

***Carbetocin versus oxytocin for the prevention  
of atonic postpartum hemorrhage after  
repeated elective cesarean sections.***

Thesis

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and Gynecology.*

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## **Abstract:**

**Objective:** to compare the effect of carbetocin versus oxytocin in prevention of postpartum hemorrhage after repeated elective cesarean section.

**Study design:** randomized controlled prospective study on 50 women were going to do repeated elective cesarean section after 38 weeks. They were randomized to receive 100 microgram of carbetocin and 5 units of oxytocin followed by 20-40 units of IV oxytocin infusion. The primary outcomes were to compare the occurrence of major obstetric hemorrhage and need for uterine massage and additional uterotonic agents. Secondary outcomes included estimated mean operative loss, objective changes in hemoglobin and hematocrit, preoperative and postoperative blood pressure and pulse, severe anemia and need for blood transfusion.

**Results:** patients received carbetocin developed less postpartum hemorrhage, required less intervention with less mean operative blood loss than oxytocin, with nearly similar safety profile

**Conclusion:** Carbetocin seems to be more effective in maintaining adequate uterine tone and preventing excessive blood loss in patients undergoing repeated elective cesarean section. Carbetocin was well tolerated with nearly similar safety profile to oxytocin.

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

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# ABBREVIATIONS

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<b>ASA</b>	American Society of Anesthesiology
<b>ACOG</b>	American College of Obstetricians and Gynecologists
<b>AMTSL</b>	Active Management of Third Stage of Labor
<b>APH</b>	Antepartum Hemorrhage
<b>BCSH</b>	British Committee for Standards in Hematology
<b>BP</b>	Blood pressure
<b>CCT</b>	Controlled Cord Traction
<b>C<sub>max</sub></b>	maximum Concentration
<b>CS</b>	Cesarean Section
<b>CTG</b>	Cardiotocography
<b>DAG</b>	Diacylglycerol
<b>DIC</b>	Disseminated Intravascular Coagulopathy
<b>DVT/ PE</b>	Deep Vein Thrombosis/Pulmonary Embolism
<b>ED<sub>95</sub></b>	The effective dose of a therapeutic agent that eradicates 95% of the target pathogen
<b>FDA</b>	Food and Drug Administration
<b>FFP</b>	Fresh Frozen Plasma
<b>FIGO</b>	International Federation Of Gynecologists and Obstetricians
<b>IM</b>	Intramuscular
<b>IP<sub>3</sub></b>	inositol tri-phosphate
<b>ITP</b>	Idiopathic Thrombocytopenic Purpura
<b>IV</b>	Intravenous
<b>MRSA</b>	Methicillin-resistant Staphylococcus epidermidis
<b>mg</b>	Milligram
<b>mL</b>	milliliter

<b>NASG</b>	Non –pneumatic antishock garment
<b>NO</b>	Nitric Oxide
<b>PET</b>	Preeclampsia Toxaemia
<b>PPH</b>	Postpartum Hemorrhage
<b>RCOG</b>	Royal College of Obstetricians and Gynecologists
<b>RIA</b>	Radioimmunoassay
<b>SAE</b>	Selective Arterial Embolization
<b>SOGC</b>	Society of Obstetricians and Gynecologists of Canada
<b>IU</b>	International Unit
<b>UTI</b>	Urinary tract infection
<b>UK</b>	United Kingdom
<b>USA</b>	United States of America
<b>VBAC</b>	Vaginal Birth After Cesarean
<b>VWD</b>	von Willebrand's Disease
<b>WHO</b>	World Health Organization

## *Introduction*

Postpartum hemorrhage (PPH) is defined as a blood loss more than 500 ml and serious PPH as a blood loss more than 1,000 ml. PPH is a serious condition remaining the single main cause of maternal morbidity and mortality (*Su et al., 2012*).

Postpartum hemorrhage (PPH) accounts for nearly one-quarter of all maternal deaths worldwide (*Moertl et al., 2011*). And was the second most frequent cause of maternal death in the UK for the 2000–2002 trienniums (*Higgins et al., 2011*).

The most frequent cause of PPH is uterine atony, contributing up to 80 % of the PPH cases. Although two-thirds of the PPH cases occur in women without predisposing factors, there are several risk factors for PPH such as previous PPH, preeclampsia, coagulopathy, multiple gestation and ante partum hemorrhage. Also cesarean section (CS) is a recognized risk factor for PPH and its prevalence is increasing (*Moertl et al., 2011*).

