

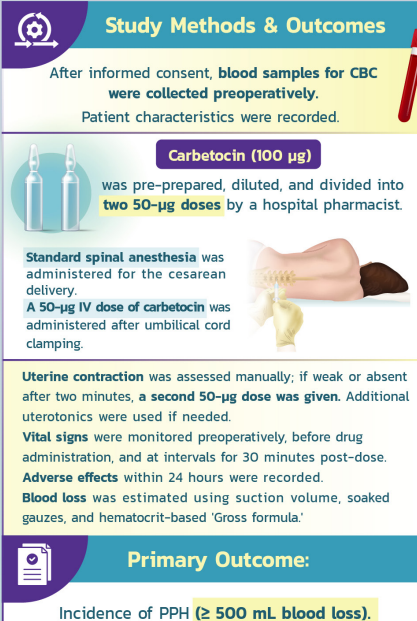
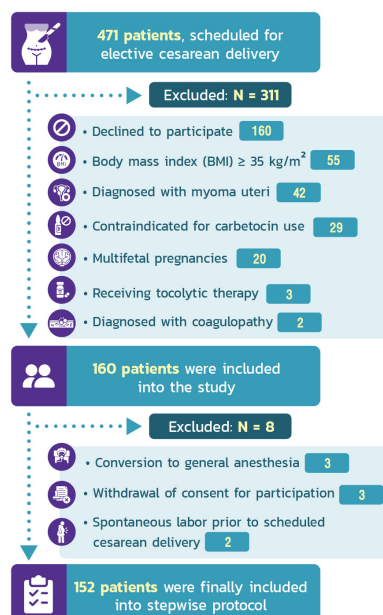
Effects of Stepwise Carbetocin Administration on Postpartum Hemorrhage after Prelabor Cesarean Delivery

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The stepwise regimen demonstrated an effectiveness of 69.7% in preventing postpartum hemorrhage (PPH) during elective cesarean deliveries with the initial 50 µg dose, which increased to 89.4% following the administration of a second dose.



Regarding PPH prevention, a single 50 mcg dose of carbetocin was effective in 69.7% of cases (106/152, 95%CI: 0.62–0.77). For the remaining 30.3% (46/152, 95%CI: 0.23–0.38) who needed a second dose, 10.5% also received other additional uterotonic agents.

Incidence of PPH (%)	
Estimated by anesthesiologist	Calculated by Hematocrit changes
32.9%	45.4%
2.0%	13.8%
	500mL
	1,000mL

Only the involvement of a resident as a surgeon emerged as a significant predictor for the need of a second carbetocin dose (OR 7.9, 95%CI: 3.6–17.1, P<0.01)

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ABSTRACT

Objective: To evaluate the effectiveness of stepwise administration of carbetocin in reducing postpartum hemorrhage (PPH) in term pregnancies undergoing elective cesarean delivery.

Materials and Methods: This study included term pregnancies scheduled for cesarean delivery. Exclusion criteria were a BMI ≥ 35 kg/m², any underlying medical conditions that contraindicated the use of carbetocin and conditions affecting uterine contraction. Following newborn delivery, an initial dose of 50 µg of carbetocin was administered, with a subsequent 50 µg given if uterine contraction was inadequate. The primary outcome was the incidence of PPH exceeding 500 mL, while secondary outcomes included total blood loss $\geq 1,000$ mL, administration of additional uterotonic agents, adverse effects, other pregnancy-related and surgical outcomes.

Results: Of the 152 pregnant women analyzed, adequate uterine contraction was observed in 69.7% of cases after the first carbetocin dose, with an additional 19.7% achieving adequate contraction after the second dose. Estimated blood loss exceeding 500 mL was 32.9% and exceeding 1,000 mL was 2.0% of cases, respectively. Recalculations based on pre- and post-hematocrit levels indicated higher rates of blood loss: more than 500 mL in 45.4% and over 1,000 mL in 13.8%. No serious adverse events or complications were reported.

Conclusion: The stepwise regimen demonstrated an effectiveness of 69.7% in preventing postpartum hemorrhage (PPH) during elective cesarean deliveries with the initial 50 µg dose, which increased to 89.4% following the administration of a second dose.

