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Original Research Article

Carbetocin, the front runner for post partum haemorrhage in heart disease complicating pregnancy at a tertiary care hospital

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ABSTRACT

Introduction: Post Partum Heamorrhage (PPH) is responsible for 47% of maternal mortality in India and one quarter of maternal deaths globally. Lack of expertise, lack of proper cold chain for oxytocin and cost limitations of heat stable carbetocin are major hurdles to prevent PPH. Restrained options for safer uterotonics in heart disease complicating pregnancy are a major concern.

Materials and Methods: This study was conducted on 30 patients with heart disease complicating pregnancy who delivered at a tertiary care centre. All patients were administered single dose of carbetocin 100 mcg IM immediately after delivery and observed for development of PPH.

Results: Carbetocin prevented PPH in 73.33% cases. Among 20% of COVID-19 positive patients, only one case had PPH. Major contributory factors in patients developing PPH include anemia before delivery, use of anticoagulant in antenatal period, instrumental delivery and high CARPREG 2 score. Less hemodynamic side effects even in patients with high CARPREG 2 score was appreciated.

Conclusion: Carbetocin is a hemodynamically safer and effective uterotonic in heart disease complicating pregnancy. Increasing its availability and implementation in current guidelines is the way forward.

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1. Introduction

Maternal mortality rate in India in 2020 is 99 per lakh live births.[1] Maternal mortality due to obstetric hemorrhage is attributed to 47% cases.[1] Postpartum haemorrhage (PPH) is commonly defined as a blood loss of 500 mL4 or more within 24 hours after birth and affects about 5% of all women giving birth[2] around the world. Globally, nearly one quarter of all maternal deaths are associated with PPH2 and, in most low-income countries, it is the main cause of maternal mortality. Prevention and treatment of PPH involves quick assessment and appropriate action. Limited availability of heat stable uterotonics, inability to maintain cold chain for available uterotonics, lack of expertise in remote areas and limited options available for heart disease complicating pregnancies are major hurdles to prevention of PPH. This study brings forth the idea of use of heat stable carbetocin in Heart disease complicating pregnancy to overcome the limitations of currently available options.

2. Materials and Methods

This study was conducted at Gandhi hospital, Secunderabad a tertiary care centre for high risk pregnancies and nodal centre for COVID-19 positive referrals in the state of Telangana, during August, September, October and November 2021. Antenatal cases with heart disease complicating pregnancy admitted for delivery were included in this study. Carbetocin 100 mcg single dose IM was given to all these patients immediately after delivery to prevent PPH after taking informed consent. Before conduct of this study approval of institutional ethics committee was taken.

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Detailed analysis of the maternal outcome of pregnancy was done.

3. Result

There were 2176 deliveries in the months of August, September, October and November 2021 out of which 1019 were vaginal deliveries and 1142 were lower segment cesarean sections. There were 45 COVID-19 positive deliveries during these four months. There was a total of 34 admissions of heart disease complicating pregnancy out of which 30 cases delivered. Among the study population 20% (6 cases) were COVID-19 positive. These 30 cases were administered carbetocin immediately after delivery and patients were assessed for development of PPH. PPH was present if there was blood loss of more than 500 ml following vaginal delivery or 1000 ml following LSCS or if there was post delivery tachycardia and hypotension was seen, difference in hemoglobin 24 hours post delivery was more than 3, difference in hematocrit $>10^3$. Blood loss was estimated visually as there was no instruments available for quantification of blood loss. Need for uterine massage, need for additional uterotonic and need for blood transfusion was also assessed. The study population had an age distribution of 19-44 years. The study population comprised 46.67% primi gravidas and 16.67% multigravidas, gestational hypertension and preeclampsia was seen in 23.44% of cases. Severity of heart disease and risk stratification was done by using CARPREG 2 score.

Table 1:

Heart disease in pregnancy	Total number of patients
Asymptomatic chronic rheumatic heart disease with changes in 2D ECHO like MS, MR or PAH	10
Congenital Heart disease asymptomatic	11
Status post-surgical correction of congenital heart disease	5
Coronary Artery disease	2
Pulmonary Hypertension (RSVP >49 mm Hg)	1
Severe LV dysfunction	1

Table 2:

Mode of termination	Total number of cases	Percentage distribution
Vaginal delivery	17	56.67%
Cesarean section	13	43.33%
Instrumental delivery	7	23.33%
Primi cesarean sections	7	23.33%

Mode of termination of pregnancy was vaginal delivery in 56.67% (17 cases) and cesarean section in 43.33% (13 cases) out which 7 primigravidas underwent cesarean section, instrumental delivery was done in 7 cases (23.33%). Duration of labour was more than or equal to 10 hours in 12 cases out of which 8 cases had no PPH. Birth weight of 3 kg or more was seen in 8 cases and male baby was born to 18 mothers. Carbetocin was effective in 73.33% cases (22 patients). The fall in hemoglobin more than or equal to 3 was seen in patients with CARPREG 2 score of 4 to 7 whereas carbetocin prevented PPH even in patients having high CARPREG score of 5-8.

