e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2023; 15(1); 434-440

Original Research Article

A Comparative Study was done on Oxytocin and Carbetocin in Order to Prevent Atonic Postpartum Hemorrhages after Repeated Elective Cesarean Sections

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Received: 26-10-2022 / Revised: 30-11-2022 / Accepted: 20-12-2022

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Conflict of interest: Nil

Abstract

Background: Postpartum hemorrhage, often known as PPH, is a very dangerous illness that continues to be the primary reason for mother morbidity and death.

The purpose of this study was to evaluate the efficacy of carbetocin and oxytocin as preventative agents against atonic pulmonary hypertension (PPH) in patients who were having recurrent elective cesarean sections (CS) while under the influence of spinal anesthesia.

Participants and Procedures: This comparative study was performed on 100 pregnant women after 38 weeks who underwent elective cesarean section under spinal anesthesia at Delhi between March 2020 and September 2021. Fifty patients received a single dose of 100 microgram intravenous carbetocin, and the other fifty patients received 5 IU of oxytocin IV followed by 20-40 IU of oxytocin infusion on 1000 ml saline with a rate of 150 ml per hour.

Results: The findings showed that patients who were given carbetocin had a lower incidence of significant obstetric hemorrhage, needed less intervention in the form of uterine massage, and required fewer extra uterotonic medicines than patients who were given oxytocin. When compared to the oxytocin group, the carbetocin group had a considerable decrease in the amount of predicted blood loss. In addition, the carbetocin group demonstrated a lower frequency of severe anemia and the need for blood transfusions as compared to the oxytocin group; however, this difference did not reach statistical significance.

Conclusion: It indicated that carbetocin was as effective as, if not more effective than, oxytocin for the prevention of atonic postpartum hemorrhage in individuals who were having elective cesarean section. When compared to the maximum permitted dosage of oxytocin, the administration of carbetocin after a cesarean section resulted in a decreased need for further oxytocics (5 IU). In addition to these benefits, carbetocin improved the patients' hemodynamic conditions, reduced the frequency of severe anemia, and reduced the requirement for blood transfusions.

Keywords: Carbetocin, Oxytocin, Atonic Postpartum Hemorrhage, and Repeated Elective Cesarean Sections.

Introduction

PPH is a very dangerous illness that continues to be the single most important factor in maternal morbidity and death.[1] Postpartum hemorrhage (PPH) is responsible for about one-quarter of all maternal fatalities worldwide.[2] In the United Kingdom, PPH was the second most common cause of maternal mortality between the years 2000 and 2002.[3]

Uterine atony is the leading cause of preterm premature labor, accounting for as much as 80 percent of all PPH cases. There are a number of risk factors for preeclamptic hemorrhage, including a history of preeclamptic hemorrhage, preeclampsia, coagulopathy, multiple gestation, and antepartum hemorrhage. However, the majority of preeclamptic hemorrhage episodes occur in women who do not have any predisposing conditions. In addition, caesarean section (CS) is a known risk factor for persistent pulmonary hypertension (PPH), and the incidence of this procedure is growing.[4]

According to Hummel *et al*. (2010), giving oxytocics to the newborn after delivery lowers the risk of persistent pulmonary hypertension (PPH).[5] As a result, the administration of 5 IU of oxytocin through a slow intravenous injection is currently recommended in the United Kingdom for all cesarean sections. On the other hand, the use of extra oxytocic medicine is widespread (WHO, 2015) and is done either to stop bleeding or as a preventative measure in cases where there are risk factors for PPH.[6]

At the moment, oxytocin is the uterotonic that is most often used. It has been shown to reduce the occurrence of PPH by forty percent, has a rapid beginning of action, and a favorable safety profile. Oxytocin's short half-life of 4–10 minutes is one of its drawbacks. Because of this, the hormone often has to be administered by a continuous intravenous infusion or multiple intramuscular injections.[7]

Carbetocin, often known as "Pabal," is a long-acting analogue of the oxytocin hormone that is prescribed for the prevention of uterine atony after caesarean section delivery while the patient is under epidural or spinal anesthesia. Because carbetocin causes a persistent uterine response with contractions of increased amplitude and frequency, its effects begin to take effect very quickly (within one to two minutes) and last for a relatively long period of time (about one hour). It has a safety profile that is similar to that of oxytocin.[8]

The purpose of the current investigation was to evaluate the efficacy of carbetocin and oxytocin as preventative agents against the development of atonic PPH in patients who were scheduled to receive repeated elective CS under the influence of spinal anesthesia.