Keywords: Carbetocin; stepwise administration; cesarean delivery; postpartum hemorrhage (Siriraj Med J 2025; 77: 513-522)

INTRODUCTION

Postpartum hemorrhage is the leading cause of maternal mortality worldwide.¹ While women with high-risk factors—such as prolonged third stage of labor, pregnancy-induced hypertensive disorders, uterine atony, birth canal injury, or retained placental tissue—are particularly susceptible, postpartum hemorrhage can also occur in low-risk pregnancies, regardless of the mode of delivery.^{1,2} To reduce its incidence, the administration of uterotonic agents in the third stage of labor is a critical intervention.³ Carbetocin is a next-generation synthetic oxytocin that acts as a long-acting oxytocin agonist. It is used to prevent postpartum hemorrhage (PPH) by promoting rhythmic uterine contractions.⁴ Recent meta-analyses have confirmed that carbetocin reduces the need for additional uterotonic agents compared with oxytocin in preventing PPH, particularly in elective cesarean delivery.^{5,6}

Determining the optimal dosage of carbetocin for PPH prevention remains a question. Initially, the standard dose of carbetocin (100 µg) was proved to be effective for preventing PPH after cesarean delivery and was recommended to be the 1st line drug for PPH prevention in guidelines.^{7,8} The standard dose of carbetocin, set at 100 µg, was based on the equivalent dose of oxytocin 5 IU.⁴ However, in a sequential allocation trial, the effective dose for 90% of cases (ED90) was found to be 14.8 µg of carbetocin.⁹ Among obese women (BMI ≥ 40 kg/m²) the

minimum effective dose of carbetocin was 62.9 µg.¹⁰ In pregnant women with abnormal labor and a history of oxytocin usage curves who underwent cesarean delivery, the minimum effective dose was 121 µg of carbetocin.¹¹

In two studies, a wide range of carbetocin doses (20-120 µg) was administered but, the results were inconclusive.^{12,13} Similar to those of oxytocin, carbetocin has some adverse effects, including nausea, vomiting, headache, hypotension, and chills.¹ Therefore, reducing the dose may also reduce adverse effects. We hypothesized that a half dose of carbetocin (50 µg) would be both sufficient and practical for effectively reducing PPH in pre-labor cesarean delivery. The aim of this prospective study was to analyze the effects of stepwise administration of carbetocin (50 µg/step) in reducing PPH in term pregnancies undergoing cesarean delivery.

MATERIALS AND METHODS

The study protocol was approved by the Institutional Review Board (IRB) on April 18, 2022 (COA No. Si 313/2022). This prospective study was conducted from January 1st to June 30th, 2023. The study employed a stepwise approach using carbetocin in women undergoing a pre-labor cesarean section. The inclusion criteria were women with a term singleton pregnancy scheduled for elective cesarean delivery at Siriraj Hospital. The exclusion criteria were women with a history of carbetocin allergy, cardiovascular, liver, kidney diseases, epilepsy, migraine,

or asthma. Additionally, obese women ($\text{BMI} \geq 35 \text{ kg/m}^2$) and those with high-risk pregnancies affecting uterine contractility, such as preeclampsia, placenta previa, placenta accreta spectrum (PAS), polyhydramnios, uterine structural abnormalities, hematologic diseases, were excluded. Women who had received tocolytic drugs within 24 hours preoperatively were also excluded. The standard anesthetic approach for pregnant women undergoing cesarean section is regional anesthesia (spinal or epidural anesthesia). Therefore, cases requiring conversion to general anesthesia, which might impact uterine contraction, are excluded from this study.

