International Journal of Clinical Obstetrics and Gynaecology

ISSN (P): 2522-6614
ISSN (E): 2522-6622

www.gynaecologyjournal.com
2019; 3(5): 318-321
Received: 24-07-2019
Accepted: 28-08-2019

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Comparison of carboprost with oxytocin in third stage of labour

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DOI: https://doi.org/10.33545/gynae.2019.v3.i5e.371

Abstract
Background: The third stage of labour commences with the complete delivery of the foetus and ends with the complete delivery of the placenta and its attached membranes. The present study was conducted to evaluate the scope of using carboprost in comparison with intramuscular oxytocin and providing single drug for third stage of labour which is effective as well as safe and associated with less side effects.
Materials & Methods: The present study was conducted on 220 females. Patients were randomly assigned into two equal groups. Third stage of labour was observed for sign of placental separation such as uterine tone, symphysis fundal height, lengthening of cord and gush of blood.
Results: Group 1 women received (10 Unit) oxytocin and group II women received (125 micrograms) carboprost. Each group had 110 patients. The mean maternal age in oxytocin group was 26.23±4.16 years and in carboprost group was 25.51±3.98 years. The mean duration of third stage of labour was 8.77±3.9 mins in oxytocin group and 7.59±3.9 mins in carboprost group. The difference was found to be statistically significant. In group I, mean blood loss was 264.69 ml and in group II was 175.15 ml.
Conclusion: Carboprost is better and cost effective alternative to intramuscular 10 units oxytocin in the prophylactic management of third stage of labor. Carboprost reduces the duration of third stage, amount of blood loss, decreases the requirements of additional oxytocin.

Keywords: Comparison, carboprost, oxytocin, labour

Introduction
The third stage of labour commences with the complete delivery of the foetus and ends with the complete delivery of the placenta and its attached membranes. The clinician immediately recognizes that from a practical perspective, the risk of complications continues for some period after delivery of the placenta [1]. The third and fourth stages of labour are usually uneventful, although significant complications can occur in this period. Postpartum hemorrhage is one of the most dreaded complications of third stage of labour. Worldwide there are an estimated 500,000 – 600,000 deaths of mothers in childbirth annually of which 25% are due to severe bleeding [2].
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 post partum eclampsia, intracerebral hemorrhage, myocardial infarction, cardiac arrest and pulmonary edema [3].
Carboprost and oxytocin both have found to be effective in the management of third stage of labour. But carboprost was associated with side effect when used in a dose of 250 microgram. It has been found to be effective when used in dose of 125 microgram with minimal side effects. Thus carboprost was found to be better uterotonic drug, the only concern being high dosage [4].
The present study was conducted to evaluate the scope of using carboprost in comparison with intramuscular oxytocin and providing single drug for third stage of labour which is effective as well as safe and associated with lesser side effects.

Materials & Methods
The present study was conducted at Dr. Ram Manohar Lohiya Combined Hospital Lucknow U.P. in Obstetrics and Gynecology Department over a period of one year August 2018 to July 2019. It comprised of 220 females. Ethical committee approval of the hospital and written informed consent was taken from patients after explaining the study.
Data such as name, age etc. was recorded. Patients were randomly assigned into two equal groups. Group I–these women received (10 Unit) oxytocin intramuscular immediately after delivery of fetus.

Complete general and systemic examination was done. Obstetrical examination include a per abdomen examination to know the fundal height, lie, presentation, foetal heart sound, per vaginal examination done to know cervical dilatation, effacement of cervix, station of presenting part, type & adequacy of pelvis. Third stage of labour was observed for sign of placental separation such as uterine tone, symphysis fundal height, lengthening of cord and gush of blood. Results were tabulated. The p-value <0.05 was considered significant.

Results

Table 1: Distribution of patients

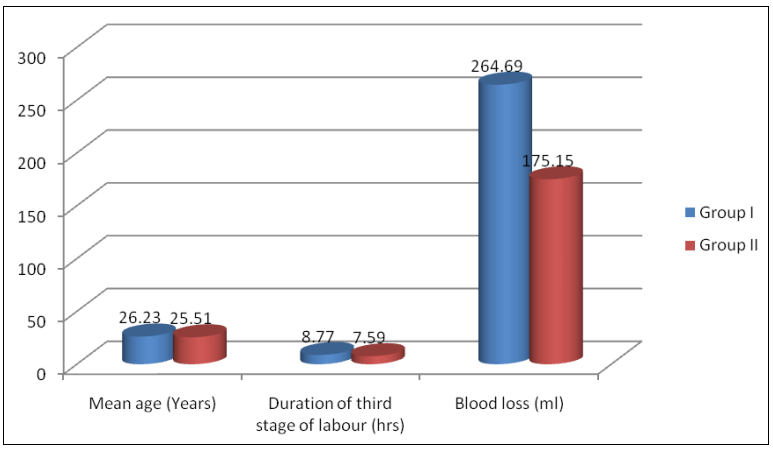
Groups	Group I	Group II
Agent	Oxytocin	Carboprost
Number	110	110

Table I shows that group 1 women received (10 Unit) oxytocin and group II women received (125 micrograms) carboprost. Each group had 110 patients.

