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Comparison between carbetocin and oxytocin in the prevention of postpartum hemorrhage in cesarean sections: a systematic review

Comparación entre carbetocina y oxitocina en la prevención de hemorragia posparto en cesáreas: revisión sistemática

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ABSTRACT

Postpartum hemorrhage is a leading cause of maternal mortality, particularly in women undergoing cesarean sections. This study aimed to compare the efficacy and safety of carbetocin versus oxytocin for the prevention of postpartum hemorrhage in women who have had a cesarean section, through a critical review and synthesis of the available evidence. A systematic review was conducted using the PRISMA guidelines. Studies comparing oxytocin and carbetocin in women with postpartum hemorrhage following cesarean section were searched in databases such as PubMed, Cochrane Library, Scopus, and Embase. The methodological quality of the studies was assessed using JADAD and Rob2 to determine the risk of bias. Seven studies published between 2015 and 2025, with a total of 848 participants, were included. The outcome parameters evaluated were blood loss (p= 0.12), use of additional uterotonics (p< 0.001), intensity of uterine tone (p= 1), and hemoglobin (p= 0.351). This systematic review concludes that there are no significant differences between the two drugs for postpartum hemorrhage (PPH) after cesarean section.

Keywords: postpartum hemorrhage, cesarean section, oxytocin, carbetocin, mortality.

RESUMEN

La hemorragia posparto es una de las principales causas de mortalidad materna, especialmente en mujeres sometidas a cesáreas. El objetivo de este estudio fue comparar la eficacia y seguridad de la carbetocina en relación con la oxitocina para la prevención de la hemorragia postparto en mujeres que han tenido una cesárea, mediante una revisión crítica y síntesis de la evidencia disponible. Se realizo una revisión sistemática utilizando las guías prisma. Se buscaron estudios en bases de datos como PubMed, Cochrane Library, Scopus y Embase, que comparen directamente la oxitocina y carbetocina en mujeres con HPP tras una cesárea. Se evaluó la calidad metodológica de los estudios con JADAD y Rob 2 para determinar el riesgo de sesgos. Se incluyeron 7 estudios en el período 2015 al 2025, un total de 848 participantes. Los parámetros de los resultados evaluados fueron pérdida de sangre (p= 0.12), uso de uterotónicos adicionales (p< 0.001), intensidad del tono uterino (P= 1) y hemoglobina (p= 0.351). Esta revisión sistemática concluye, que no existen diferencias significativas entre ambos fármacos para la HPP post cesárea.

Palabras clave: hemorragia posparto, cesárea, oxitocina, carbetocina, mortalidad.

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INTRODUCTION

Postpartum hemorrhage (PPH) is one of the most serious obstetric complications and one of the three leading causes of maternal mortality worldwide, even in settings with advanced medical care (Briones, 2025). It is classically defined as blood loss exceeding 500 ml after a vaginal delivery or more than 1,000 ml after a cesarean section, although this quantification may be underestimated in clinical practice (Castiblanco et al., 2022). Early postpartum hemorrhage occurs during the first 24 hours after birth and is generally the most severe, requiring the most immediate attention (Ortuanya et al., 2024). The most frequent causes of PPH include uterine atony (the most common), birth canal trauma, retained placental products, and coagulation disorders (Anaposala et al., 2023). Although the diagnosis is primarily clinical, most cases of postpartum hemorrhage (PPH) can be prevented by implementing an active and systematic strategy during childbirth, using appropriate pharmacological and non-pharmacological interventions (Nucamendi et al., 2024).

Postpartum hemorrhage is the leading direct cause of maternal mortality and morbidity, responsible for approximately 140,000 deaths annually worldwide. In Latin America, it accounts for more than 30% of direct causes of death, with slightly higher rates in developing or low-income countries (Jin et al., 2019; Delorme et al., 2020; Ibrahim et al., 2020). In Ecuador, according to the National Institute of Statistics and Censuses (INEC), postpartum hemorrhage is the second leading cause of maternal mortality, accounting for 7.87% of deaths (Guillén-Terán & Viracocha-Toapanta, 2025). The Ecuadorian Ministry of Public Health reports maternal deaths weekly in its Epidemiological Gazette of Maternal Mortality. So far in 2025, 17 reports have been issued, documenting a total of 27 deaths. The province of Guayas had the highest number with 9 deaths, followed by Pichincha with 5. Obstetric hemorrhage was the second leading cause of death, accounting for 14.81% of cases (Ministerio de Salud Pública, 2025).

The Ministry of Public Health of Ecuador reports maternal deaths weekly in its Epidemiological Gazette of Maternal Mortality. Carbetocin is an analogue of oxytocin because it has a similar chemical structure, but it differs by the presence of a methyl group instead of a disulfide bond, and cysteine is replaced by a hydrogen bond. These molecular differences allow for longer uterine responses in terms of frequency and amplitude, making carbetocin a long-acting drug and a novel uterotonic agent. This medication commonly presents various adverse effects such as nausea, vomiting, and dysarteriotonia, which are still under investigation (Delgado, 2020).