After obtaining informed consent, blood samples for a complete blood count were collected the day prior to surgery. Characteristics of the women were recorded. Carbetocin was prepared in advance from a 100 µg ampule (Duratocin®, Ferring Pharmaceutical Co., Ltd, Thailand), divided into two syringes, and diluted with normal saline to 5 mL per syringe by a hospital pharmacist on the day of surgery. Women underwent cesarean delivery under spinal anesthesia, which was administered using local anesthetic combined with intrathecal morphine, with standard intraoperative monitoring. Following fetal delivery and clamping of the umbilical cord, a 50-µg dose of diluted carbetocin was administered intravenously. The assessment of uterine contraction was performed through manual palpation by the surgeon, and was categorized as strong, moderate, weak, or absent. If after two minutes of administration, uterine contraction was assessed weak or absent, a second dose of 50 µg was administered. Additional uterotonic agents were administered if uterine contractions remained inadequate. The anesthesia team monitored and recorded the pulse and blood pressure before surgery, before drug administration, and then two minutes after administration, and subsequently every five minutes for 30 minutes. Any adverse effects within the first 24 hours post-operatively were documented by interviewing the patient, with medications used for treatment recorded. To estimate blood loss during surgery, the anesthesiologist documented the volume of blood collected in the suction canister and from weighed soaked gauzes or swabs. Twenty-four hours postoperatively, a blood sample was obtained from the patient for a complete blood count (CBC), and the results were subsequently used to calculate the volume of blood loss utilizing the 'Gross formula', a method for assessing blood loss based on changes in hematocrit levels.¹⁴

The primary outcome of this study was the incidence of PPH (blood loss $\geq 500 \text{ mL}$).¹ Secondary outcomes included total blood loss, blood loss $\geq 1,000 \text{ mL}$, administration of additional uterotonic agents, adverse effects, other

pregnancy-related and surgical outcomes including operative time, pre- and post-operative hemoglobin and hematocrit levels, adverse events after operation.

The sample size was calculated based on 2022 data from Siriraj Hospital. The retrospective data of 50 pregnant women undergoing elective cesarean delivery in early 2022 showed average rate of blood loss exceeding 500 mL following cesarean delivery was 40%. Considering a type I error rate of 0.05 and a power of 0.8, the calculated sample size was 145. To account for potential dropout, an additional 10% was added, bringing the total to 160 pregnant women.

Statistical analyses

Data analysis was conducted using SPSS Statistics version 18.0 for Windows (IBM Corp., Armonk, NY, USA). Descriptive data were presented as numbers and percentages (n, %) for categorical variables and as mean $\pm$ standard deviation (SD) or median (IQR) for continuous variables, depending on data distribution.

Normality of continuous variables was assessed using the Kolmogorov-Smirnov or Shapiro-Wilk test. If normally distributed, variables were summarized as mean $\pm$ SD and compared using the independent t-test or one-way ANOVA. If non-normally distributed, data were reported as median (IQR) and compared using the Mann-Whitney U test or the Kruskal-Wallis test. Categorical variables were presented as n (%) and compared using the Chi-square test. Fisher's exact test was used when any expected count was <5 . A p-value < 0.05 was considered statistically significant.

To identify factors associated with the need for an additional dose of carbetocin, univariate analysis was first performed for each predictor variable. Variables with $p \leq 0.2$ in the univariate analysis were considered for further evaluation in multivariate analysis. Multivariate logistic regression was then conducted using SPSS stepwise regression (both forward and backward selection), which iteratively adds or removes variables based on statistical significance criteria. The final model retained only independent predictors with p-values < 0.05 . Results were reported as odds ratios (ORs) with 95% confidence intervals (CIs). A p-value of < 0.05 was considered statistically significant.

RESULTS

A total of 471 pregnant women participated, with 152 included (Fig 1). Scheduled cesarean deliveries occurred at approximately 38 weeks of gestation. The majority of pregnant women were overweight (55.3%) or obese (13.8%). Maternal anemia ($\text{Hb} < 11 \text{ g/dL}$) was observed in 19.7% of cases (Table 1).

