Carbetocin in Reducing Blood Loss during and after Cesarean Section

Thesis

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By

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Sherouk Osama El Attar

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List of Abbreviations

Abbr.	Full-term
ACOG	: American College of Obstetricians and Gynecologists
CBC	: Complete blood count
CT	: Computed tomography
DIC	: Disseminated intravascular coagulation
EDD	: Expected delivery date
FAST	: Focused assessment with sonography in trauma
FDA	: Food and Drug Administration
FFP	: Fresh frozen plasma
Hb	: Hemoglobin
IM	: Intramuscular
ITP	: Idiopathic thrombocytopenic purpura
IV	: Intravenous
LFTs	: Liver function tests
LMP	: Last menstrual period
MRI	: Magnetic resonance imaging
NSAID	: Non-steroidal anti-inflammatory drug
OCT	: Oxytocin challenge test
OXY	: Oxytocin
PPH	: Postpartum hemorrhage
PRBCs	: Packed red blood cells
PT	: Prothrombin time

PTT : Partial thromboplastin time

SD : Standard deviation

SOGC : Society of Obstetricians and Gynaecologists of Canada

SPSS : Statistical package for social science

U/S : Ultrasonography

UK : United Kingdom

USAID : United States Agency for International Development

WHO : World Health Organization

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Abstract

Background: Postpartum hemorrhage (PPH) is defined as blood loss more than 500 ml in vaginal delivery and 1,000 ml during cesarean section. PPH is a serious condition remaining the single main cause of maternal morbidity and mortality. **Aim of the Work:** This study aims to compare the efficacy of carbetocin with that of oxytocin in reducing blood loss in women undergoing C.S. **Patients and Methods:** This randomized controlled trial was conducted at Ain Shams University maternity Hospital on 80 women with age group 20-35 years old undergoing elective or emergency cesarean section after 37 weeks of gestation either primigravida or multigravida. **Results:** The estimated blood loss was lower in carbetocin group compared to the oxytocin group; this result was with statistically significant; also the study revealed less intervention in the form of uterine massage and less additional uterotonic agents in carbetocin group than those in the oxytocin group also this different was statistically non-significant. **Conclusion:** Carbetocin seems to be more effective than oxytocin in decreasing blood loss and incidence of post partum hemorrhage, though statistically insignificant. **Recommendations:** Many studies are recommended on large population to report the incidence of adverse effects, the effect of carbetocin on the hemodynamic states, blood pressure, cardiovascular disease risk, and major PPH should be assessed to evaluate if the efficiency and benefits of carbetocin exceeds its cost.

Key words: carbetocin, blood loss, cesarean section, women

Introduction

Postpartum hemorrhage is potentially life threatening and is a significant contributor to maternal mortality and morbidity worldwide, so prevention of postpartum hemorrhage is therefore of great importance in the pursuit of improved health care for women ***(Khan et al., 2006).***

Postpartum hemorrhage is defined as loss of greater than 500ml of blood following vaginal delivery or 1000 ml of blood following cesarean section, it is more likely to occur while placenta is separating or soon after ***(Leduc et al., 2010).***

The incidence of postpartum hemorrhage varies widely, depending upon criteria used to define the disorder, reasonable estimate is 1 to 5 percent of deliveries. It is associated with nearly one quarter of all maternal deaths globally ***(Carroli et al., 2008).***

Postpartum hemorrhage has many potential causes, but the most common, by a wide margin is uterine atony ***(Anderson and Etches, 2007).***

Risk factors of postpartum hemorrhage include:

- Postpartum hemorrhage in a previous pregnancy
- Retained placenta
- Failure to progress during the second stage of labor
- Placenta accreta

- Lacerations
- Instrumental delivery
- Large for gestational age newborn
- Hypertensive disorders
- Induction of labor
- Augmentation of labor with oxytocin

(Sheiner et al., 2005).