Carbetocin acts as a selective oxytocin receptor (OTR) agonist. Its mechanism of action is based on binding to the G protein-coupled receptor (GPCR), which activates the phospholipase C (PLC) pathway. This pathway converts phosphatidylinositol 4,5-bisphosphate (PIP2) into inositol triphosphate (IP3) and diacylglycerol (DAG). IP3 stimulates the release of intracellular calcium from sarcoplasmic reticulum deposits, causing uterine smooth muscle contraction and myometrial retraction. This helps compress blood vessels and prevents postpartum hemorrhage (PPH). Additionally, DAG activates protein kinase C (PKC) (Gupta, 2023).

In a multicenter clinical trial involving 23 hospitals in 10 countries, it was reported that intramuscular administration of 100 µg of heat-stable carbetocin resulted in less postpartum blood loss in relation to the prevention of postpartum hemorrhage (PPH). The WHO even recommended the use of carbetocin for PPH prevention in all cases of childbirth, especially when oxytocin is unavailable (Ai et al., 2021).

Oxytocin is a synthetic analogue of the natural hormone. It helps induce or stimulate labor, but is also used to prevent or treat postpartum hemorrhage (PPH) due to uterine atony. It can be administered intravenously or intramuscularly to act on oxytocin receptors in the myometrium, helping to increase the frequency and strength of uterine contractions. It has a rapid onset but a relatively short plasma half-life of less than 5 minutes (Brun et al., 2024).

Oxytocin binds to specific receptors in the myometrium, which are considered G protein-coupled receptors. This binding triggers an intracellular signaling cascade that increases calcium levels in uterine smooth muscle cells, thus generating more effective uterine contractions. During pregnancy, these receptors increase, resulting in more receptors to which oxytocin can bind, thus helping to prevent or treat postpartum hemorrhage (PPH) due to uterine atony (Whitley et al., 2025). The response to intravenous oxytocin is almost instantaneous, and it is rapidly eliminated from the plasma by the liver and kidneys, with only a minimal amount reaching the urine and being excreted unchanged (Li et al., 2022; Albazee et al., 2023).

Oxytocin has proven effective in reducing the incidence of PPH. Its efficacy is based on its ability to increase myometrial contractility, promoting uterine contractions. Although its use is widespread and considered effective, it is considered a medication requiring close monitoring. While there are variations in dosage protocols, its effectiveness in preventing PPH is recognized by multiple studies (Gök & Kaleli, 2023).

The controversy stemmed from marked differences between the drugs, related to their

duration, efficacy, cost, and even storage conditions. Oxytocin is effective and economically viable, but it requires continuous administration or multiple doses, and its storage method necessitates refrigeration. In contrast, carbetocin, being long-acting, facilitates administration with lower doses but with a sustained effect. When administered intravenously, it produces uterine contractions lasting approximately 6 minutes, followed by rhythmic contractions for 60 minutes. When administered intramuscularly, it generates sustained contractions lasting approximately 11 minutes and rhythmic contractions for 120 minutes. Oxytocin, when administered, acts for 3 to 5 minutes, and its plasma half-life is 1 to 6 minutes, thus requiring infusion to maintain its effect. Furthermore, carbetocin offers a significant advantage in distribution and storage, as it does not require refrigeration.

The uterotonics described above have extensive literature, but there is a lack of comprehensive reviews comparing the benefits of both, leaving the true efficacy of each unclear. Given the large network of clinical trials available in medical databases, it is important to compile these into a systematic review to properly clarify the pharmacological choice for medical personnel in terms of stability, efficacy, and storage. Currently, there is limited evidence to support one over the other, leaving uncertainty about whether to prioritize the economic accessibility and well-established efficacy of oxytocin or the stability, better adherence, and longer duration offered by carbetocin. (Tixe et al., 2023; Patil et al., 2024). Therefore, this systematic review aimed to compare the efficacy and safety of carbetocin versus oxytocin for the prevention of postpartum hemorrhage in women who have undergone a cesarean section, through a critical review and synthesis of the current available evidence. The following research question was also posed: Which medication is truly effective in preventing postpartum hemorrhage in patients undergoing a cesarean section?

METHODOLOGY

This article was developed through an analytical research process using a qualitative methodological approach based on a systematic and documentary literature review of the topic. The research began with the PICO method for developing the research protocol for this qualitative synthesis review of randomized controlled trials, following the international guidelines of the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines (Page et al., 2021).

Information sources, inclusion and exclusion criteria: Randomized controlled trials (RCTs) evaluating interventions aimed at preventing postpartum hemorrhage in patients undergoing cesarean section were considered. Studies comparing carbetocin and oxytocin as uterotonic agents in the context of preventing postpartum hemorrhage following cesarean section were included. Articles published in indexed scientific journals and available in recognized databases such as PubMed, Cochrane Library, Scopus, and Embase were considered. Articles published between 2015 and 2025, in English or Spanish, were also included. Publications that did not directly evaluate the prevention of postpartum hemorrhage in the context of cesarean section, or that focused on other causes or types of hemorrhage, were excluded, as were studies lacking comparative data between carbetocin and oxytocin. Articles with unclear or ambiguous methodologies that hindered the interpretation of results, as well as duplicate articles across different databases, were also excluded.