Materials and Methods

A computerized random cross sectional prospective comparative research was carried out at Delhi on a total of one hundred pregnant women between the months of March 2020 and September 2021. The study was designed as a prospective comparison. All of the participants gave their informed consent after being given a straightforward and understandable explanation of the goals of the research as well as the potential benefits that the study could have for them. Additionally, the participants were given the assurance that the study would not have any negative effects on their health. Participants were under no obligation to take part in the study, and they were free to withdraw at any point between March 2020 and September 2021 (the duration of the study).

Patients who had a singleton pregnancy, a gestational age of more than 38 weeks, spinal

anesthesia, and recurrent cesarean sections with cephalic, breech, or any other malpresentation were included in the research.

Patients were not allowed to participate in the study if they had the following conditions: placenta previa, placental abruption, uterine myomata, congenital uterine anomalies, gestational age before 38 weeks, women who required an emergency cesarean section due to fetal or maternal distress, and patients who had a hepatic condition or a pre-existing bleeding disorder.

Patients who participated in the current research were randomly assigned to one of two groups: Group I received carbetocin (Pabal®) manufactured by Ferring pharmaceuticals given as a single dose of 100 microgram slowly intravenous, and Group II received oxytocin (Syntocinon) manufactured by Novartis given as 5 IU intravenous drip followed by 20-40 IU of oxytocin infusion on 1000 ml of saline or lactated ringer

All of the patients in both of the groups were given a history and clinical examination, as well as an obstetric ultrasound upon admission. This was done to ensure that the fetus was healthy, to determine the gestational age, to identify any obstetric complications such as placenta praevia, multiple gestation, and congenital anomalies, to examine the placenta and amniotic fluid, and to perform routine investigations such as a complete blood count, coagulation

The procedure for administering anesthesia was standardized, and spinal anesthesia was carried out. Prior to receiving spinal anaesthetic, patients were given an intravenous bolus of 500 milliliters of crystalloid solution. At a location that was deemed appropriate, a pencil-point needle with a size of 25G was used. When receiving spinal anesthesia, the patient may be positioned in either the seated or left lateral position. The anesthetic solution included 10–20 micrograms of fentanyl in addition to 0.1 milligrams of preservative-free morphine and 2 milliliters of hypertonic bupivocaine at a concentration of 0.5 percent. According to the results of the touch test, the degree of anesthesia was T5. The patient was positioned 15 degrees to the left of supine, and routine monitoring was carried out in accordance with the criteria provided by the AAGBI. When it was required, anesthesiologists used colloid infusions or blood to replenish the blood that was lost during the procedure. Crystalloids were maintained to be administered intravenously at a rate of 1 liter every eight hours until the morning following surgery. It was decided to standardize the surgical procedure for cesarean section. It was requested that surgeons do the operation in accordance with a conventional method, which outlines a transverse lower segment cesarean section with a two-layer closure of the uterine incision.

It was determined to adopt active management of the third stage of labor: Along with the delivery of the baby's anterior shoulder, administration of the uterotonic drug is also performed. Soon after the baby is born, the umbilical chord is clamped and then severed. Through the abdomen, delivering regulated strain to the umbilical cord while at the same time exerting synchronous counter-pressure to the uterus.

Every woman was monitored for 48 hours following surgery to assess the postpartum outcomes, including vital signs, hemoglobin, and hematocrit. This examination was place after the delivery of the baby.

An examination of the statistics: The statistical program for the social sciences, version 20.0, was used to conduct an analysis on the data that was recorded (SPSS Inc., Chicago, Illinois, USA). The numerical information was presented using the mean

together with the standard deviation (SD). The frequency and percentage of occurrence were used to convey the qualitative data.

