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Carbetocin vs oxytocin in prevention of PPH during caesarean section

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Abstract
Postpartum hemorrhage (PPH) is the leading cause of maternal death worldwide, with uterine atony accounting for 70% of cases. This study aimed to compare the efficacy of carbetocin and oxytocin in preventing PPH during cesarean sections. Conducted at P.C. SETHI hospital in Indore, the prospective comparative study involved 480 women undergoing cesarean delivery with at least one risk factor for PPH. Group 1 received oxytocin, while Group 2 was administered carbetocin. Outcomes, including blood loss, uterine tone, and the need for additional uterotonics, were analyzed. Results indicated that patients receiving carbetocin experienced significantly lower blood loss, reduced need for additional uterotonics, and fewer adverse effects compared to the oxytocin group. Carbetocin was associated with better uterine contractility and lower incidence of uterine atony. The study concludes that carbetocin is more effective than oxytocin for PPH prevention, offering better clinical outcomes during cesarean sections.

Keywords: PPH, caesarean section, carbetocin vs oxytocin

Introduction

Postpartum hemorrhage (PPH) is severe bleeding after giving birth. It's a serious and dangerous condition. PPH usually occurs within 24 hours of childbirth, but it can happen up to 12 weeks postpartum. When the bleeding is caught early and treated quickly, it leads to more successful outcomes. Primary PPH is define as blood loss more than 500 ml after vaginal delivery and more than 1000 after caesarean section that occure in first 24 hr after delivery [1].

Postpartum hemorrhage (PPH) accounts for 125,000 deaths per year worldwide and is the leading cause of maternal death [2]. Uterine atony is its principal cause, responsible for nearly 70% of the cases [3]. Active management of delivery with uterotonic agents is thus recommended by all national guidelines and is reported to halve the PPH rate [4]. According to a 2013 Cochrane review, prophylactic oxytocin can prevent PPH, and an intravenous (IV) bolus dose of 10 IU is recommended as part of active management of the third stage of labor [5]. The World Health Organization recommendations for PPH treatment and prevention also advise the use of 10 units of oxytocin (intramuscularly or intravenously) for the prevention of PPH in all births [6, 7]. This injection is often followed by a maintenance dose of 10 IU over several hours because the half-life of oxytocin is 4 to 10 minutes. Carbetocin, a synthetic oxytocin analog with a half-life of 40 minutes, has been available for 20 years and is hoped to provide better efficacy and a greater ease of use. The main indication for which carbetocin has been proposed is cesarean delivery as it is associated with a higher prevalence of severe PPH and requires invasive second-line therapies three times more often than vaginal deliveries do [8]. It has been evaluated in women with cesareans in small randomized trials and by subjective or post hoc judgment criteria (use of other uterotonics or fundal height in the immediate postpartum period). A 2018 Cochrane meta-analysis concluded that prophylactic carbetocin does not result in a lower incidence of PPH >500 mL in cesarean deliveries, with a risk ratio of 0.71 (0.47–1.07) [9]. This result was nonetheless limited by the number of studies available for this outcome (only six trials and 678 women with cesareans) and the moderate quality of the studies. On the other hand, blood loss and the need for additional uterotonic agents fell significantly, and other recent meta-analyses appear to show that carbetocin is superior to oxytocin [10, 11]. In 2012, our tertiary referral center replaced oxytocin by carbetocin for use in preventing PPH in cases of caesareans before or during labor.

Aims & Objectives

The objective of this study was to investigate whether the use of a single injection of carbetocin was more effective than an oxytocin bolus and 24-hour infusion for preventing PPH in a large sample of women with a cesarean delivery before or during labor.

Materials & Method

This is prospective comparative study done in P.C.SETHI hospital Indore. The study duration was of 18 months from 1st June 2020 to 1st Dec 2021.The study included total 480 patients on the basis of selection criteria who underwent caesarean section for live birth after 34 weeks with at least one risk of PPH. There was selection criteria which involves inclusion and exclusion factors. Inclusion criteria included multiple pregnancy, multigravida, foetal macrosomia, polyhydramnios, uterine fibroid, previous caesarean section. Exclusion criteria included hypertension, preeclampsia, cardiac diseases, renal and liver diseases, epilepsy, general anaesthesia and history of hypersensitivity of carbetocin.

Inclusion criteria	Exclusion criteria
Multiple pregnancy Multigravida Foetal macrosomia Polyhydramnios Uterine fibroid Previous caesarean section	Hypertension and preeclampsia Cardiac diseases Renal and liver diseases Epilepsy General anaesthesia History of hypersensitivity of carbetocin

These 480 patients were divided into two groups of 240 patients. Group 1 received oxytocin infusion of 10 international unit and group 2 received 100 mcg carbetocin as an intravenous bolus just after delivery of baby. Outcome measures such as blood loss, uterine tone, vital sign, haemoglobin level, need of additional uterotonics, and adverse effect were all documented.