To increase the precision of the search strategy, keywords and descriptors were established beforehand, defined using the DeCS (Health Sciences Descriptors) and MeSH (Medical Subject Headings) thesauri. Subsequently, the terms were combined to obtain the most relevant results in the main scientific databases. The search equations that yielded the best results were: (carbetocin vs. oxytocin) AND (cesarean delivery) AND (postpartum hemorrhage), as well as (carbetocin OR oxytocin) AND (postpartum hemorrhage) AND (cesarean section OR cesarean). These helped to search the databases comprehensively and efficiently.

Titles and abstracts were then reviewed, discarding those that did not meet the research objectives or whose methodology was inadequate. The preselected studies were fully evaluated and subjected to bias analysis, using tools such as the JADAD scale to assess the methodological quality of the trials (De Cassai et al., 2023).

In addition, the revised ROB 2.0 tool, designed by Cochrane and frequently used to assess the risk of bias in randomized controlled trials (Sterne et al., 2019), was included. Its application allowed for a more in-depth calculation of the internal validity of the studies used. Five domains are included: randomization, intervention deviations, missing data, outcome measurement, and selective reporting.

To assess the overall certainty of the evidence, the GRADE approach was used. This tool is useful for classifying results into different levels (high, moderate, low, or very low), facilitating the interpretation of clinical results (Page et al., 2021). Only studies that met the established

methodological standards and provided evidence relevant to the objectives of this review were included.

The JADAD scale was initially used to assess the methodological quality of clinical trials. Subsequently, the revised Cochrane RoB 2 tool for risk of bias was applied independently. This tool evaluates each article across five domains: D1, corresponding to the randomization process; D2, related to intervention deviations; D3, concerning the lack of outcome data; D4, which analyzes bias in outcome measurement; and D5, focused on the selection of reported outcomes. This provides an overall score for each article by ROBS 2 (Sterne et al., 2019).

The certainty of the evidence was assessed using GRADE (Grading of Recommendations Assessment, Development and Evaluation). The results were summarized in an individual table for the selected studies, including primary and secondary outcomes, each with its respective p-value.

RESULTS AND DISCUSSION

The search and selection process for studies was conducted following the PRISMA guidelines, ensuring a systematic, transparent, and reproducible approach. Based on the defined strategy, records were identified in both scientific databases and complementary academic sources. After applying the established eligibility criteria and following a rigorous screening and methodological evaluation process, seven studies were ultimately selected that met the inclusion and quality requirements. These studies form the basis of this systematic review and provide relevant evidence comparing carbetocin and oxytocin in the prevention of postpartum hemorrhage during cesarean sections.

The complete selection process is summarized in the PRISMA flowchart in Figure 1. The PRISMA flow diagram results indicate that, out of 27 initially identified records, 17 were screened for eligibility. Following a detailed assessment, 10 records were excluded for not meeting inclusion criteria (8), being duplicates (2), or having methodological shortcomings such as unclear methodology (7), not focusing on postpartum hemorrhage prevention (8), lacking direct carbetocin-oxytocin comparative data (4), or low JADAD quality scores (2). Consequently, a total of 7 articles were included in the final systematic review or meta-analysis.

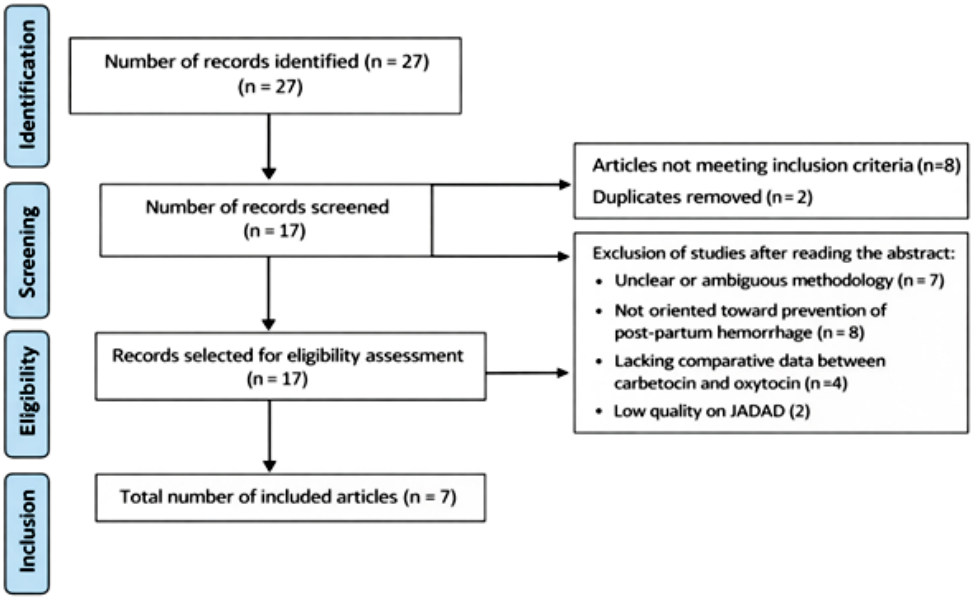

Figure 1. PRISMA flowchart.

