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A COMPARATIVE STUDY IN EFFICACY BETWEEN INTRAMUSCULAR CARBOPROST (125µg) VERSUS INTRAMUSCULAR OXYTOCIN (10UNITS) FOR ACTIVE MANAGEMENT OF THIRD STAGE OF LABOR

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ABSTRACT A hospital based randomized comparative study was performed in the department of obstetrics and gynaecology, Midnapore Medical College between January 2017 to June 2018. A total of 200 women fulfilling the inclusion criteria were recruited and were divided into two groups, each having 100 women. One group received injection oxytocin (10 units) IM and the other group received injection carboprost tromethamine (125 mcg) IM after delivery of the baby. Both the groups were comparable demographically. Mean duration of third stage of labor, mean amount of blood loss and mean haemoglobin changes and the need for additional oxytocics were significantly lower in the group receiving injection carboprost. On the other hand incidences of side effects were significantly higher in the injection carboprost group.

KEYWORDS : Intramuscular Carboprost, Intramuscular Oxytocin, Active Management, Third Stage Of Labor, Efficacy

INTRODUCTION

In spite of marked improvement in management, postpartum haemorrhage (PPH) remains a significant contributor to maternal morbidity and mortality both in developing and developed countries[1,2], This complication is amongst the most challenging which a clinician will face. The third stage of labour is the most crucial stage of labour and the proper management of third stage of labour will reduce maternal mortality significantly as post partum haemorrhage is the leading cause of maternal mortality in India contributing 30% of maternal deaths[3]. Prevention, early recognition and prompt appropriate intervention are the keys to minimizing its impact. Persons providing intra-partum care should routinely take steps to prevent PPH. Practices should be established to facilitate the identification of women who may be at particularly high risk for PPH and to allow prompt intervention should excessive bleeding occur. Appropriate medications and instruments should be readily available and known to all staffs.

Globally about 11 % of women having live births have severe PPH amounting to 14 million women a year[4]. The major burden of this is borne by women in the underdeveloped and developing countries. Desai and Jani quote the incidence of PPH to be 3-6% of all normal deliveries[5]. The incidence is higher in operative deliveries especially when conducted under general anaesthesia. The incidence is said to be3.9% in vaginal deliveries and 6.4% in caesarean sections. In rural India where women have limited access to healthcare facilities the incidence of PPH is bound to be higher, although, the exact incidence in difficult to obtain. PPH is a major cause of maternal death. In India PPH is responsible for 15.15% maternal deaths[6]. 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 after delivery of the fetus and a transition from expectant to active intervention[7,8]. Drugs conventionally used for prophylaxis against PPH include oxytocin, methylergometrine and 15 methylPGF2α (Carboprost)[9]. Recent studies have shown that there are still wide variations in practice around the world in the management of third stage of labour[10,11]. Prophylactic use of oxytocic agents after delivery of the fetus 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, intra cerebral haemorrhage, myocardial infarction, cardiac arrest and pulmonary oedema[12] Carboprosttromethamine is a PGF2α analogue. It is given as a single intramuscular injection. It is free from side effects such as hypertension[13]. The WHO trial also demonstrated that the addition of CCT did almost nothing to reduce haemorrhage. The women who received CCT bled 10 ml less (on average) than women who delivered their placenta by their own effort. There was a real difference, however, in terms of the length of the third stage: third stage was six minutes longer among those women who did not receive CCT. The authors acknowledged that this can be an important amount of time, not so much for the woman, but for the management of a busy labour room and delivery unit.

Parenteral PGF2α (marketed as Carboprost) is mainly used in the management of intractable PPH. Experience parenteral PGF2α for routine use in the third stage is limited. Available data suggest that intramuscular prostaglandins are more effective than injectable oxytocin and ergometrine in reducing blood loss in the third stage of labour. However concerns regarding safety, side effects and cost have limited their routine use in low risk women.[14]

The present study is an attempt at comparing the efficacy, side effects and safety of intramuscular PGF2α (Carboprost) 125 mcg and intramuscular oxytocin (10 units) for the active management of third stage of labour.