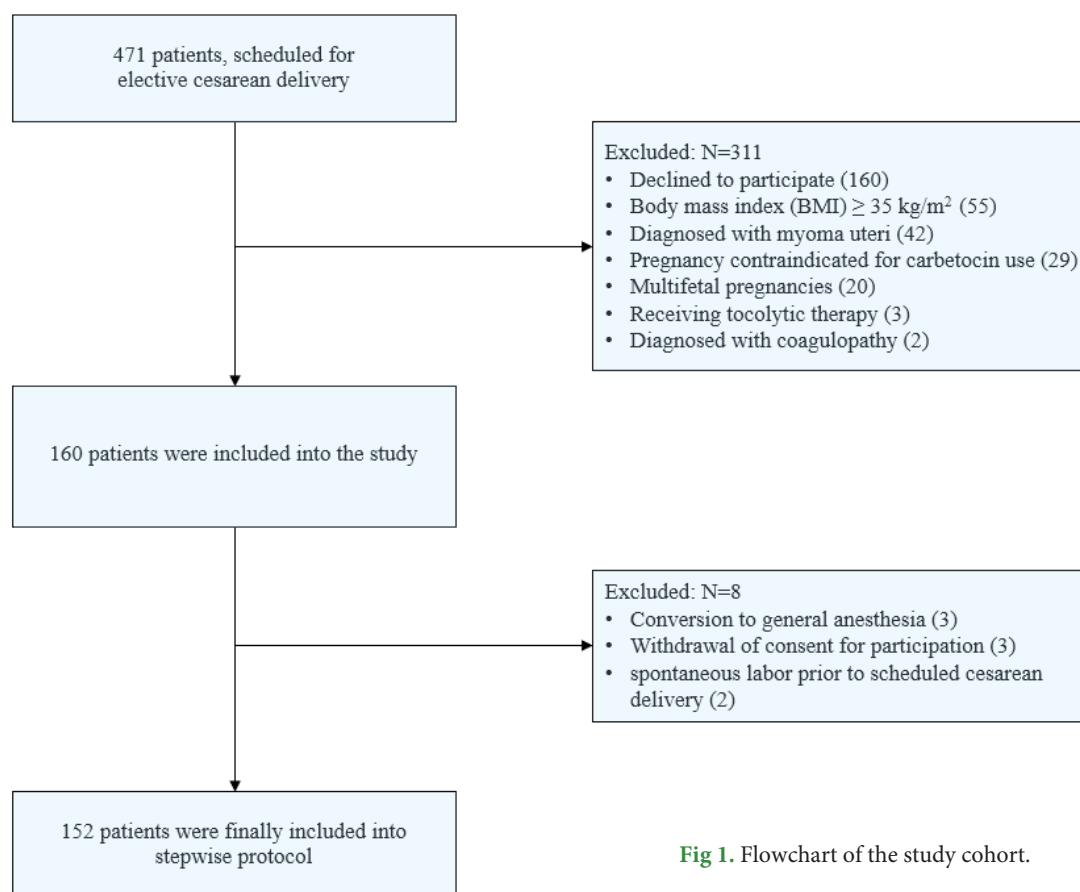


Fig 1. Flowchart of the study cohort.

TABLE 1. Characteristics of study population (N=152).

Characteristic	Mean ± SD or N (%) (n=152)
Age (year)	34.01 ± 4.78
Body weight on admission (kg)	69.10 ± 9.85
Weight gain (kg)	13.58 ± 5.03
Gestational age (week)	38.18 ± 0.55
BMI (kg/m ²)	26.65 ± 3.35
BMI (kg/m ²)	
Underweight (<18.5)	2 (1.3)
Normal weight (18.5-24.9)	45 (29.6)
Overweight (25.0-29.9)	84 (55.3)
Obesity (30.0-35.0)	21 (13.8)
Baseline hemoglobin (g/dL)	11.95 ± 1.03
Baseline hematocrit (%)	36.42 ± 2.94
Maternal anemia	30 (19.7)
Fetal birth weight (g)	3122.76 ± 377.94

Carbetocin was effective as a single dose in 69.7% (106/152, 95% CI: 0.624–0.770), while 30.3% (46/152, 95% CI: 0.230–0.376) required an additional dose, with 10.5% also receiving other uterotonic agents. Based on the estimate of the anesthesiologist, 32.9% of pregnant women experienced blood loss exceeding 500 mL and 2.0% exceeded 1,000 mL, increasing to 45.4% and 13.8%, respectively, when assessed by hematocrit changes. Those requiring a second dose or additional uterotonic agents had significantly greater blood loss and hematologic changes ($P < 0.05$). Hypotension ($\geq 20\%$ decrease in SBP or DBP) occurred in 74% (113/152) of pregnant women, with 48% (54/113) requiring vasopressors. Vasopressor use did not differ significantly between groups (50 μ g: 34% vs. 100 μ g: 39%, $P \geq 0.05$). No severe adverse events occurred, and adverse effects did not differ between groups (Table 2).