Table 1 presents the methodological quality assessment of seven randomized controlled trials comparing the efficacy of carbetocin *versus* oxytocin for postpartum hemorrhage prevention. The overall quality is variable, with one study (Trivedi et al., 2025) demonstrating a low risk of bias across all domains, while three raised some concerns. Two other studies (Fahmy et al., 2016; Al Zubaidi et al., 2022) also received an overall "low risk" rating. However, concerns were identified in several studies, primarily related to blinding of participants and personnel (D2) and selective reporting (D5). Specifically, Mannaerts et al. (2018) and McDonagh et al. (2022) were rated with an overall "some concerns", the latter due to high/unclear risk in random sequence generation, allocation concealment, and selective reporting. All studies demonstrated low risk regarding blinding of outcome assessment (D3) and handling of incomplete outcome data (D4), indicating consistent strength in these areas of trial conduct.

For the JADAD bias assessment, Table 2 indicates the methodological quality evaluation of the clinical trials included in the review. Key aspects of trial design are assessed, such as randomization, blinding, and the description of losses during follow-up, assigning positive or negative scores according to the demonstrated methodological rigor.

Table 1. Methodological quality assessment of the efficacy of carbetocin *vs.* oxytocin in postpartum hemorrhage prevention

Study (Year)	Experimental intervention	Comparison intervention	Primary outcome measured	D1a	D1b	D2	D3	D4	D5	Overall
Fahmy et al. (2016)	Carbetocin (100 µg)	Oxytocin (20 IU)	Blood loss (ml)	+	+	!	+	+	+	+
Mannaerts et al. (2018)	Carbetocin 100 µg IV	Oxytocin 5 IU IV	Comparable blood loss between groups, measured by Hb decrease 48h post-cesarean	+	+	+	+	+	!	!
Al Zubaidi et al. (2022)	Carbetocin 100 mcg IV slow bolus (1 mL) immediately after delivery	Oxytocin 10 IU IV slow bolus (1 mL) immediately after delivery	Use of additional uterotonics within the first 24 hours	+	+	!	+	+	!	+
McDonagh et al. (2022)	Carbetocin 20 µg	Oxytocin 0.5 IU	Uterine tone intensity at 2 minutes assessed by VNRS scale (0–10)	!	!	+	+	+	!	!
Yesmin et al. (2022)	Carbetocin 100 µg IV bolus	Oxytocin 10 IU IV	Incidence of PPH (Postpartum hemorrhage)	+	+	+	+	+	!	!
Turner et al. (2025)	Carbetocin 80 µg IV bolus + placebo infusion	Oxytocin 1 IU IV bolus + 4.8 IU/h infusion	Uterine atony at 3 minutes (VNRS scale 0-10)	+	+	+	+	+	!	+
Trivedi et al. (2025)	Carbetocin 100 mcg IV just after delivery	Oxytocin 10 IU IM at the time of postpartum	Estimated volume of blood loss	+	+	+	+	+	+	+

D1a: Random sequence generation; D1b: Allocation concealment; D2: Blinding of participants and personnel; D3: Blinding of outcome assessment; D4: Incomplete outcome data; D5: Selective reporting; +: Low risk of bias; -: High risk of bias; !: Some concerns / Unclear risk of bias.

Table 2. Bias assessment according to JADAD

Reference	Qualification	JADAD scale						
		Is the study randomized?	Is the study described as double-blind?	Are losses and withdrawals from the study described?	Is the randomization method adequate?	Is the double-blind method appropriate?	Total score	Quality
Fahmy et al. (2016)	Comparative study between the effect of carbetocin and Oxytocin on isoflurane-induced uterine hypotonia in twin pregnancy patients undergoing cesarean section	1	1	0	1	1	4	High quality
Mannaert (2018)	Adverse effects of carbetocin versus oxytocin in the prevention of postpartum haemorrhage after caesarean section: a randomized controlled trial	1	1	1	1	1	5	High quality
Yesmin et al. (2020)	Carbetocin *vs.* oxytocin in the prevention of postpartum haemorrhage after caesarean section	1	1	0	0	1	3	High quality
Al Zubaidi & Alhaidari (2022)	Heat-stable carbetocin *vs.* oxytocin for the prevention of post-partum hemorrhage in emergency caesarean delivery: a randomized controlled trial	1	1	1	1	1	5	High quality
McDonaghe t al. (2022)	Carbetocin *vs.* oxytocin at elective caesarean delivery: a double-blind, randomized, controlled, non-inferiority trial of low- and high-dose regimes	1	1	1	1	1	5	High quality
Ambika et al. (2024)	Carbetocin *vs.* oxytocin in primigravida for active management of the third stage of labor: a prospective study	1	0	0	1	0	2	Low quality