High-quality evidence suggests that active management of the third stage of labor reduces the incidence and severity of postpartum hemorrhage ***(Adegbola et al., 2009).***

Oxytocin is the most widely used uterotonic agent used for enhancing uterine contraction after delivery, it is routinely administered after delivery to initiate and maintain adequate uterine contractility after placenta! delivery, It has only a half-life of 4-10 minutes and must be administered as a continuous IV infusion to achieve sustained uterotonic activity, however adverse hemodynamic effects are known to occur after i.v oxytocin, notably tachycardia, hypotension and ECG changes (***Butwick et al., 2010).***

Among the agents that have been studied, oxytocin agonist carbetocin appears to be the most promising for this indication ***(Chong, 2003).***

Several data of literature suggest that prophylactic administration of carbetocin may be a good alternative to oxytocin to prevent postpartum hemorrhage ***(Attilakos et al., 2010).***

Carbetocin is a long-acting synthetic octapeptide analogue of oxytocin (l-deamino-l-monocarbo-(2-O-Methyl-tyrosine) with agonist properties firstly described in 1987,It has a half-life of 40 minutes (around 4-10 times longer than oxytocin) and uterine contractions occur in less than two minutes after intravenous administration of optimal dosage of 100 (µg) ***(Carroli et al., 2012).***

Carbetocin has been approved for use immediately following an elective Cesarean section when a local or spinal anesthesia has been administered, Since the uterus cannot contract on its own during cesarean section, exogenous administration of oxytocin or an analog is necessary to restore uterine tone and prevent hemorrhage ***(Moertl et al., 2011).***

In pharmacokinetic studies, intravenous injections of carbetocin produces tetanic uterine contractions within 2 minutes lasting 6 minutes, followed by rhythmic contractions for a further hour, while intramuscular injection produces tetanic contractions within 2 minutes, lasting about 11 minutes, and followed by rhythmic contractions for an additional 2 hours, so the prolonged duration of activity after

intramuscular compared with the intravenous carbetocin injection was significant ***(Hunter et al., 1992).***

A single dose of carbetocin has been hypothized to act as a 16 hours intravenous oxytocin infusion regarding the increase in uterine tone and the reduction of the risk of PPH in elective cesarean section ***(Boucher et al., 1998).***

It must be administered only after delivery of the infant by cesarean section and should be given as soon as possible after delivery preferably before removal of the placenta, no further doses of carbetocin should be administered ***(Attilakos et al., 2010).***

Ten to forty percent of patients receiving carbetocin will experience nausea, vomiting, abdominal pain, itching skin, increased body temperature, trembling and weakness. One to five percent of patients may experience back and chest pain, dizziness, anemia, chills and sweating, metallic taste, tachycardia and respiratory distress ***(Attilakos et al., 2010).***

Aim of the Work

This study aims to compare the efficacy of carbetocin with that of oxytocin in reducing blood loss in women undergoing C.S.

Chapter 1
Postpartum Hemorrhage

The third stage of labor refers to the period following the completed delivery of the newborn until the completed delivery of the placenta. The third stage of labor is potentially the most dangerous part for the mother, and active management is necessary in high risk patient ***(Su et al., 2012).***

DEFINITION:

Postpartum hemorrhage is traditionally defined as blood loss greater than 500 ml during a vaginal delivery or greater than 1000 ml with a cesarean delivery. Significant blood loss can be well tolerated by most young healthy women ***(Begley et al., 2010).***

INCIDENCE AND PREVALENCE:

Globally, postpartum hemorrhage is the leading cause of maternal mortality. The condition is responsible for 25% of delivery-associated deaths, postpartum hemorrhage is the second leading single cause of maternal mortality, ranking behind preeclampsia/eclampsia ***(World Health Organization, 2008).***

The prevalence of PPH and severe PPH was estimated approximately 6% of all deliveries, with a wide variation across regions of the world. The majority of maternal deaths