Table 3 demonstrates median (IQR) values for pulse rate, SBP, and DBP post-carbetocin administration. Median vital sign changes were minimal, with no significant differences in pulse rate and SBP ($P \geq 0.05$). However, DBP was significantly lower in the 100 μ g group at 2 and 5 minutes post-administration (49.0 (17) vs. 57.0 (14) mmHg, $P < 0.01$ at 2 min; 49.0 (14) vs. 56.0 (12) mmHg, $P < 0.01$ at 5 min).

TABLE 2. Outcomes and factors associated with the stepwise protocol (N=152).

	N (%) (n=152)	Carbetocin dose N (%)		p-value*
		50 ug group (n=106)	100 ug group (n=46)	
Parity				
Nullipara	72 (47.4)	58 (54.7)	14 (30.4)	0.01
Multipara	80 (52.6)	48 (45.3)	32 (69.6)	
Previous cesarean section				
Yes	70 (46.1)	43 (40.6)	27 (58.7)	0.04
No	82 (53.9)	63 (59.4)	19 (41.3)	
Surgeon				
Attending physician	99 (65.1)	84 (79.2)	15 (32.6)	<0.001
Resident	53 (34.9)	22 (20.8)	31 (67.4)	
Maternal anemia (Before cesarean section)	30 (19.7)	22 (20.8)	8 (17.4)	0.63
Maternal anemia (After cesarean section)	79 (52.0)	53 (50.0)	26 (56.5)	0.46
Need of additional uterotonic agents	16 (10.5)	0 (0.0)	16 (34.8)	<0.001
Need of vasopressor drugs	54 (35.5)	36 (34.0)	18 (39.1)	0.54
Operative time	55.7 (18.2)	51.9 (17.0)	64.4 (17.9)	<0.01
Blood loss				
Estimated blood loss				
< 500 mL	99 (65.1)	82 (77.4)	17 (37.0)	<0.001
≥ 500-999 mL	50 (32.9)	23 (21.7)	27 (58.7)	<0.001
≥ 1,000 mL	3 (2.0)	1 (0.9)	2 (4.3)	0.17
Calculated blood loss				
< 500 mL	62 (49.6)	57 (51.0)	8 (17.4)	0.03
≥ 500-999 mL	69 (45.4)	42 (39.6)	27 (58.7)	0.03
≥ 1,000 mL	21 (13.8)	10 (9.4)	11 (23.9)	0.02
Adverse effects				
Headache	3 (2.0)	3 (2.8)	0 (0.0)	0.25
Dizziness	24 (15.8)	16 (15.1)	8 (17.4)	0.72
Nausea/vomiting	63 (41.4)	40 (37.7)	23 (50.0)	0.16
Flushing	4 (2.6)	1 (0.9)	3 (6.5)	0.05
Bitterness	10 (6.6)	6 (5.7)	4 (8.7)	0.49
Chills	28 (18.4)	19 (17.9)	9 (19.6)	0.81
Shivering	15 (9.9)	12 (11.3)	3 (6.5)	0.36
Pruritus	74 (48.7)	55 (51.9)	19 (41.3)	0.23

TABLE 2. Outcomes and factors associated with the stepwise protocol (N=152). (Continue)