Table 3:

Birth weight	Number of cases	Gender of baby	Number of cases
<3 kg	22	Male	18
>=3 kg	8	Female	12

Table 4:

Fall in hemoglobin post delivery	CARPREG 2 score	Number of cases
>3	4 to 7	4 (13.33%)
<3	4 to 8	8 (26.67%)

Incidence of PPH was 26.66% cases (8 patients). Out of which 2 patients had CARPREG score of 6, one patient had score of 7 and one patient had score of 8. On admission NYHA classification of 3 was seen in one case and NYHA classification of 4 was seen in one case. All the 8 patients needed uterine massage and use of additional uterotonic like misporostol for control of PPH. Among patients having PPH, delivery was done by emergency LSCS in 4 patients and vaginal delivery in 4 patients of which 2 patients.

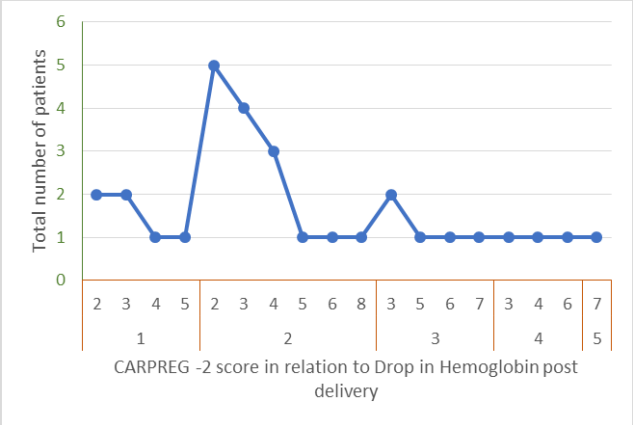

Fig. 1: Relationship between drop in hemoglobin levels following administration of carbetocin in comparison to CARPREG-2 score

Underwent instrumental delivery. Birth weight of 3.75 kg was seen in one case and 3 kg was seen in 3 cases. Anticoagulant was used in antenatal period in 5 cases out of which 3 patients did not have PPH. Blood transfusion was

required in 3 cases. Only 16.66% (1 case) developed PPH in the COVID-19 positive group. She was a primi with term gestation delivered vaginally by instrumental delivery, she had severe preeclampsia, there was anticoagulant usage in antenatal period and she had high CARPREG 2 score of 8.

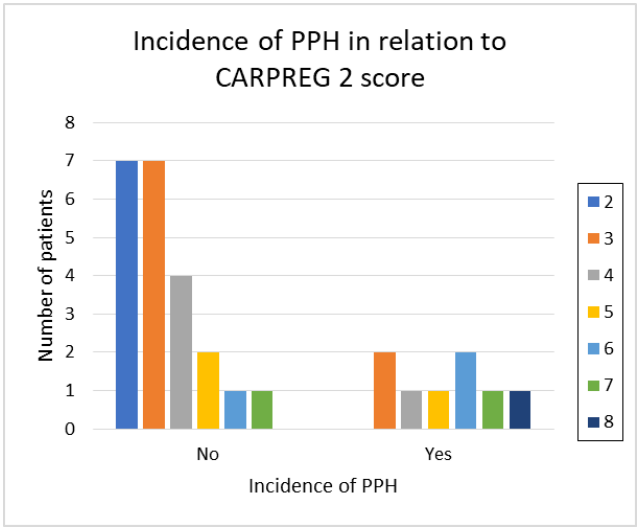

Fig. 2: Incidence of PPH in study group following administration of carbetocin and overall risk stratification of study group by CARPREG-2 score

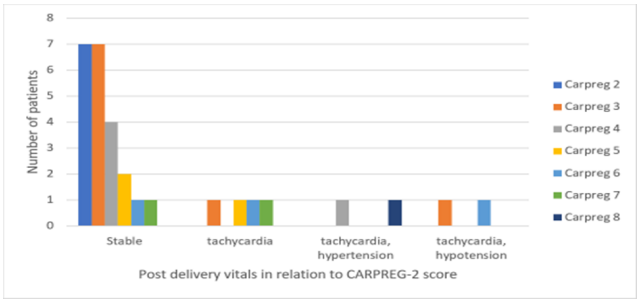

Fig. 3: Relationship between fall in hematocrit after delivery and development of tachycardia and hypotension in the back drop of CARPREG -2 score. Patients with high CARPREG-2 score of 5,6,7 were also stable.