The aims and objectives of this study were –

[1] To compare the effectiveness of intramuscular oxytocin (10units) and intramuscular carboprost tromethamine (125µg) in prophylaxis of post partum haemorrhage.
[2] To compare the amount of blood loss in third stage of labour.
[3] To compare the duration of third stage of labour.
[4] To evaluate the side effects

MATERIALS AND METHODS

STUDY DESIGN –

Hospital based Randomized comparative study was done at Department of Gynaecology and Obstetrics, Midnapore Medical College and Hospital from January 2017 to June 2018.

SAMPLE SIZE –

The sample size was 200, with 100 cases in each group.

INCLUSION CRITERIA-

Primigravida or multigravida with singleton pregnancy with cephalic presentation with no obstetric complication in whom vaginal delivery was anticipated.

EXCLUSION CRITERIA-

1. Patient with hypersensitivity to drugs,

2. Preeclampsia, Eclampsia,
3. Severe anaemia <7gm/dl,
4. Multiple pregnancies,
5. Poly or Oligohydramnios,
6. Grand multipara,
7. Previous history of lower segment caesarean section.
8. Gestation age <37week and >41week,
9. Induction of labour,
10. Instrumental delivery,
11. Prolonged labour,
12. IUFD,
13. Placenta previa and other cause of APH,
14. Macrosomia fetal wt >4kg,
15. Respiratory disease, Cardiac disease, Renal or Liver disease, Epilepsy, Psychiatric disease,
16. Past history of PPH,
17. Patients unwilling to participate.

STUDY TOOLS-

[1] Relevant medical, surgical, personal history of mothers.
[2] Bed head ticket of mothers.
[3] Biochemical, haematological test of mothers.
[4] USG for FPP.

DATA COLLECTION AND LAB INVESTIGATIONS-

[1] The amount of blood loss during third stage of labour and immediate postpartum period (1hr after delivery) was estimated by use ofbedpans (immediately after the cord was clamped and cut, blood collection was started by placing a bedpan under the buttocks of the woman delivering on a delivery table).
[2] Haemoglobin in gm % was estimated, at the time of admission and 24 hours after delivery.
[3] Third stage complications such as nausea, vomiting, diarrhoea, shivering and fever, retained placenta, and need for second injection of additional oxytocics were noted.

STUDY TECHNIQUE-

Informed written consents were obtained from all the women who participated in the study. All the consents were taken in the languages the enrolled women understood.

This study was performed on 200 women, with 100 women in each group.

Patients who were assigned to Group 1, received 10 units oxytocin intramuscularly; and the patients assigned to Group 2 received carboprost tromethamine 125microgram (mcg)intramuscularly after delivery of fetus.

RESULT AND ANALYSIS

For statistical analysis data were entered into a Microsoft excel spreadsheet and then analyzed by SPSS 24.0. Data had been summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables. Two-sample t-tests for a difference in mean involved independent samples or unpaired samples. Paired t-tests were a form of blocking and had greater power than unpaired tests. Unpaired proportions were compared by Chi-square test or Fischer's exact test, as appropriate. p-value ≤ 0.05 was considered statistically significant.

We found that in injection carboprost (125mcg) IM, the mean age (mean±s.d.) of patients was 21.1500 ± 2.3371 years with range 18.0000 - 28.0000 years and the median was 21.0000 years. In injection oxytocin (10 units) IM, the mean age (mean±s.d.) of patients was 21.0500 ± 2.3543 years with range 17.0000 - 27.0000 years and the median was 21.0000 years. Association of age in two groups was not statistically significant (p=0.7634).