Table 2: Comparison of parameters in both groups

Groups	Group I	Group II	P value
Mean age (Years)	26.23	25.51	0.842
Duration of third stage of labour (hrs)	8.77	7.59	0.05
Blood loss (ml)	264.69	175.15	0.01

Table II, graph I shows that the mean maternal age in oxytocin group was 26.23±4.16 years and in carboprost group was 25.51±3.98 years. The mean duration of third stage of labour was 8.77±3.9 mins in oxytocin group and 7.59±3.9 mins in carboprost group. The difference was found to be statistically significant. In group I, mean blood loss was 264.69 ml and in group II was 175.15 ml.



Graph 1: Comparison of parameters in both groups

Table 3: Mean Duration of the third stage of labor in various studies

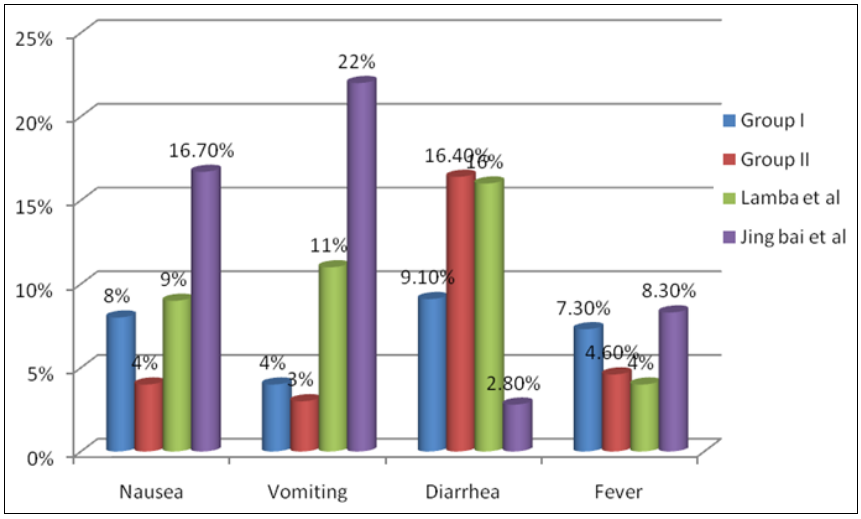
Study	Group I	Group II
Sunil Kumar KS *et al.* [5]	7.02 mins	6.05 mins
Bhide P *et al.* [6]	6.30 mins	3.15 mins
Present study	8.77 mins	7.59 mins

Table III shows mean duration of the third stage of labor in various studies.

Table 4: Side effects in both groups and in various studies

Side effects	Group I	Group II	Lamba *et al.* [7]	Jing bai *et al.* [8]
Nausea	8%	4%	9%	16.7%
Vomiting	4%	3%	11%	22%
Diarrhea	9.1%	16.4%	16%	2.8%
Fever	7.3%	4.6%	4%	8.3%

Table IV, graph II shows that common side effect in group I was diarrhoea seen in 9.1% and 16% in group II. In study by Lamba *et al*, 16% patients had diarrhoea and Jing bai *et al* found that 22% had vomiting.



Graph 2: Side effects in both groups and in various studies

Table 5: Distribution of subjects according to additional drugs used

Drugs	Group I	Group II	P value
Percentage	29.1%	7.3%	0.001

Table V shows that 29.1% in group I and 7.3% in group II required additional drugs in the form of methylergomertine, misoprostol and carboprost (250 microgram).

Table 6: Comparison of Estimated Blood Loss in present and in various studies

Study	Methyl ergometrine	Carboprost	Oxytocin
Reddy *et al.*	202 ml	127 ml	-
B. jajupuroshotam	169 ml	111 ml	-
Devi PK *et al.*	283 ml	99.8ml	-
Sunil Kumar KS *et al*	-	170.2 ml	281.05 ml
Present study	-	175.15 ml	264.69 ml

Table VI shows ccomparison of estimated Blood Loss in ml in Various Studies.

Table 7: Cost of the whole treatment

Drugs	Ampoule	Cost
Oxytocin	One	Rs 25-36
Carboprost	One (250 microgram)	Rs 150-175
Carboprost	Half (125microgram)	Rs 75-90
Misoprostol	One tablet	Rs 75-100

Table VII shows cost of treatment in our study.