	Mean ± SD (n=152)	Mean ± SD 50 ug (n=106)	100 ug (n=46)	p-value*
Estimated blood loss (mL)	416.1 ± 179.2	378.8 ± 161.5	502.2 ± 189.7	<0.001
Postoperative hemoglobin (g/dL)	11.9 ± 1.0	11.9 ± 1.0	12.1 ± 1.0	0.16
Postoperative hematocrit (%)	36.4 ± 2.9	36.2 ± 3.0	36.9 ± 2.8	0.16
Postoperative hemoglobin (g/dL)	11.0 ± 1.2	11.0 ± 1.2	10.9 ± 1.3	0.57
Postoperative hematocrit (%)	33.4 ± 3.4	33.5 ± 3.3	33.2 ± 3.7	0.52
	Median (IQR) (n=152)	Median (IQR) 50 ug (n=106)	100 ug (n=46)	p-value*
Calculated blood loss (mL)	419.6 (625.0)	364.5 (577.0)	555.9 (820.0)	0.02
Change of Hemoglobin (g/dL)	0.9 (1.4)	0.8 (1.2)	1.3 (1.6)	0.03
Change of Hematocrit (%)	2.7 (4.1)	2.4 (3.75)	3.6 (4.7)	0.03

* Statistical significance (P<0.05)

Abbreviations: SD: standard deviation, IQR: interquartile range

Multiparity, previous cesarean delivery, resident and operative time were identified as significant factors in the univariate analysis (Table 2). However, the only significant predictor of requiring an additional carbetocin dose was surgeries performed by residents (OR: 7.9, 95% CI: 3.6–17.1, $P < 0.001$), whereas multiparity and prior cesarean delivery were not retained in the final model ($P > 0.05$) (Table 4). Additionally, surgeries performed by residents were significantly longer than those conducted by attending physician (68.3 ± 17.8 vs. 49.0 ± 14.5 minutes, $P < 0.01$). However, the incidence of PPH did not significantly differ between groups. The proportion of cases with blood loss ≥ 500 mL was 44.4% in faculty-performed surgeries and 47.2% in resident-supervised surgeries ($P > 0.05$). For blood loss $\geq 1,000$ mL, the rates were 11.1% and 18.9%, respectively ($P > 0.05$).

DISCUSSION

This study demonstrated that a single 50 µg dose of carbetocin effectively prevented PPH after cesarean delivery in 69.7% of cases, while 30.3% required an additional dose. Pregnant women requiring additional uterotonic agents experienced greater blood loss and more pronounced hematologic changes. However, no

severe adverse events were reported. These findings support the efficacy of carbetocin in reducing the need for additional uterotonic agents.

Postpartum hemorrhage is the leading cause of maternal mortality worldwide.³ Current evidence unequivocally supports the pivotal role of medical interventions in reducing the incidence of PPH. According to a meta-analysis by Gallos *et al.*, carbetocin may be considered as the preferred agent for preventing PPH during elective cesarean deliveries.⁶ While its efficacy in this context has been well established, the cost-effectiveness of carbetocin remains the subject of debate in clinical practice. Studies conducted in developed countries have demonstrated its cost-effectiveness and potential to reduce overall patient care costs; however, these findings have not been consistently replicated in developing countries.¹⁵⁻¹⁷ Based on the findings of this study, reducing the carbetocin dosage to 50 mcg may be a viable and clinically appropriate strategy. However, cost-effectiveness analyses of the half-dose regimen are needed to support its wider clinical implementation.

The potential for reducing carbetocin dosage to use for PPH prevention among elective cesarean deliveries has been demonstrated in clinical research. Previous studies indicate the efficacy of various carbetocin regimens, especially in lower doses, in sustaining sufficient uterine

TABLE 3. Pulse and blood pressure after drug administration (N=152).