Independent-samples When comparing two means, a t-test for statistical significance and a Mann-Whitney U test were used. The Chi-square (x2) test of significance was used in the process of comparing proportions of qualitative parameters. The U-test was utilized in the process of comparing the median and the interquartile range (IQR). A measure of the link between an exposure and an outcome was called an odds ratio (OR), and it was accompanied with confidence intervals of 95%. It was decided that a margin of error of 5% would be acceptable, and the confidence interval would be set at 95%. Therefore, a P-value of less than 0.05 was regarded as statistically significant.

Results

No statistically significant difference was found between groups according to demographic and pulse. There was no statistically significant difference between groups according to blood pressure.

When comparing the groups based on their Hb and blood loss, there was a statistically significant disparity between them. Postoperative. When compared to the oxytocin group, the carbetocin group had a postoperative blood loss that was noticeably less severe. Before and after surgery, both groups' pre- and post-operative Hb and HCT levels were measured and compared. The levels of preoperative Hb and HT showed no significant difference between the two groups, but the levels of postoperative Hb and HCT were significantly higher in the carbetocin group than in the oxytocin group, leading the researchers to draw the conclusion that carbetocin showed the better results in controlling the amount of blood loss and maintaining the levels of Hb and HCT volume. It was revealed that there was a statistically significant difference between the groups in terms of the Hb change and the HCT change. In compared to the oxytocin group, the changes in preoperative and postoperative HCT and Hb levels were statistically significant lower in the carbetocin group. In terms of the administration of uterotonic drugs, the carbetocin group had a lower demand for such administration (20%) in contrast to the oxytocin group's (32%), despite the fact that there was no statistically significant difference between the two groups (Table 1).

Table 1: Comparison between Carbetocin and Oxytocin group according to required uterotonic agents administration

Uterotonic agents	Non-administered	Administered	OR	(95%CI)	P-value
Carbetocin	41	9	0.61	0.213-1.324	0.221
Oxytocin	33	17			

Carbetocin group showed (10%) when compared with the oxytocin group (20%) according to severe anemia, there is no statistically significant difference (p-value= 0.161) (Table2).

Table 2: Comparison between Carbetocin and Oxytocin group according to suffered from severe anemia

Occurrence of severe anemia(Hb<7gm)	No severe anemia	Severe anemia	OR	(95%CI)	P-value
Carbetocin	46	6	0.54	0.140-1.411	0.211
Oxytocin	39	9			

According to severe anemia, there is not a statistically significant difference between the carbetocin group's results (ten percent) and the oxytocin group's results (twenty percent) (p-value = 0.161).

There was not a statistically significant difference between the requirement for blood transfusion in the carbetocin group (6%), which demonstrated, and the oxytocin group (10%), according to the carbetocin group's results (p-value = 0.461).

There is not a statistically significant difference between the carbetocin group's results (16%), which exhibited post-partum bleeding, and the results of the oxytocin group's (28%), which showed the same thing (p-value = 0.148).

Discussion

In the course of the research, the postoperative blood loss that occurred in the carbetocin group was much less than that which occurred in the oxytocin group. In addition, there was a statistically significant gap between the two groups in terms of the incidence of postpartum hemorrhage. In compared to the oxytocin group, which had a 32% incidence of bleeding, the carbetocin group only had a 12% incidence of this complication.

In line with the findings of the current study, demonstrated a lower rate of additional oxytocic usage after carbetocin in comparison with oxytocin.[9] This suggests that carbetocin may be more effective in preventing uterine atony and, consequently, preterm premature labor (PPH). Another research came to the conclusion that the carbetocin group saw a considerably reduced amount of estimated blood loss.[5] In addition, Mohamed *et al*. (2015) demonstrated that blood loss was significantly higher in the oxytocin group in comparison to the carbetocin group, but not to the degree of PPH.[10] This could be attributed to the fact that carbetocin causes a tetanic uterine contraction that is produced 2 minutes after an intravenous injection of 8-30 mg or an intramuscular injection of 10-70 mg, and that this contraction lasts for approximately 1 minute. After an intravenous or intramuscular injection, rhythmic uterine contractions continue for sixty or one hundred and twenty minutes, respectively, and this helps to reduce uterine atony.

