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INTRAVENOUS INJ. CARBETOCIN VERSUS INTRAVENOUS INJ. OXYTOCIN DRIP FOR PREVENTION OF PRIMARY ATONIC POSTPARTUM HAEMORRHAGE IN CESAREAN SECTION

Obstetrics & Gynaecology

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ABSTRACT

Introduction: Postpartum hemorrhage (PPH) is the most common cause of maternal mortality worldwide and accounts for nearly one-quarter of all maternal pregnancy-related deaths. Postpartum haemorrhage (PPH) remains one of the principal causes of maternal deaths in developing nations. **Methodology:** The present prospective study was conducted in women undergoing cesarean section in department of Obstetrics & Gynecology of a tertiary health care centre, during a period of 24 months from July 2022 to July 2024. **Results:** Total 110 women undergoing caesarean section enrolled in this study with 55 in each groups. Mean age of pregnant women among Inj. Oxytocin group was 23.47±4.02 years & among Inj. Carbetocin group was 24.18±5.27 years. There was no significant difference among both group in relation to blood loss after LSCS, blood transfusion, tone of uterus & requirement of additional uterotonics. There was highly significant difference in duration of action of drug in relation to time taken for placental separation & time taken to regain uterine tone. There was no significant difference among both groups in Hb & Hematocrit value. **Conclusion:** The duration of action of Carbetocin is prolonged. It results in a prolonged uterine response with more frequent and intense contractions. A single Carbetocin injection is more practical than an injection of oxytocin bolus that must be followed by an oxytocin infusion for a few hours. After Carbetocin is administered, there are very few chances of requirement of additional uterotonics. But compared to Oxytocin, delays placental detachment and uterine tone not returning right away.

KEYWORDS

Inj. Carbetocin, Inj. Oxytocin, PPH

Postpartum hemorrhage (PPH) is the most common cause of maternal mortality worldwide and accounts for nearly one-quarter of all maternal pregnancy-related deaths.[1] Postpartum haemorrhage (PPH) remains one of the principal causes of maternal deaths in developing nations.[2] It has been estimated that over 300,000 women, mostly from developing countries, lose their lives during pregnancy and childbirth every year.[3] Aside from increased mortality, increased rates of PPH can also increase maternal and neonatal morbidity via potential blood transfusion, increased length of hospital stay, and reduced ability to care for the newborns. Resource utilization may also be increased because of these factors.[4]

Notwithstanding the progress achieved in technology over the last few decades, postpartum haemorrhage (PPH) continues to be a significant contributor to maternal mortality in developing countries.[5] Uterine atony is the most prevalent foetal aetiology factor.[6] However, prophylactic use of uterotonics is effective in reducing PPH, with oxytocin being the preferred uterotonic. In addition to stimulating the contraction of the uterine muscles, oxytocin increases prostaglandin production, which further intensifies the contractions. Oxytocin has a short half-life of 4-10 min due to which it requires a continuous intravenous infusion or repeated intramuscular injections to maintain uterotonic activity.[7-10] Moreover, large doses of oxytocin are associated with dose dependent adverse effects such as hypotension, nausea, vomiting, tachycardia, arrhythmias, ST-T changes, pulmonary edema, water intoxication, and convulsions.[9-11] Therefore, the search for an alternative ideal uterotonic drug continues and carbetocin appears to be a promising substitute.

In recent times, carbetocin, a more recent substitute for oxytocin, has been introduced. It has an approximate half-life of forty minutes and is long-acting; it is also prescribed for the prevention of uterine atony following caesarean section. Carbetocin binds to the myometrial oxytocin receptors with a similar affinity to oxytocin. [7,12] Its main advantage over oxytocin is a four-fold longer half-life, which means there is no need for a continuous infusion.[13,14]

Although the difference between carbetocin and oxytocin in terms of hemodynamic changes, postpartum blood loss and incidence of side effects is not statistically significant,[15,16] carbetocin is superior to oxytocin in terms of additional dosing and cost-effectiveness. [17] However, there is not enough clinical information regarding the hemodynamic side effects of carbetocin and oxytocin. Hence, this research work was done to compare safety, efficacy and the haemodynamic effects of oxytocin and carbetocin.