	Median (IQR) (n=152)	Carbetocin dose		p-value*
		Median (IQR)		
		50 ug (n=106)	100 ug (n=46)	
Pulse (bpm)				
2 min	91.0 (17)	90.5 (16)	93.5 (16)	0.35
5 min	89.0 (19)	88.5 (22)	90.0 (14)	0.88
10 min	88.5 (15)	90 (15)	87.5 (18)	0.42
15 min	88.0 (16)	88.0 (16)	87.5 (16)	0.99
20 min	87.0 (17)	86.0 (17)	88.0 (17)	0.86
25 min	84.0 (18)	83.0 (16)	85.0 (20)	0.32
30 min	82.0 (16)	82.0 (15)	82.0 (20)	0.67
Systolic blood pressure (mmHg)				
2 min	110 (16)	111 (16)	105 (21)	0.06
5 min	111 (17)	112 (16)	110 (21)	0.32
10 min	111 (15)	109.5 (16)	111 (16)	0.33
15 min	113 (17)	112.5 (17)	116.0 (18)	0.50
20 min	112 (19)	111.0 (17)	112.0 (20)	0.25
25 min	115 (16)	114.5 (17)	115.0 (18)	0.40
30 min	115 (15)	115.0 (15)	115.0 (14)	0.76
Diastolic blood pressure (mmHg)				
2 min	54 (15)	57.0 (14)	49.0 (17)	<0.01
5 min	54 (14)	56.0 (12)	50.0 (13)	<0.01
10 min	53.5 (11)	54.0 (13)	53.0 (9)	0.61
15 min	55 (11)	54.0 (11)	58.5 (9)	0.55
20 min	56 (13)	55.0 (11)	57.0 (13)	0.34
25 min	60 (12)	60.0 (12)	60.0 (11)	0.80
30 min	61 (13)	61.0 (13)	63.0 (11)	0.29

*Statistical significance (P<0.05)

Abbreviations: bpm: beat per minute, IQR: interquartile range

TABLE 4. Multiple logistic regression analysis of factors associated with 100 ug carbetocin.

Variable	Multivariate analysis				
	beta	SE	χ^2	p-value*	OR (95%CI)
Multiparity	1.24	0.79	2.48	0.12	3.4 (0.74-16.01)
Previous CS	-1.39	0.80	2.98	0.08	0.3 (0.05-1.21)
Operative time > 60 minutes	-1.32	0.50	0.07	0.79	0.9 (0.33-2.31)
Resident	2.29	0.52	18.83	<0.01	9.8 (3.50-27.61)
Constant	-1.78	0.34	28.10	<0.01	0.2

*Statistical significance (P<0.05), SE: standard errors, χ^2 : Wald χ^2 , OR: odds ratios, and 95% CI: 95% confidence intervals, CS: cesarean section

contraction during cesarean delivery across different patient conditions.^{9,10,13} Building on these findings, our study suggests that a reduced dose of 50 µg of carbetocin is adequate for promoting uterine contraction in elective cesarean deliveries. However, we excluded pregnant women with a BMI over 35 kg/m² for ethical reasons, as these cases required carbetocin doses greater than 50 µg.¹⁰ It's important to note that despite excluding pregnancies preoperatively diagnosed with myomas, we encountered 8 cases with intraoperative diagnoses of myomas, highlighting the need for careful risk assessment when applying this stepwise protocol.

The stepwise administration of 50 µg of carbetocin demonstrated its efficacy in reducing PPH following elective cesarean delivery. In our study, two-third of pregnant women (69.7%) required only a single dose, while one-third (30.3%) required an additional dose. The need for additional uterotonic agents was low (10%), with no severe adverse events reported. These findings align with previous research highlighting carbetocin's role in minimizing PPH risk.^{5,18,19}

Blood loss during cesarean delivery is frequently underestimated due to the inherent limitations of traditional measurement techniques, such as suction canister readings and visual estimation of gauze saturation, both of which are susceptible to significant error. Our analysis revealed that conventional estimates underreported blood loss by a factor of 0.7 for cases exceeding 500 mL (32.9% estimated vs. 45.4% recalculated) and by a factor of seven for losses greater than 1,000 mL (2.0% estimated vs. 13.8% recalculated). While hematocrit-based recalculations provide a more objective assessment, their accuracy remains influenced by intraoperative fluid administration and physiological variations. Despite these constraints, hematocrit-based estimation represents an improvement over the conventional method. To further enhance accuracy and optimize postpartum hemorrhage management in cesarean deliveries, the implementation of advanced quantitative blood loss measurement tools, similar to those used in vaginal deliveries, may improve accuracy and enhance PPH management in cesarean deliveries.^{20,21} Multiple logistic regression analysis identified surgical inexperience as a significant factor associated with the need for additional doses of carbetocin. Conducted at a tertiary care center, our residency training program follows a standard structure comparable to other university hospitals worldwide. First-year residents assisted in cesarean delivery under faculty supervision, progressing to independent performance in later years, with oversight and consultation available as needed. In practice, the decision to administer an additional dose was guided by the study protocol rather than anesthesiologist warnings