Observations

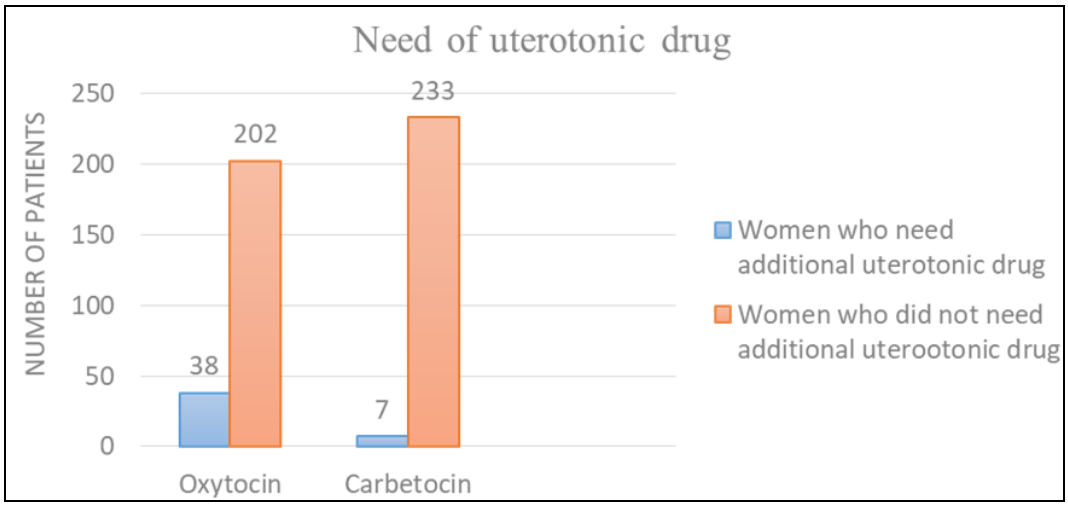

Fig 1: Showing the need of additional uterotonic drug

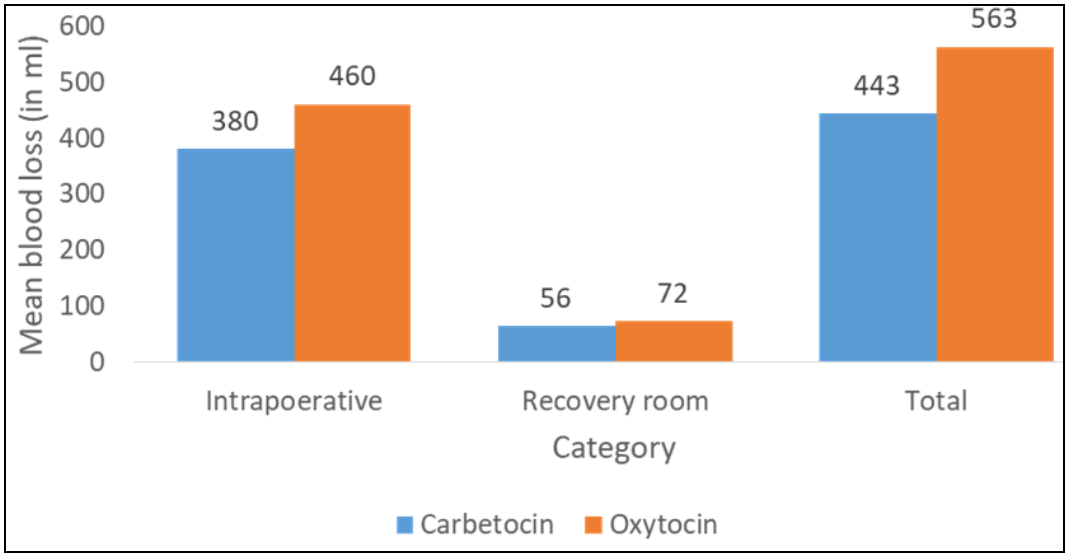

Fig 2: Showing mean blood loss in intraoperative and recovery room in both groups