Methodology:

The present prospective study was conducted in women undergoing cesarean section in department of Obstetrics & Gynecology of a tertiary health care centre, during a period of 24 months from July 2022 to July 2024. This study include 110 women undergoing cesarean section who were willing to participate. Women with moderate anaemia, DIC & other blood dyscrasias, abnormal placentation, cardiac disease, renal diseases were excluded from study.

With informed consent, demographic details of women with cesarean section complications were recorded. Detailed history taking and examination were done. Data was documented in case report form (CRF) and data collection sheets was prepared. Women were allocated in two groups. The inj. oxytocin groups was considered as control group as group A and inj. carbetocin was considered as study group as group B. Monitoring vitals i.e. pulse, BP, RR, temperature, urine output, spo2, uterine tone, bleeding PV was done every 15 minutes. Blood pressure, uterine tone (sufficient, atony) were monitored 2 hours ,4 hrs, 6 hrs ,10 hr and upto 24 hrs after cesarean sections.

The statistical software SPSS 21 was used for all analyses. Frequency & percentage were calculated for categorical data. Means and standard divisions calculated for metric data. Independent samples Student's-test or chi-square test is used to compared demographic and clinical results. If the P-value was < 0.05, the differences were considered significant.

RESULTS:

Total 110 women undergoing caesarean section enrolled in this study with 55 in each groups. Mean age of pregnant women among Inj. Oxytocin group was 23.47±4.02 years & among Inj. Carbetocin group was 24.18±5.27 years. In Inj. Oxytocin group, about 21 (38.18%) pregnant women belong to age group of 26-30 & among Inj. Carbetocin group, about 20 (36.36%) pregnant women aged 21-25 years. Among Inj. Oxytocin group, about 26 (47.27%) pregnant women living in rural area & among Inj. Carbetocin group, 28 (50.91%) pregnant women living in rural area. . Among Inj. Oxytocin group, about 15 (27.27%) pregnant women belong to upper class & among Inj. Carbetocin group, 27 (49.09%) pregnant women belong to upper middle class. Among both groups majority of the women were Hindu by religion & had booked pregnancy. In Inj. Oxytocin group , about 21 (38.18%) were para one & 2 (3.64%) were multipara. Inj. Carbetocin group, about 28 (50.91%) were para1 & 3.45 (49.09%) were multipara. (Table 1)

There was no significant difference among both group in relation to blood loss after LSCS, blood transfusion, tone of uterus & requirement of additional uterotonics. ($p > 0.05$). There was highly significant difference in duration of action of drug in relation to time taken for

placental separation & time taken to regain uterine tone. (p<0.01) (Table 2)

Mean Hb in Inj. Oxytocin was 10.47±0.47 gm/dl & in Inj. Carbetocin group was 10.58±0.51 gm/dl. There was significant difference among both groups (p 0.843). Mean hematocrit in Inj. Oxytocin group was 29.15±4.14 & in Inj. Carbetocin group was 31.13±4.57. There was no significant difference among both groups.(p 0.637) (Table 3)

Most common side effect in Inj. Oxytocin group was nausea 2(3.64%) followed by vomiting 1(1.82%) & tachycardia 1(1.82%). In Inj. Carbetocin group, most common side effect was vomiting 1 (1.82%), flushing of skin 1(1.82%) & headache 1 (1.82%). (Table 4)

DISCUSSION:

Primary PPH is a common obstetric emergency which can lead to Maternal morbidity and mortality in developing nations.[1] Therefore, management of PPH is crucial for the prevention of maternal mortality and morbidity. In our study, we have studied various aspects of safety, efficacy of Inj. Oxytocin and Inj. Carbetocin and we also studied in terms of changes in hemoglobin level, Hematocrit level, need for additional uterotonics, blood transfusion requirement & side effects.