or concerns about liability for PPH. Nevertheless, the diverse levels of experience among these surgeons may have impacted their decisions regarding the administration of additional doses of carbetocin. While residents were more likely to administer an additional dose, the study found no significant difference in the incidence of PPH between surgeries performed by residents and those performed by faculty. This finding suggests that surgical experience affects clinical decision-making during cesarean delivery rather than directly influencing the occurrence of complications.

In line with prior research, the most frequently reported adverse effects included pruritus (48.7%), nausea/vomiting (41.4%), chills (18.4%), and dizziness (15.8%).^{11,22,23} Hypotension was also prevalent, and observed in 74.3% of pregnant women, with a subset requiring vasopressor intervention. It's important to note that some of these adverse effects cannot be definitively attributed to carbetocin alone as they could be caused by other anesthetic agents used during surgery. For example, spinal block anesthesia can cause a drop in diastolic blood pressure (DBP) due to reduced parasympathetic tone and intrathecal morphine is known to cause pruritus, as well as nausea and vomiting. Nevertheless, it's worth emphasizing that all these clinical manifestations were not severe and were manageable.

A major strength of this study is its prospective experimental design, which provides a structured evaluation of a low-dose carbetocin regimen with a stepwise administration protocol in a real-world setting. The preparation of the diluted carbetocin dose was conducted under strict quality control by the Siriraj pharmacist unit, ensuring accuracy and consistency. Additionally, blood loss assessment incorporated both intraoperative estimates and an objective standardized equation based on pre- and postoperative hematocrit levels, offering a more comprehensive evaluation of actual blood loss.

However, the study has certain limitations. As a single-center study, the findings are influenced by institutional protocols and patient demographics, which may limit their direct applicability to other healthcare settings. Nevertheless, the documentation and analysis of clinical practice in a controlled manner provide valuable insights that may inform broader clinical implementation. Furthermore, the study employed a single-unblinded design to reflect real-world clinical decision-making. This approach may have introduced variability in the administration of additional uterotonic agents, as the determination of uterine tone relied on individual clinical judgment.

Given the widespread use of oxytocin as the first-line agent for PPH prevention, further research is needed to compare the efficacy and safety of this stepwise carbetocin regimen with standard oxytocin protocols. Multicenter randomized trials could clarify its benefits in uterine tone stabilization, blood loss reduction, and broader clinical applications.

CONCLUSION

The stepwise regimen demonstrated an effectiveness of 69.7% in preventing postpartum hemorrhage (PPH) during elective cesarean deliveries with the initial 50 µg dose, which increased to 89.4% following the administration of a second dose.

Data Availability Statement

The data supporting this study are not publicly available due to ethical concerns and patient confidentiality but may be obtained from the corresponding author upon reasonable request and with appropriate institutional approval.

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DECLARATION

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Conflict of Interest

Tripop Lertbunnaphong has received a speaker honorarium from Ferring Pharmaceutical Co., Ltd, Thailand. The other authors have no relevant financial or non-financial interests to disclose.

Registration Number of Clinical Trial

TCTR20231009002 (retrospective registration on October 9, 2023)

Author Contributions

P.B.: Protocol development, Material preparation, Data collection, Data analysis, Manuscript writing, Funding management. T.L.: Protocol development, Manuscript editing, Funding management. P.L.: Data collection, Data analysis. A.P.: Material preparation, Data collection. P.N.: Protocol development, Manuscript editing. N.T.: Protocol development, Manuscript editing. All authors reviewed and agreed to the final version of the manuscript.

Use of Artificial Intelligence

During the preparation of this work, the authors used ChatGPT to refine the English language for publication. After utilizing this tool, the authors reviewed and edited the content as necessary and took full responsibility for the final version of the publication.

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