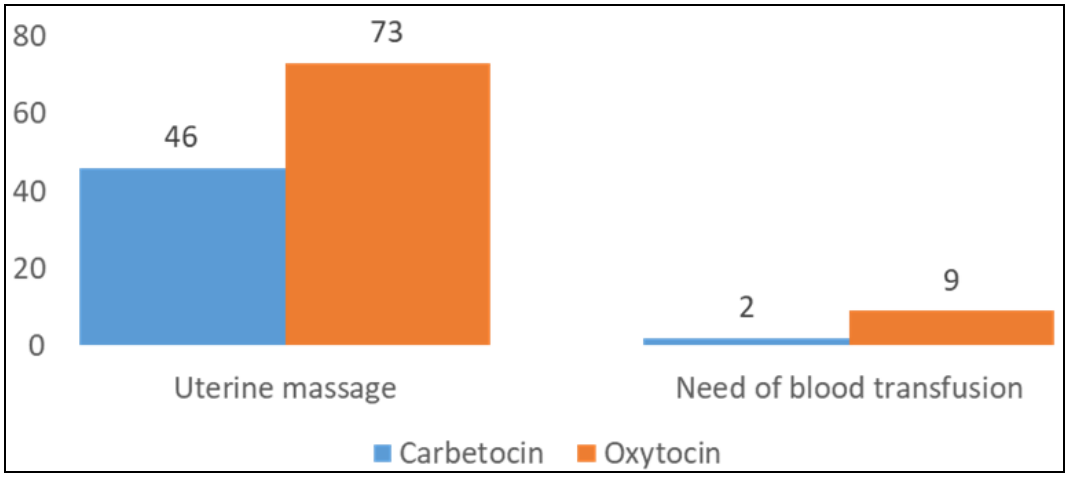

Fig 3: Showing the need of uterine massage and need for blood transfusion in both the groups

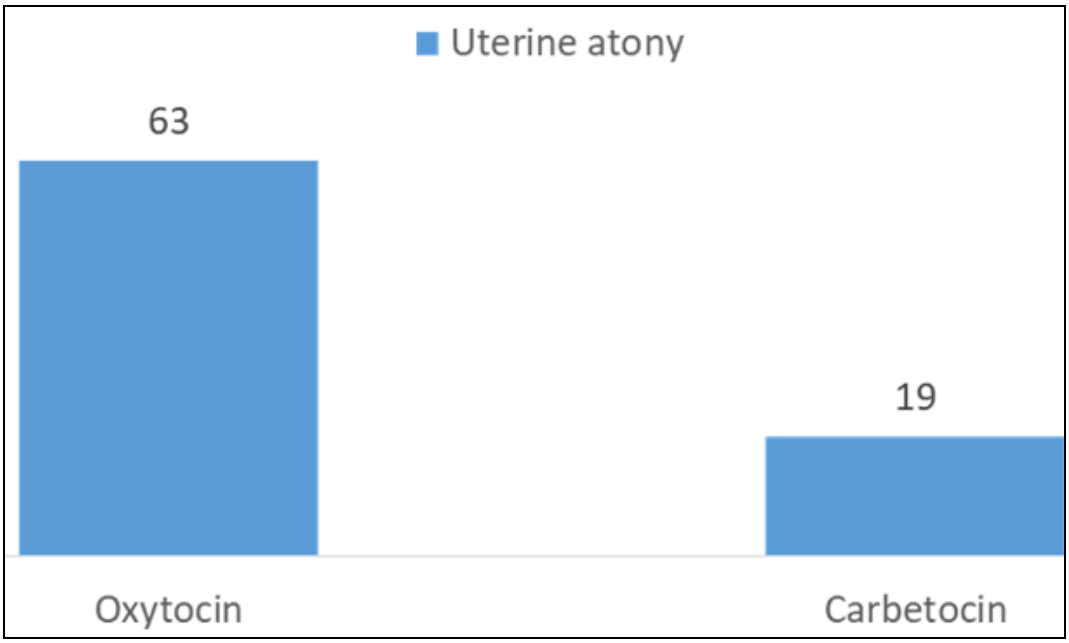

Fig 4: Showing association of uterine atony with oxytocin and carbetocin

Table 5: Showing the association of adverse effects associated with carbetocin and oxytocin

Variables	Carbetocin (N=240)	Oxytocin (N=240)
Nausea	12(5%)	31 (13%)
Vomiting	7(3%)	28(12%)
Tachycardia	45(19%)	19(8%)
Hypotension	5(2%)	40(17%)
Hypertension	21(9%)	9(4%)
Palpitation	7(3%)	5(2%)
Total	97 (40.4%)	132 (55%)