Reference	Qualification	JADAD scale						
		Is the study randomized?	Is the study described as double-blind?	Are losses and withdrawals from the study described?	Is the randomization method adequate?	Is the double-blind method appropriate?	Total score	Quality
Brun et al. (2024)	Intramyometrial and intravenous oxytocin compared to intravenous carbetocin for prevention of postpartum hemorrhage in elective cesarean section—a quasi-randomized controlled phase IV non-inferiority interventional trial	1	0	0	1	-1	1	Low quality
Trivedi et al. (2025)	The role of oxytocin versus carbetocin in prevention of postpartum hemorrhage in caesarean section: a randomized control trial	1	1	0	1	1	4	High quality
Turner et al. (2025)	Oxytocin *vs.* carbetocin at elective caesarean delivery in parturients with class III obesity: a double-blind randomized controlled noninferiority trial	1	1	1	1	1	5	High quality

Table 3 refers to the assessment of the certainty of evidence for the included studies, using the GRADE methodology. This approach analyzes multiple domains that can affect the validity of the results, allowing the overall certainty of each study to be classified as high, moderate, low, or very low.

Table 3. Assessment of the certainty of evidence from studies using the GRADE methodology

Reference	Certainty assessment						Certainty
	Study design	Risk of bias	Inconsistency	Indirect evidence	Printing	Other considerations	
Fahmy et al. (2016)	Randomized trials	Serious	It's not serious	It's not serious	Serious	None	⊕⊕⊕◯ Moderate
Mannaerts et al. (2018)	Randomized trials	It's not serious	It's not serious	It's not serious	Serious	None	⊕⊕⊕◯ Moderate
Al Zubaidi & Alhaidari (2022)	Randomized trials	It's not serious	It's not serious	It's not serious	It's not serious	None	⊕⊕⊕⊕ High
McDonagh et al. (2022)	Randomized trials	It's not serious	It's not serious	It's not serious	It's not serious	None	⊕⊕⊕⊕ High
Yesmin et al. (2020)	Randomized trials	It's not serious	It's not serious	It's not serious	Serious	None	⊕⊕⊕⊕ High
Turner et al. (2025)	Randomized trials	It's not serious	It's not serious	It's not serious	It's not serious	None	⊕⊕⊕⊕ High
Trivedi et al. (2025)	Randomized trials	It's not serious	It's not serious	It's not serious	Serious	None	⊕⊕⊕◯ Moderate

Table 4 presents a summary of individual results, indicating the main findings of the included clinical trials, which focused on evaluating the efficacy of carbetocin versus oxytocin for preventing hemorrhage in cesarean sections. For each study, key methodological aspects are presented, such as design, sample size, and inclusion criteria, along with the interventions used and the findings in terms of primary and secondary outcomes.

The main finding of this review was a reduction in the need for additional uterotonics and in blood loss after cesarean section, thus contributing to a decrease in the incidence of postpartum hemorrhage (PPH) in women who received carbetocin compared to those treated with oxytocin. However, the reduction in blood loss was demonstrated in only one article, while the others found no statistically significant differences.

Table 4. Summary of individual results

Reference	Design, period, and country	Number of participants	Inclusion/exclusion criteria	Intervention	Primary result	Secondary result
Fahmy et al. (2016)	Prospective double-blind controlled RCT. Period: November 2012 to June 2016 Country: Egypt	60 patients 30 patients with carbetocin 30 patients with oxytocin	Inclusion criteria: Twin pregnancy, ASA physical status I, age: 28 to 36 years, general anesthesia, and signed informed consent. Exclusion: Patients with chronic diseases, coagulation disorders, or use of anticoagulants, drug allergies, and preoperative anemia	Carbetocin 100 µg diluted in 10 ml of saline solution. Oxytocin 20 IU diluted also in 10 ml of saline solution	Efficacy of uterine contraction, assessed using a clinical scale (0 = atony, up to 4 = very good contraction) at 2 minutes, p <0.001	Estimated amount of blood loss p <0.001, need to administer additional uterotonics p <0.001, need for blood transfusion p <0.001.
Mannaerts et al. (2018)	Single-center double- blind RCT Period: 2011–2017 Country: Belgium	58 women (Carbetocin: 32; dOxytocin: 26)	Inclusion Women pregnant at term (≥37 weeks), scheduled cesarean section, singleton pregnancy, spinal or combined anesthesia	Carbetocin 100 µg IV in 10 ml NaCl at the end of fetal extraction, followed by an infusion of 1000 ml of crystalloid over 24 h Oxytocin 5 IU IV in 10 ml NaCl at the end of fetal extraction, followed by an infusion of 10 IU in 1000 ml of crystalloid for 24 h	Blood loss was comparable between groups, measured by the decrease in Hb 48 h and Hct after cesarean section: Hb = 1.50 g/ dL in the oxytocin group and 1.45 g/ dL in the carbetocin group, with a p = 0.8 and a p = 0.7, respectively, which were not significant.	The presence of nausea was lower in the carbetocin group (6%) compared to oxytocin (15%), although without statistical significance p = 0.256. The need for vasopressors was similar between both groups: carbetocin 25% (8/32) and oxytocin 23% (6/26), with no significant differences, p = 1.0
Al Zubaidi & Alhaidari (2022)	Single-center, double-blind, non-inferiority RCT Period: January 1 – August 1,	300 participants 100 participants treated with carbetocin	Inclusion criteria: pregnant women aged 18–43 years, singleton pregnancy at term, emergency cesarean section. Exclusion criteria: fibroids, longitudinal uterine incision,	Carbetocin 100 µg IV bolus, 1 mL over 1 min immediately postpartum Oxytocin	The need for additional uterotonics within 24 hours post-surgery was lower in the group using	The need for blood transfusion was lower in the carbetocin group, but this was not statistically significant (p= 0.05). Blood loss was greater in the