4. Discussion

Post Partum Heamorrhage (PPH) is defined by blood loss of more than 500 ml in vaginal delivery and more than 1000 ml in ceasarean section[3] or blood loss associated with signs and symptoms of hypovolemia.[4] PPH is responsible for 47% maternal mortality in India.[1] Incidence of PPH in India is 2-4% after vaginal delivery and 6% after cesarean delivery.[5] Pregnancy is a hemodynamic state associated with increase in cardiac output and decrease in systemic vascular resistance. Major hemodynamic changes include

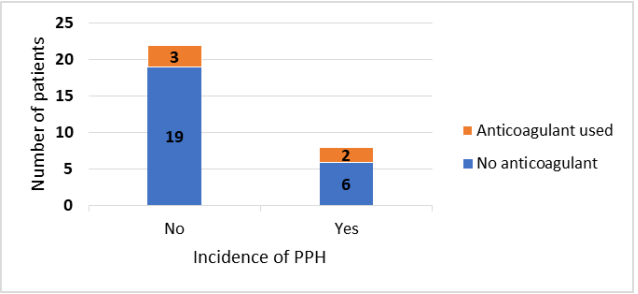

Fig. 4: Incidence of PPH in study group in relation to anti-coagulant use

dilutional anemia, decreased systemic vascular resistance and decrease in preload due to compression of uterus on the inferior vena cava.[6] Cardiac output increases by 60 to 80% immediately after delivery, due to increase in heart rate, preload and circulating catecholamines.[7] Heart disease complicating pregnancy has crucial aspects in management during labour and immediate post Partum mainly because 1) duration of second stage of labour need to be reduced to avoid increase in cardiac output 2) increased incidence of instrumental delivery implies more traumatic PPH 3) adverse cardiovascular effects of spinal and general Anesthesia in case cesarean delivery[8] 4) limited options available for uterotonics with safe cardiovascular profile.

Oxytocin is used in the prevention and treatment of PPH. It exerts its effect by binding to g-protein coupled receptor leading to a direct contractile effect on the myometrium and increased production of prostaglandins f 2 alpha in the endometrium. Oxytocin receptors undergo rapid homologous desensitisation.[9] Oxytocin has a short half life of 3-17 min hence continuous infusion is required for sustained uterotonic activity. Large doses of oxytocin infusion is associated with adverse effects like hypotension, water intoxication, dysrhythmias, ST-T changes, pulmonary edema.[10]

Other uterotonic agents like ergometrine is an absolute contraindication and carboprost is a relative contraindication in heart disease complicating pregnancy.[11]

Carbetocin is a long acting synthetic analogue of oxytocin. It has a half life of 40 mins and has enhanced stability. It acts by binding to myometrial oxytocin receptors leading to rhythmic contraction of uterus. A single dose of carbetocin 100 mcg given IV lasts for 1 hour and if given IM lasts for 2 hours. It has less affinity for V2 receptors and has less cardiovascular side effects. One dose of carbetocin is equivalent to 16 hours of oxytocin infusion.[12] Carbetocin is stable at 30°C for 3 years, at 40°C for 6 months, at 50°C for 3 months and at 60°C for 1 month.[13]

CARPREG 2 (Cardiac Disease in Pregnancy Study) score was used in this study to quantify the severity of heart disease. Risk stratification was done as a predictor of morbidity and mortality in mothers.[14] The risk of primary

cardiac event is 5% with score of 1, risk of 10% with score of 2, 15% with score of 3, 22% with score of 4 and 41% with score greater than 4.

Table 5:

Predictor	Score
Prior cardiac events or arrhythmias	3
Baseline NYHA 3-4 or cyanosis	3
Mechanical Valve	3
Systemic ventricular dysfunction LVEF <55%	2
High risk valve disease or left ventricular outflow tract obstruction (aortic valve area <1.5 cm2, subaortic gradient >30, or moderate to severe mitral regurgitation, mitral stenosis <2.0 cm2	2
Pulmonary hypertension, RVSP >49 mm Hg	2
High risk Aortopathy	2
Coronary artery disease	2
No prior cardiac intervention	1
Late pregnancy assessment	1

In our study we conclude that carbetocin was effective in reducing PPH in 73.33% cases. It was observed that carbetocin is appreciably effective in 26.67% patients with high CARPREG 2 score of 4-8. PPH was seen in 26.66% of cases where additional factors were contributory like multigravida, big baby, anemia before delivery, use of anticoagulant, instrumental delivery. In all these cases PPH was controlled by the use of additional uterotonics like misoprostol. Fewer cardiovascular side effects like hypotension and tachycardia in majority of cases was also appreciated.

5. Conclusion

PPH is dreaded complication of delivery which need to be addressed with adequate preventive measures and prompt action. In case of heart disease complicating pregnancy, PPH can be more challenging due to limited availability of hemodynamically safer uterotonics. Carbetocin can prove to be a safer and effective solution to this major problem. It is especially useful in low resource countries as it does not require a cold chain or IV access or expertise for dose calculation. Therefore recommendation of carbetocin in national and international guidelines and increasing its availability is the need of the hour.

6. Source of Funding

None.

7. Conflict of Interest

The authors declare no conflict of interest.

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