Results

In this study 480 patients were included in the study after choosing from the selection criteria as depicted. The patients were allocated into two categories as Group 1 (given Oxytocin) and Group 2 (given Carbetocin). It was observed that 38 patients (15.8%) needed additional uterotonic drug in Group 1 and 7 patients (2.9%) needed additional uterotonic drug in Group 2 as depicted in table 1. It was observed that mean blood loss was more with Group 1 rather with Group 2. It was seen that 460 ml of mean blood loss was seen with Group 1 patients during intraperative period. However, 380 ml of mean blood loss was seen with Group 2 patients during intraperative period. Moreover, 72 ml and 56 ml were average blood loss in recovery room for Group 1 and Group 2, respectively. Also, it was seen that the total associated blood loss was 563 ml in Group 1 and 443 ml in Group 2. It is shown in table 3 that uterine massage was needed in 73 patients (30.4%) in Group 1 and 46 patients (19.1%) in Group 2. However, need for blood transfusion was seen in 9 patients (3.7%) in Group 1 and 2 patients (0.8%) in Group 2. It was found that uterine atony was associated with 63 patients (26.2%) in Group 1 and 19 patients (7.9%) in Group 2. There were numerous adverse effects associated with both the drugs. The reported incidence of adverse effects was more commonly seen in Group 1 with oxytocin in 55% of the cases rather than in Group 2 with carbetocin in 40%. of the cases. The incidence of nausea was more common in Group 1 w.r.t Group 2

with reported incidence of 13% and 5%, respectively. The incidence of vomiting was also more common in Group 1 w.r.t Group 2 with reported incidence of 12% and 3%, respectively. The incidence of tachycardia was observed more in Group 2 rather than Group 1 with reported incidence of 19% and 8%, respectively. The incidence of hypotension was also observed more in Group 1 rather than Group 2 with reported incidence of 17% and 2%, respectively. The incidence of hypertension was more commonly seen with Group 2 rather than Group 1 with reported incidence of 9% and 4%, respectively. The incidence of palpitation was more commonly observed with Group 2 rather than Group 1 with reported incidence of 3% and 2%, respectively. The Overall adverse effects were commonly seen with Group 1 than with Group 2.

Discussions

In our study, it was observed that carbetocin is overall more effective than oxytocin for prevention of PPH during caeserean section. Danzereau *et al*. firstly described a lower additional uterotonic need for treatment of uterine atony in women who took carbetocin soon after delivery [12]. However, with a similar safety profile and minor antidiuretic effect, single dose of carbetocin appears to be more effective than a continuous infusion of oxytocin to maintain adequate uterine tone in the third stage and in the first 24 hours after delivery defined "four stage of labor" [13].

In the study by Giovanni *et al*., the effectiveness of carbetocin compared to oxytocin regarding the uterine contraction and tonicity was studied. It was observed that the uterine contractility was better in the carbetocin group at 2, 12 and 24 hours after caesarean section, as well as the fundus was significantly below 2 cm from the umbilical point in patients of carbetocin group after 2 and 12 hours. In our study, the uterine atonicity was more commonly seen in Group 1 that is with oxytocin rather than carbetocin. Hence, providing evidence that carbetocin is better drug than oxytocin [14].

Table 1: Comparison of characteristics and clinical indications of oxytocin and heat-stable carbetocin [15]

Characteristics	Oxytocin	Heat stable carbetocin
Brief description	Synthetic cyclic peptide form of the naturally occurring posterior pituitary hormone Binds to oxytocin receptors in the uterine myometrium, stimulating contraction of this uterine smooth muscle by increasing the sodium permeability of uterine myofibrils	Long-acting synthetic analogue of oxytocin with agonist properties. Binds to oxytocin receptors in the uterine smooth muscle, resulting in rhythmic contractions, increased frequency of existing contractions, and increased uterine tone
Pharmacokinetics	Intravenous (IV): almost immediate action with peak concentration after 30 minutes Intramuscular (IM): slower onset of action, taking 3–7 minutes, but produces a longer lasting clinical effect of up to 60 minutes Half-life: 1–6 minutes	IV: sustained uterine contractions within 2 minutes, lasting for about 6 minutes and followed by rhythmic contractions for 60 minutes IM: sustained uterine contractions lasting for about 11 minutes and rhythmic contractions for 120 minutes Half-life: 40 minutes
Storage and transport	Requires protection from light, and storage at 2–8°C continuously, to preserve its activity	Storage conditions: up to 30°C
Clinical indications	Oxytocin	Heat stable carbetocin
Induction of labour	Yes	No
Augmentation of labour	Yes	No
Augmentation of labour	Yes	No
Prevention of PPH	Yes	Yes
Treatment of PPH	Yes	No

Conclusion

Patients who received Carbetocin had reduced need for additional uterotonic agent. The difference was highly significant in mean blood loss and in reduction of the requirement of blood transfusion in Carbetocin group. Patients who received Carbetocin have sufficient uterine contraction and prevent uterine atony. Regarding the haemodynamic effects. The reduction in diastolic blood pressure was significant in patients who received oxytocin. Patients who received Carbetocin associated with higher incidence of tachycardia (pulse > 100 beats per minute within 60 minutes after delivery.

Conflict of Interest

Not available

Financial Support

Not available

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