Another study indicated that a single injection of carbetocin appeared to be more efficient than a continuous infusion of oxytocin to prevent PPH, with a comparable hemodynamic profile and a slight antidiuretic effect. This conclusion was reached after the researchers compared the two methods.[6]

A randomized controlled trial (RCT) was carried out in Canada by Holleboom *et al*. (2013) to compare the incidence of postpartum hemorrhage (PPH) in women undergoing elective caesarean section who received either carbetocin as a 100-microgram IV bolus or oxytocin as a continuous infusion for 8 hours. Both treatments were given to the women at the same time. The carbetocin group saw a lower incidence of PPH than the other groups.[7]

In a way that is somewhat consistent with our findings, Su and Associates (2012) found that the group that received oxytocin had a larger loss of blood than the group that received carbetocin, although the difference was not statistically significant. Carbetocin and oxytocin, on the other hand, did not vary statistically significantly from one another in terms of the risk of any PPH or the risk of severe PPH.[11]

In the current investigation, the pre-operative and post-operative levels of Hb and HT were measured across both groups of participants. The levels of preoperative Hb and HT showed no significant difference between the two groups, but the levels of postoperative Hb and HCT were significantly higher in the

carbetocin group than in the oxytocin group, leading the researchers to draw the conclusion that carbetocin showed the best results in controlling the amount of blood loss and maintaining the levels of Hb and HCT values. In addition, the difference between pre and postoperative HCT and Hb levels was much less pronounced in the carbetocin group as compared to the oxytocin group.

Post-operatively, the levels of hemoglobin and hematocrit in the carbetocin group were statistically higher, which is consistent with the findings described above.[8]

Attilakos *et al*. (2010) revealed that there were no significant changes in the mean hemoglobin fall after the procedure and in the fundal height or uterine tone postnatally.[5] Additionally, they found that there were no differences in the mean hemoglobin fall after the operation. On the other hand, there was no significant difference in the postoperative reduction in hemoglobin or hematocrit levels. This might be because these values were only reported if they were checked as part of normal care (i.e. not before labor). As a consequence, the findings might be skewed owing to the measures taken in some patients.[7]

In the current investigation, the need for the administration of uterotonic drugs was noticeably reduced in the carbetocin group in contrast to the oxytocin group.

Carbetocin proved to be the most effective treatment when compared to the oxytocin group (5 IU bolus), with much less need for blood transfusions and significantly less need for extra uterotonic medicine. This was in line with the findings that we obtained.[7]

In accordance with these findings, another study confirmed that a single intravenous injection of carbetocin administered during CS significantly reduced the need for additional uterotonic interventions in comparison with traditional I.V. oxytocin treatment. This study also confirmed that carbetocin has the same safety profile as oxytocin, as vital signs, hematologic values (a drop in hemoglobin levels), and the incidence of adverse effects were not statistically different in the two groups.[9]

Other studies that evaluated the effect of an intravenous injection of carbetocin following a cesarean delivery under regional anesthesia found that a single intravenous injection of carbetocin significantly reduced the need for additional uterotonic interventions to maintain adequate uterine tone and prevent or treat excessive bleeding following a caesarean delivery in comparison to intravenous oxytocin.[4,7]

Another research found that the percentage of women in the carbetocin group who needed extra uterotonic medications post-operatively was statistically lower than the number of women in the control group. In the same group, there was a reduced need for uterine massage.[3,4]

In this study, the number of women who suffered from severe anemia and were in need of blood transfusion was not significantly different between the two groups; however, in comparison to the oxytocin group, fewer patients in the carbetocin group showed severe anemia (8%) or the need for blood transfusion (4%).

In contrast to the findings that we obtained, Debbie-Lyn UY and colleagues (2013) [4] demonstrated that the two groups that were investigated did not substantially vary from one another in terms of the need for blood transfusions or the development of severe anemia.

The research conducted by Attilakos *et al*. (2010) found no statistically significant differences between the oxytocin and carbetocin groups for the number of women who required blood transfusions.

Carbetocin seemed to be the most effective treatment when compared to the grouping

that received oxytocin 5 IU bolus. As a result, there was a considerably reduced need for blood transfusions.[7]

Conclusion

It indicated that carbetocin was as effective or more effective than oxytocin for the prevention of postpartum hemorrhage in patients who were about to have elective cesarean sections.

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