It was found that in injection carboprost (125mcg) IM, the mean BMI (mean±s.d.) of patients was 18.5640 ± 4679 kg/$m^2$with range 18.0000 - 21.0000 kg/$m^2$and the median was 18.5000kg/m^2.In injection oxytocin (10 units) IM, the mean BMI (mean±s.d.) of patients was 18.4830 ± .3654 kg/$m^2$with range 17.9000 - 19.2000 kg/$m^2$and the median was 18.5000kg/m^2.Difference of mean BMI in two groups was not statistically significant (p=0.1740).

We found that in injection carboprost (125mcg) IM, the mean gestational age (mean±s.d.) of fetal was 39.0180 ± .4370 with range 38.0000 - 40.1000 and the median was 39.0000.In injection oxytocin (10 units) IM, the mean gestational age (mean±s.d.) of patients was 38.9540 ± .4349 with range 38.0000 - 40.0000 and the median was 39.0000.Difference of mean gestational age in two groups was not statistically significant (p=0.3005).

It was found that in injection carboprost (125mcg) IM, the mean of duration of 3rd stage of labour (mean±s.d.) of patients was 5.5100 ± 2.1296 minutes with range 2.0000 - 13.0000 minutes and the median was 5.0000 minutes. In injection oxytocin (10 units) IM, the mean of duration of 3rd stage of labour (mean±s.d.) of patients was 6.8700 ± 2.1445 minutes with range 2.0000 - 15.0000 minutes and the median was 7.0000 minutes. Difference of mean duration of 3rd stage of labour in the two groups was statistically significant (p<0.0001).

We found that in injection carboprost (125mcg) IM, the mean amount of blood loss (mean±s.d.) of patients was 160.2000 ± 67.8230 ml with range 50.0000 - 345.0000 ml and the median was 152.5000 ml. In injection oxytocin (10 units) IM, the mean amount of blood loss (mean±s.d.) of patients was 248.5500 ± 76.9110 ml with range 50.0000 - 525.0000 ml and the median was 250.0000 ml. Difference of mean amount of blood loss in two groups was statistically significant (p<0.0001).

We found that in injection carboprost (125mcg) IM, the mean Hb change (mean±s.d.) of patients was .5607 ± .2031 with range 0.2000 - 1.1000 and the median was 0.5500.

In injection oxytocin (10 units) IM, the mean Hb Change (mean±s.d.) of patients was. 8076 ± .2210 with range 0.2000 - 1.6000 and the median was 0.8000. Difference of mean Hb Change in two groups was statistically significant (p<0.0001).

It was found That in injection carboprost (125mcg) IM group, 4(4.0%) patients had additional oxytocics required. In injection oxytocin (10 units) IM group, 18(18.0%) patients had additional oxytocics required. Association of additional oxytocics required in two groups was statistically significant (p=0.0015).

We found that according to side effects in injection carboprost (125mcg) IM, 10(10.0%) patients had diarrhea, 6(6.0%) patients had nausea, 5 (5%) patients had vomiting and 79(79.0%) patients had no side effects. According to side effects in injection oxytocin (10 units) IM, 2(2.0%) patients had headache, 4(4.0%) patients had nausea,3 (3%) patients had vomiting, 87(87.9%) patients had no side effects and 3(3.0%) patients had shivering. Association of side effect in two groups was statistically significant (p=0.0061).

Table: Distribution of mean age, BMI, gestational age, duration of 3rd stage of labor, Amount of blood loss (ml) and Hb Change in two groups