The administration of oxytocics after the delivery of the neonate reduces the likelihood of PPH (*Hummel et al., 2010*). and 5 IU oxytocin by slow intravenous injection is currently recommended in the UK for all cesarean sections (*Attilakos et al., 2010*). However, the use of additional oxytocic medication is common (*WHO, 2009*) to arrest bleeding, or prophylactically if there are risk factors for PPH (*Tharakan and Jha, 2008*).

Oxytocin is currently the uterotonic of first choice. It has proven to decrease the incidence of PPH by 40 % and has a rapid onset of action and a good safety profile (*Winter et al., 2007*).

A disadvantage of oxytocin is its short half life of 4–10 min, regularly requiring a continuous intravenous infusion or repeated intramuscular injections (*Dansereau et al., 1999*).

Carbetocin (Pabal) is a long-acting oxytocin analogue indicated for the prevention of uterine atony after child birth by CS under epidural or spinal anesthesia. Carbetocin has a rapid onset of action (within 1–2 min) and a prolonged duration of action (approximately 1 h) because of sustained uterine response with contractions of higher amplitude and frequency. Its safety profile is comparable to that of oxytocin (*Moertl et al., 2011*).

The current pharmacological policy for the prevention of PPH is oxytocin. Most hospitals use a bolus of oxytocin 5 or 10 IU; some add an infusion of oxytocin for a couple of hours.

## *Aim of the Work*

The aim of the study is to compare the prophylactic effects of carbetocin with those of oxytocin in the prevention of uterine atony in patients undergoing repeated elective CS under spinal anesthesia.

## *Planned Elective Repeat Cesarean Section*

### **Definition:**

It is a scheduled timing for a fetus birth by making an incision in the abdominal wall (laparotomy) and the uterine wall (hysterotomy)(*Tita et al., 2009*).

### **Description of the condition:**

The rate of cesarean section in high-income countries is increasing, accounting for 23.7% of all births in the United Kingdom, 26% in Ireland (*Dat a, 2011*), and 32.8% in the United States (*Hamilton BE, 2012*). Reported rates from South America are higher, reaching over 50% in private hospitals in Chile, Argentina, Brazil and Paraguay (*Belizan et al., 1999*). Suggested reasons for the high proportion of cesarean births over the last few decades have included medico legal issues, the increasing use of electronic fetal heart rate monitoring, and reduced training in operative vaginal and vaginal breech births. Repeat cesarean section is the most common primary obstetric indication for repeat cesarean in the United States ~48%.(*Benson&Pernoll, 2015*).

Concerns about the increasing cesarean section rate resulted in a consensus statement by the American College of Obstetricians and Gynecologists, that “most women with one previous cesarean delivery with a low-transverse incision are candidates for and should be counseled about Vaginal birth after cesarean (VBAC)”(*Cheng et al., 2011*). However, there is considerable variation in both the proportion of women attempting labour after cesarean birth (28% to 82%), as well as reported success rates (49% to 87%)(*Guise JM, 2010*).

### **Indications for elective Cesarean Delivery(*Liu et al., 2007; Zanardo et al., 2010; Barber et al., 2011.*)**

- 1- Placenta praevia with no active bleeding.
- 2- Malpresentation.
- 3- Previous cesarean delivery: for patients who are not candidates for trial of labor e.g previous two sections or pervious classical cesarean section, hysterectomy and vertical incision C.S.
- 4- Past history of repair of vesico-vaginal or recto-vaginal fistula or stress incontinence.
- 5- Twins or more children.
- 6- Invasive cervical carcinoma.

### **Description of the intervention:**

For a woman with a previous cesarean birth, the decision regarding planned mode of birth in a subsequent pregnancy will be influenced by many factors, including previous experience of a vaginal birth, desire to achieve a vaginal birth, feelings about the previous cesarean birth, and family considerations (including an easier recovery). There are benefits and harms associated with both repeat elective cesarean and vaginal birth (*Zanardo et al., 2010*).

Repeat elective cesarean birth is associated with an increase in the risk of complications such as:

- 1- Bleeding.
- 2- The need for blood transfusion.
- 3- Infection.
- 4- Damage to the bladder and bowel.
- 5- Deep venous thrombosis.