Reference	Design, period, and country	Number of participants	Inclusion/exclusion criteria	Intervention	Primary result	Secondary result
	2018 Country: Iraq	200 participants treated with oxytocin	placental pathologies, coagulopathies, allergies, chronic diseases (cardiac, hepatic, renal, endocrine).	10 IU IV bolus followed by 1 mL over 1 min immediately postpartum	carbetocin compared to oxytocin, with an RR of 0.36 and a p= 0.051, so it is not statistically significant.	carbetocin group (13%) compared to oxytocin (10.5%), with an RR: 1.24; but this difference was not statistically significant, CI 95%: 0.65–2.37; p= 0.52.
McDonagh et al. (2022)	RCT, prospective double-blind Period: May 25, 2017 to December 17, 2020. Country: Canada	277 patients 70 women treated with low-dose carbetocin. 69 women treated with high-dose carbetocin 69 women with low-dose oxytocin. 69 women on high-dose oxytocin	Inclusion: Pregnant women from 37 +0 to 40 +6 weeks of gestation undergoing elective cesarean section under spinal anesthesia. Exclusion criteria: Refusal of informed consent; allergy or hypersensitivity to oxytocin or carbetocin; BMI ≥40 kg/m2; conditions that predispose to uterine atony and PPH.	Carbetocin They received 20 µg + IV placebo infusions They received 100 µg + IV placebo infusions Oxytocin They received a low dose of 0.5 IU bolus + infusion of 40 mIU /min They received a high dose of 5 IU bolus + infusion of 40 mIU/min	Intensity of uterine tone on a 0-10 non-restrictive uterine tone scale (NRS), assessed by the obstetrician 2 minutes after completion of the bolus injection of the study drug. p = 1	Use of additional uterotonics in the operating room p= 0.48; adverse effects after injection of the study drug up to 2 hours after delivery p= 0.61; and estimated blood loss p= 0.83.
Yesmin et al. (2020)	ECA and controlled Period: February – July 2015 COUNTRY: Bangladesh	64 pregnant women. 32 women received IV carbetocin, while 32 women received IV oxytocin.	Inclusion: women with term pregnancy undergoing elective or emergency cesarean section under spinal anesthesia and with risk factors for HPP, such as multiple pregnancy. Exclusion: Hypertension, preeclampsia, placenta previa, heart, kidney, or liver disease, allergy to carbetocin or oxytocin	Carbetocin They received a bolus injection of 100 µg by IV oxytocin They received 10 IU IV	Blood loss after cesarean section in both groups was not statistically significant either preoperatively or 12h after cesarean section, p-value: 0.121 and p-value: 0.066, respectively	Regarding the pre- or post-operative hemoglobin level, the difference was not statistically significant between the two groups with a p:0.351 in both periods. Furthermore, the blood transfusion requirements were not statistically significant with p= 0.119.

Reference	Design, period, and country	Number of participants	Inclusion/exclusion criteria	Intervention	Primary result	Secondary result
Turner et al. (2025)	double-blind non-inferiority RCT Period: July 2021-December 2022 Country: Canada	47 participants 23 participants treated with carbetocin 24 participants treated with oxytocin	Inclusion: Pregnant women with BMI ≥ 40 kg/m², elective cesarean section, without labor. Exclusion criteria: Drug allergy, active labor, general anesthesia, pathologies predisposing to postpartum hemorrhage (placenta previa, multiples, preeclampsia, etc.)	Carbetocin 80 µg IV bolus + placebo infusion Oxytocin IV bolus of 1 IU + continuous infusion of 4.8 IU/h	Uterine tone at 3 minutes showed no statistically significant difference between the oxytocin and carbetocin groups, with a p-value = 0.06.	Uterine tone at 5 and 10 minutes showed no significant differences between the groups since there was no difference in the medians; in the need for additional uterotonics, both groups had similar results and were not statistically significant by their p-value=1.
Trivedi et al. (2025)	Single-center double-blind RCT Period: February 8, 2023, to February 8, 2024 Country: India	42 women Intervention Group: 21 Control Group: 21	Inclusion criteria: Full-term, singleton pregnancy, elective or emergency cesarean section, regional anesthesia, no drug allergies Exclusion criteria: Multiple pregnancy, placenta previa, placental abruption, chronic diseases, and thromboembolic disorders	Carbetocin They received 100 µg within one minute of delivery. Oxytocin They received 10 IU IM within one minute of delivery.	The HPP in the participants reported a p of 0.343, which was not statistically significant since there was no difference between the groups.	Blood loss reported a significant p-value of 0.006, indicating a reduction in blood loss with the use of carbetocin. Regarding hemoglobin before and after delivery, there was no significant difference with a p= 0.052 and 0.765, respectively.