		Number	Mean	SD	Minimum	Maximum	Median	p- value
Age	Injection Carboprost (125MCG) IM	100	21.1500	2.3371	18.0000	28.0000	21.0000	0.7634
	Injection Oxytocin (10 Units) IM	100	21.0500	2.3543	17.0000	27.0000	21.0000	
BMI	Injection Carboprost (125MCG) IM	100	18.5640	.4679	18.0000	21.0000	18.5000	0.1740
	Injection Oxytocin (10 Units) IM	100	18.4830	.3654	17.9000	19.2000	18.5000	
Gestational age	Injection Carbopro St (125MCG) IM	100	39.0180	.4370	38.0000	40.1000	39.0000	0.3005
	Injection Oxytocin (10 Units) IM	100	38.9540	.4349	38.0000	40.0000	39.0000	
Duration of 3rd stage of labor	Injection Carbopro ST (125MCG) IM	100	5.5100	2.1296	2.0000	13.0000	5.0000	<0.0001
	Injection Oxytocin (10 Units) IM	100	6.8700	2.1445	2.0000	15.0000	7.0000	
Amount of blood loss (ml)	Injection Carboprost (125MCG) IM	100	160.2000	67.8230	50.0000	345.0000	152.5000	<0.0001
	Injection Oxytocin (10 UNITS) IM	100	248.5500	76.9110	50.0000	525.0000	250.0000	
Hb Change	Injection Carboprost (125MCG) IM	100	.5607	.2031	0.2000	1.1000	0.5500	<0.0001
	Injection Oxytocin (10 Units) IM	100	.8076	.2210	0.2000	1.6000	0.8000	

Table: Association of Additional oxytocics required and side effects with groups

		Injection Carboprost (125MCG) IM	Injection Oxytocin (10 Units) IM	Total	Chi-square value	p-value
Additional oxytocics required	**No**	96	82	178	10.0102	0.0015
	Row %	53.9	46.1	100.0		
	Col %	96.0	82.0	89.0		
	Yes	4	18	22		
	Row %	18.2	81.8	100.0		
	Col %	4.0	18.0	11.0		
	Total	100	100	200		
	Row %	50.0	50.0	100.0		
	Col %	100.0	100.0	100.0		
Side effects	**DIARRHEA**	10	0	10	16.2809	0.0061
	Row %	100.0	0.0	100.0		
	Col %	10.	0.0	5.0		
	HEADACHE	0	2	2		
	Row %	0.0	100.0	100.0		
	Col %	0.0	2.0	1.0		
	NAUSEA	6	4	10		
	Row %	60.0	40.0	100.0		
	Col %	6.0	4.0	5.0		
	NO	79	87	166		
	Row %	47.6	52.4	100.08		
	Col %	79.0	87.9	3.4		
	SHIVERING	0	3	3		
	Row %	0.0	100.0	100.0		
	Col %	0.0	3.0	1.5		
	VOMITING	5	3	8		
	Row %	62.5	100.0	100.0		
	Col %	5.0	3.03	4.0		
	TOTAL	100	99	199		
	Row %	50.3	49.7	100.0		
	Col %	100.0	100.0	100.0		

DISCUSSION

The two groups were comparable in respect to age, gestational age and BMI and there was no statistically significant difference between the groups as far as background demographic characteristics were concerned.

As far as the duration of the third stage of labour was concerned, mean duration of third stage was significantly less in the injection carboprost group. The studies performed by K. S. Sunil Kumar et al [21] , Jing Bai et al [22] and Lamont et al [23] found similar results as the present study.

The mean amount of blood loss was significantly lower in the injection carboprost group. K.

S. Sunil Kumar et al[21] also found that injection carboprost was associated with less blood loss in third stage of labour.

The mean change in Haemoglobin concentration in the injection carboprost group was lower than in the injection oxytocin group.

As far as the requirement of additional oxytocics was concerned, the injection carboprost group needed fewer additional oxytocics. K. S. Sunil Kumar et al [21] in their study also concluded that use of injection carboprost reduces the need of additional oxytocics in the third stage of labour.

The women in the injection carboprost group suffered from more side effects than in the injection oxytocin group. Jing Bai et al [22] also found similar results.

CONCLUSION:

So it can be concluded from the study performed, that injection carboprost tromethamine (125 microgram) IM in the active management of third stage of labour is more effective than injection oxytocin (10 unit) IM albeit with an increased incidence of side effects.

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