In this present study, in Inj. Oxytocin group majority of pregnant women undergoing cesarean section belong to age group of 26-30 years & in Inj. Carbetocin group about aged below <20years. As compare to other studies, mean age group was lower in present study. In Delorme P et al(2020)[18] study mean age group was higher than present study.

As compare to other studies, the mean age of participants was much lower, this might be because of early marriages are very common in India.[NFHS 5][19]

In this study, majority were para one. The study conducted by Delorme P et al (2020)[18]75% were para one in both groups. About 66.7% in Inj. Oxytocin group & 70.4% in Inj. Carbetocin group were para one in the study conducted by Paljk Likar et al (2022)[20]. In the study conducted by Terblanche N Cs et al (2023)[21], >90% were para one in both the groups. In present study, in Inj. Oxytocin group, only 5.45% pregnant women had >1000 ml blood loss after LSCS and in Inj. Carbetocin group, 3.64% pregnant women had >1000 ml blood loss after LSCS. There was no comparable difference in both group in blood loss (p 0.131). Similar finding was found in study conducted by Paljk Likar et al (2022)[20], Bashir K et al (2023)[22] & GursoyA et al (2021)[23]

There was no comparable difference in requirement of blood transfusion, tone of uterus & requirement od additional uterotonic among both group in present study. In the study conducted by Brun R et al (2024)[24] found that, no one require blood transfusion among both the groups during and after LSCS.

Table 1 : Distribution of women according to demographic parameter.

Demographic Parameter		Group A (Inj Oxytocin)		Group B (Inj Carbetocin)		p Value
		Frequency	Percentage	Frequency	Percentage	
Age Group	≤ 20	5	9.09	5	9.09	0.657
	21 – 25	16	29.09	20	36.36	
	26 – 30	21	38.18	18	32.73	
	31 – 35	11	20.00	8	14.55	
	≥ 36	2	3.64	5	9.09	
Address	Rural	26	47.27	28	50.91	0.145
	Urban	29	52.73	27	49.09	
SES	I -Upper class	14	25.45	9	16.36	0.318
	II- Upper middle	15	27.27	24	43.64	
	III- Lower middle	6	10.91	7	12.73	
	IV- Upper lower class	9	16.36	9	16.36	
	V- Lower class	11	20.00	6	10.91	
Religion	Hindu	32	58.18	33	60.00	0.609
	Muslim	17	30.91	14	25.45	
	Other	5	9.09	8	14.55	
Pregnancy status	Booked	41	74.55	37	67.27	0.401
	Un-booked	14	25.45	18	32.73	
Parity	P1	21	38.18	28	50.91	0.372
	P2	26	47.27	17	30.91	
	P3	7	12.73	6	10.91	
	MULTIPARA	2	3.64	3	5.45	

Table 2: Distribution of women according to Clinical outcome

Clinical outcome		Group A (Inj Oxytocin)		Group B (Inj Carbetocin)		p Value
		Frequency	Percentage	Frequency	Percentage	
Blood loss	<500	32	58.18	42	76.36	0.124
	500-1000	20	36.36	11	20.00	
	>1000	3	5.45	2	3.64	
Blood transfusion	Yes	3	5.45	1	1.82	0.308
	No	52	94.55	54	98.18	
Time taken for placental separation (sec)	<30	31	56.36	3	5.45	0.0001
	30-60	21	38.18	17	30.91	
	>60	3	5.45	35	63.64	
Time taken to regain uterine tone (sec)	<30	30	54.55	2	3.64	0.001
	30-60	20	36.36	15	27.27	
	>60	5	9.09	38	69.09	
Tone of uterus	Sufficient	37	67.27	39	70.91	0.679
	Insufficient	18	32.73	16	29.09	
Uterotonic used	Yes	18	32.73	15	27.27	0.532
	No	37	67.27	40	72.73	

Table 3: Comparison of Hb & hematocrit level among both groups during and after LSCS within 24 hours