Regarding the uterine tone intensity and pre- and postoperative hemoglobin levels, no significant differences were found between the two groups. However, in the latter parameter, carbetocin showed a greater tendency to maintain normal hemoglobin levels, which, although minimal, is highly relevant in the obstetric context. All these findings support the use of carbetocin in cesarean sections as a result of its potential clinical benefits, but interpretation should be cautious due to the limitations of the available studies that make this comparison. Among the main limitations are the small sample size, very narrow confidence intervals, and the heterogeneity of the primary and secondary outcomes.

Primary outcome: blood loss

According to most studies (Mannaerts et al., 2018; Yesmin et al., 2020; Al Zubaidi & Alhaidari, 2022; Turner et al., 2025), no clinically relevant differences were found between carbetocin and oxytocin in terms of reducing blood loss during cesarean section. Although some studies describe slight variations, such as slightly less blood loss with carbetocin or slightly more with oxytocin, these differences do not reach statistical significance and are largely due to methodological factors rather than a direct effect of the drug.

In studies in which oxytocin was administered intravenously as an initial bolus followed by continuous infusion (Turner et al., 2025: 1 IU plus infusion of 4.8 IU/h; Mannaerts et al., 2018: 5 IU plus infusion; McDonagh et al., 2022: 5 IU plus 40 mIU/min), the drug's short plasma half-life was effectively offset by sustained administration. This dosing strategy enabled oxytocin to achieve a pharmacodynamic effect comparable to that of carbetocin, which is characterized by a longer half-life. Consequently, both uterotonic agents demonstrate similar clinical efficacy in reducing intraoperative blood loss during cesarean section.

However, one of the analyzed clinical trials (Trivedi et al., 2025) did find a significant difference between the use of carbetocin and oxytocin ($p = 0.006$), in which carbetocin was administered intravenously (100 µg), while oxytocin was administered intramuscularly (10 IU). The difference in the routes of administration is important because oxytocin administered intramuscularly has a slower onset of action. Consequently, Trivedi et al. (2025) reported that 95.24% of patients treated with carbetocin experienced blood loss of <100 mL, compared to 80.95% of patients in the oxytocin group.

Consistent with the meta-analysis by Kalafat et al. (2021), which included 30 studies, the risk of postpartum hemorrhage after cesarean section was found to be similar between the two

uterotonics (RR: 0.69; 95% CI: 0.45–1.05; p > 0.05), indicating no statistically significant differences.

Secondary results

Use of additional uterotonics

Regarding the need for additional uterotonics in postpartum hemorrhage after cesarean section, the included studies presented conflicting results. McDonagh et al. (2022) reported that 24.6% of patients treated with carbetocin and 15.9% with oxytocin required additional uterotonics. Similarly, Turner et al. (2025) mention that 22% of patients treated with carbetocin and 25% with oxytocin required supplemental uterotonic medication. Both studies show no clinically significant difference between the drugs (Turner et al., 2025). However, the studies by Fahmy et al. (2016) indicate that 13.3% of patients receiving carbetocin and 50% of those receiving oxytocin required additional uterotonic drugs. Likewise, Al Zubaidi & Alhaidari (2022) reported that 7% of those prescribed carbetocin and 19.5% of those prescribed oxytocin requested uterotonic agents (Al Zubaidi & Alhaidari, 2022). This resulted in a significant reduction in the need for additional uterotonics with carbetocin administration. A meta-analysis and systematic review included 17 studies that evaluated additional uterotonics in postpartum hemorrhage (PPH) after cesarean section. The results showed that carbetocin reduces the use of additional uterotonics compared to oxytocin, with an OR of 0.53; CI: 0.39–0.72; I^2: 41%; and Z: 3.99 (p < 0.0001) (Maged et al., 2025).