Discussion

Postpartum hemorrhage is one of the most important cause of maternal death throughout the world. Everyday about 1500 women dies from pregnancy and child birth related complications [7]. Active management of third stage of labour and use of prophylactic oxytocin has reduced its incidence in many countries. The primary aim in the management of post partum hemorrhage should be its prevention. The Active management of the third stage with routine prophylactic administration of oxytocin immediately with the delivery of fetus has been shown to reduce the risk of postpartum hemorrhage by about 40% [8]. Routine use of active management of third stage of labour for all vaginal singleton births in health facilities is recommended by the International Federation of Gynaecologist and Obstetrician (FIGO) and the International Confederation of midwives (ICM) as well as by WHO [9, 10] Various drugs and routes of administration have been tested with varying success. Recent studies show that there are still wide variations around the world in the management of third stage of labour. Oxytocin is the most commonly used drug for prevention and treatment of excessive bleeding following delivery. Oxytocin use is recommended by WHO. The most significant benefits of oxytocin is rapid action without causing elevated blood pressure or tetanic contractions. However, the use of oxytocin is limited by the dose. Myometrial oxytocin receptor saturation may affect its effectiveness and excessive dosage may result in coronary artery contraction, hypotension and antidiuretic effect induced water intoxication [11]. Though commonly used it is not the potent drug and many times requires additional drugs and blood loss is more compared with other drugs. The production of PGF2alpha in the decidual tissue and its release in the circulation increases during labour [12]. PGF2alpha is a powerful uterotonic agent with a physiological role in human parturition. Carboprost tromethamine is the synthetic 15-methyl analogue of PGF2 alpha. It may be administered via intramuscular injection at a dose of 0.25 mg and may be repeated every 15 mins until a maximum total dose of 2 mg has been administered [13]. Carboprost has been reported to be 84-96% effective in the treatment of persistent hemorrhage due to uterine atony and may avoid the need for surgical intervention [14]. The discovery of prostaglandins and their analogues as uterotonics has improved the managment of postpartum hemorrhage due to their significant influence on uterine tone, which results in minimizing the blood loss; this outweighs its cost.

In the present study, the mean maternal age in oxytocin group was 26.23±4.16 years and in carboprost group was 25.51±3.98 years. The z value is 0.34 and p value is 0.842 i.e >0.05. No significant difference was found in proportion of various age groups between the two drugs. The majority of women in both groups belonged to the age group of 25-34 years. The distribution of the patients according to the parity in both groups was almost similar. No significant difference was found in

proportion of parity types between the 2 groups (p=0.892). In present study mean duration of third stage of labour was 8.77±3.9 mins in oxytocin group and 7.59±3.9 mins in carboprost group the difference was found to be statistically significant. Our study results are in accordance with the study of Anjaneyulu *et al*. [15] There are various studies to compare mean duration of third stage of labour.

In our study duration of third stage of labour is minimum for primipara with carboprost and maximum for multipara in oxytocin group. We found that as the parity increases incidence of postpartum hemorrhage increases. In the present study the mean blood loss during third & fourth stage of labour was 264.69±81.40 ml while in the carboprost group the mean blood loss was 175.15±65.99 ml. The significant difference was found in mean blood loss between the 2 drug groups ($p<0.001$).

In our study the summary of blood loss during third and fourth stage of labour according to drug, age, & parity shows minimum loss for primipara with carboprost drug while the maximum loss was found for multipara among the oxytocin group. In our study 29.1% cases of oxytocin group and 7.3% cases of carboprost group required additional oxytocin in the form of methylergomertine, misoprostol and carboprost (250 microgram). Highly significant difference was found in between the 2 groups ($p<0.001$).

In our study 7.3% cases of oxytocin group had side effects which were minimal in the form of shivering and headache whereas in carboprost group 16.4% cases had side effects. Diarrhea was seen in 9.1% cases and other common side effects seen were nausea, vomiting. But these side effects are not life threatening and can be easily managed.

Vaid *et al*. [16] compared prophylactic sublingual misoprostol, intramuscular methergin and intramuscular carboprost for the active management of the third stage of labour and observed that the three drugs were equally effective in the prevention of postpartum hemorrhage although diarrhea was more common in the patients who received carboprost. Lamont *et al*. [17] compared carboprost and syntometrine for the prevention of post partum hemorrhage and revealed that 2 drugs were equally effective in the prevention of postpartum hemorrhage but diarrhea occurred in 21% of the patients who received carboprost compared with only 0.8% of the patients who received syntometrine.

Conclusion

Authors found that intramuscular 125 microgram carboprost is better and cost effective alternative to intramuscular 10 units oxytocin in the prophylactic management of third stage of labor. Carboprost reduces the duration of third stage, amount of blood loss, decreases the requirements of additional oxytocin.

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