a practical alternative in low-resource settings, though its higher side effect burden warrants caution. These findings support a context-specific, tiered approach to uterotonic selection in clinical practice.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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