Intensity of uterine tone or efficacy of uterine contraction

According to McDonagh et al. (2022), there is no significant difference regarding uterine tone, since when administering both high and low doses of carbetocin and oxytocin (20 and 100 µg of carbetocin and 0.5-5 IU of oxytocin) relatively similar values of uterine tone were evident since medians of 7 and 8 points on a scale of 10 were presented, in addition to the fact that there was no need to use additional uterotonics because both drugs generated a good intensity of uterine tone (McDonagh et al., 2022). Furthermore, according to Turner et al. (2025), it agrees with McDonagh et al. (2022), but this study focuses more on women with class 3 obesity, where uterine tone was measured 3 minutes after administering the drugs (carbetocin 80 µg IV or oxytocin 1 IU IV) and in both groups an equal value of 8 points was observed, it was re-evaluated at 5 and 10 minutes and there was no difference, showing that there is very good contractility (Turner et al., 2025). This evidence aligns with the meta-analysis conducted by Gallos et al. (2025), as the study

showed carbetocin to have a similar effect to oxytocin in cases of hemorrhage greater than 500ml and even >1000ml. Furthermore, there is no statistically significant difference between the drugs evaluated (RR = 0.93; 95% CI: 0.81–1.07; p = 0.27). Although the RR suggests a slight decrease in risk, the inclusion of a null value in the CI prevents us from concluding that there is a real superiority. In addition, the heterogeneity was low (I^2 = 17%), demonstrating consistency among the analyzed studies, which increases the reliability of this meta-analysis, reinforcing that the information given regarding the comparable efficacy of both drugs is valid (Gallos et al., 2025). The evidence from these three studies supports the information that, in terms of uterine tone intensity or contraction effectiveness, both carbetocin and oxytocin offer similar benefits; neither drug is superior to the other, regardless of the obstetric context or the patient.

Preoperative and postoperative hemoglobin (Hb) levels

Regarding an important secondary outcome for quantifying the efficacy of uterotonics in postpartum hemorrhage (PPH), the quantification of preoperative and postoperative hemoglobin (Hb) levels is highlighted. These serve as an indirect indicator of blood loss, thus effectively detecting occult PPH. In the studies by Mannaerts et al. (2018), Yesmin et al. (2020), and Trivedi et al. (2025) all three agree that there was no statistically significant difference between the groups treated with carbetocin versus oxytocin. However, it is important to mention that in the two articles mentioned at the beginning, the drop in postoperative Hb compared to baseline showed that the magnitude of Hb loss was greater in the groups that received oxytocin. The drop in hemoglobin in patients treated with carbetocin was 6.84% in the first study and 4.67% in the second, while those who received oxytocin had a decrease of 11.54% and 8.26%, respectively. The meta-analysis by El-Goly et al. (2025), which included eight articles analyzing hemoglobin levels, revealed that patients using carbetocin were associated with less postoperative hemoglobin loss compared to those using oxytocin, demonstrating its greater usefulness in preventing occult postoperative hemorrhage (PPH). The mean difference was 0.37, with a confidence interval of 0.04 to 0.71 and a z-value of 2.22 (P=0.03). This differs from the articles presented in the review, which consider that pre- and postoperative hemoglobin levels were not statistically significant between the groups. Following the analysis of the articles that present hemoglobin (Hb) quantification as an indicator of occult postpartum hemorrhage (PPH), it is noteworthy that the use of carbetocin tends to have a favorable response. Although the reduction in Hb is minimal in the maternal context, these small differences are highly relevant because maintaining values closer to normal helps prevent

complications such as PPH and the risk of anemia. These benefits occur because carbetocin has a greater affinity for peripheral myometrial receptors, thus producing an effect eight times longer lasting than oxytocin, causing rhythmic and prolonged contractions and thereby reducing blood loss.

Regarding the overall evaluation of primary and secondary outcomes, it can be observed that women treated with carbetocin showed a slight decrease in the need for additional uterotonics, post-cesarean blood loss, and a slight reduction in postoperative Hb compared to those who received oxytocin. These benefits of carbetocin are related to its longer half-life of approximately 40 minutes, compared to oxytocin's 1 to 6 minutes. This allows for more effective and prolonged uterine contractions, leading to a decrease in the incidence of postpartum hemorrhage (PPH). Furthermore, it is important to consider the advantages of transporting and storing carbetocin in resource-limited countries that are more prone to healthcare system crises. Unlike oxytocin, carbetocin may not require refrigeration for storage and distribution in vulnerable healthcare systems or those with limited infrastructure. For these reasons, future research must expand its sample sizes to inform significant changes in protocols for pregnant women worldwide, ultimately aiming to reduce maternal morbidity and mortality.

CONCLUSIONS

Based on the review of the seven included and analyzed clinical trials, it was observed that carbetocin and oxytocin function quite similarly when it comes to preventing postpartum hemorrhage in cesarean sections; the studies show no clear differences in the amount of bleeding, the decrease in hemoglobin, or the need for additional uterotonics. Despite this, some studies do mention that carbetocin offers a certain advantage over oxytocin, as it reduces the need for additional medication and is associated with less variation in postoperative hemoglobin. Although both medications are valid, the final decision depends on several practical aspects that will allow for choosing the optimal drug, such as its duration of action, stability, and what each healthcare system is able to provide. Furthermore, it is important to mention that the reviewed studies do have certain limitations, such as: most of the research uses small sample sizes, there are differences in methodological design, and not all use the same criteria for measuring blood loss.

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CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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