Blood variables	Mean	S.D.	t	p Value	
Hb	Group A (Inj Oxytocin)	10.47	0.47	-1.734	0.843
	Group B (Inj Carbetocin)	10.58	0.51		
Hematocrit	Group A (Inj Oxytocin)	29.15	4.14	0.637	0.637
	Group B (Inj Carbetocin)	31.13	4.57		

Table 4 : Distribution of pregnant women according to side effects

Side effects	Group A (Inj Oxytocin)		Group B (Inj Carbetocin)	
	Frequency	Percentage	Frequency	Percentage
Nausea	2	3.64	0	0
Vomiting	1	1.82	1	1.82
Flushing of skin	0	0	1	1.82
Headache	0	0	1	1.82
Dyspnea	0	0	0	0
Tachycardia	1	1.82	0	0

In other studies conducted by, Delorme P et al (2020)[18], Kwon K et al (2020)[25], and Terblanche N Cs et al (2023)[21] found that nearly 2% pregnant women required blood transfusion after LSCS, which was lesser than present study findings. Also there was no significantly higher risk for blood transfusion in Inj. Oxytocin group compare to Inj. Carbetocin group in any study (p >0.05). In the study conducted by Mistri S (2023)[26] found that, in Inj. Oxytocin group 42% & in Inj. Carbetocin group 97% had sufficient tone of uterus after LSCS. In the study conducted by Gursoy A et al (2021)[23] 16.7 % in Inj. Oxytocin & 11.9 % in Inj. Carbetocin group required uterotonic drug. In Delorme P et al (2020)[18], 3% in group A & 2% in group B required uterotonic drug, which was much lesser than present study finding.

In present study, Inj. oxytocin group has early placental separation & there was some delay in placental separation (>one minute) in Carbetocin group. In present study, Inj. Oxytocin group has early regain of uterine tone & some delay (>60 sec) in attainment of adequate uterine tone in Inj. Carbetocin group. However, once the adequate tone was attained in Inj. Carbetocin group (after one minute of drug administration) it then sustained throughout LSCS. In contrast there was early return of adequate uterine tone in oxytocin group , but this uterine tone was not maintained. The study conducted by Bashir K et al (2023)[22] also shows similar findings.

Mean Hb in Inj. Oxytocin group was 10.06±1.47 gm/dl & in Inj. Carbetocin group was 10.58±1.51 gm/dl. There was no comparable difference among both groups (p 0.843). In the study conducted by Paljk Likar et al (2022)[20] the Mean Hb among Inj. Oxytocin group 11.99±0.96 gm/dl & among Inj. Carbetocin group was 11.84±0.93/dl

&there was comparable difference in mean Hb level among both groups.

Similar finding was also found in Bahr MH et al (2023)[27] that was, there was no statistically significant difference in blood loss between the two groups studied, with minimal HB deference in pre-operative and post-operative values in the two groups and no blood transfusions were required intraoperative or post-operative.

In present study, mean haematocrit in Inj. Oxytocin group was 29.15±4.14 & in Inj. Carbetocin group was 31.13±4.57. There was no comparable difference among both groups (p 0.637).In the study conducted by Paljk Likar et al (2022)[20], mean haematocrit in Inj. Oxytocin group was 33.35±2.64 & in Inj. Carbetocin group was 35.9±2.68. There was no comparable difference among both groups.

CONCLUSION:

The duration of action of Carbetocin is prolonged. It results in a prolonged uterine response with more frequent and intense contractions. A single Carbetocin injection is more practical than an injection of oxytocin bolus that must be followed by an oxytocin infusion for a few hours. After Carbetocin is administered, there are very few chances of requirement of additional uterotonics. But compared to Oxytocin, delays placental detachment and uterine tone not returning right away.

There was no statistically significant difference between the two drugs with the blood loss after LSCS, requirement of additional uterotonic drug & postoperative Haemoglobin & haematocrit count. So, both drugs have the same good prophylactic effect from PPH.

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