Hemodynamic Changes in Women with Severe Preeclampsia Following Administration of Carbetocin, Oxytocin or Misoprostol for Prevention of Atonic Postpartum Hemorrhage during Cesarean Section

"A Randomized Controlled Trial"

Thesis

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By

Aya Osama Abd El Galil
(M.B.B.CH) Cairo University (2009)
Ob/ GYN Registrar at Boulak El-dakror general hospital

Supervised by

Prof. Dr. Hisham Fathi
Professor of Obstetrics & Gynecology
Faculty of Medicine – Ain Shams University

Prof. Dr. Ihab Fouad Serag El Din Allam
Prof. of Obstetrics & Gynecology
Faculty of Medicine – Ain Shams University

Ass.Prof. Dr. Sherif Ashoush
Ass.Prof. of Obstetrics & Gynecology
Faculty of Medicine – Ain Shams University

Faculty of Medicine
Ain Shams University
2015

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List of Abbreviations

Abbrev.	Full term
ACOG	: American College of Obstetricians and Gynecologists
AFLP	: Acute fatty liver of pregnancy (AFLP)
AHFS	: American Hospital Formulary Service
C.S	: Cesarean section
FIGO	: International Federation of Gynecologists and Obstetricians
HUS	: Hemolytic uremic syndrome
ICM	: International Confederation of Midwives
LDH	: Lactate dehydrogenase
NICE	: National Institute for Health and Care Excellence
NSAID	: Non-steroidal anti-inflammatory drugs (NSAID)
OTR	: Oxytocin receptor
PPH	: Postpartum hemorrhage
SD	: Standard deviation
SLE	: Systemic lupus erythematosus
TTP	: Thrombotic thrombocytopenic purpura
WHO	: World Health Organization

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Introduction

Postpartum hemorrhage is defined as blood loss of 500 ml or more and severe postpartum hemorrhage as 1000 or more in third stage of labor ***(Begley et al., 2010).***

Postpartum hemorrhage is a potentially life threatening complication and is one of the major contributors to maternal mortality and morbidity worldwide. Maternal death often occurs within a short period of time due to irreversible shock. The effects of maternal morbidity include anemia, fatigue and depression ***(Lewis et al., 2004).***

Active management of the third stage of labor has been proven to be effective in the prevention of postpartum hemorrhage. It includes using uterotonic drugs, early cord clamping and controlled cord traction ***(Begley et al., 2010).***

The most widely used uterotonic agents include oxytocin, oxytocin has only a half life of 4-10 minutes and must be administrated as continuous intravenous infusion to achieve sustained uterine activity. It has some side effects like nausea, vomiting and hypertension, hence, the need to look for another uterotonic agents ***(Begley et al., 2010).***

Promising results have been published recently with the use of misoprostol for prevention of postpartum hemorrhage,

Misoprostol is a prostaglandin E1 analogue can be given orally, rectally, vaginally or sublingually and has along half life, stable at room temperature, thus opinion articles, guidelines and studies have been published support the widespread distribution of misoprostol at the community level for prevention of postpartum hemorrhage ***(Diadhiou et al., 2011).***

Recent interest has been focused on prophylactic use of Oxytocin receptor agonist (Carbetocin) for prevention of postpartum hemorrhage ***(Leduc et al., 2009).***

Carbetocin is along acting synthetic analogue of Oxytocin, oxytocin analogues are group of drugs that mimic the activity of oxytocin by binding to oxytocin receptor on myometrial cells, oxytocin is a natural hormone acting to decrease postpartum blood loss ***(Leduc et al., 2009).***

One of the recommendations from the society of obestetricians and gynecologists of Canada for postpartum hemorrhage prevention is that carbetocin 100 µg given as intravenous infusion over one minute, should be used instead of continuous oxytocin infusion in elective cesarian section. For prevention of postpartum hemorrhage and decrease need for uterotonic agents ***(Leduc et al., 2009).***

Carbetocin can be administrated either intravenously or intramuscularly, intravenously administrated carbetocin has a

half life of 40 minutes, around 4-10 times longer than reported for oxytocin ***(Rath, 2009).***

Adverse events reported by at least 10% of women who received prophylactic intravenous carbetocin following C.S. where headache, tremors, hypotension, flushing, nausea, abdominal pain, itching and feeling of warmth ***(Rath, 2009).***

Oral and rectal administration of misoprostol, a synthetic analogue of misoprostol E1, have demonstrated lower efficacy than injectable uterotonic agents in preventing excessive bleeding due to its thermal effect and the difficult mode of administration ***(Joy et al., 2003).***

It was found that postpartum bleeding (more than 500ml) is 1.6 times more common in preeclampsia than normotensive women.

Eskild and Vatten showed that the incidence of severe postpartum bleeding (more than 1500ml) was two times more common in women with preeclampsia than in normotensive women ***(Eskild et al., 2009).***

It is not clear whether this increased risk is secondary to presence of angiogenic factors in maternal circulation or impaired uterine contractility due to the use of magnesium sulfate or increased risk of antepartum hemorrahge (placental abruption) ***(Levien et al., 2004).***

Any bleeding in preeclamptic patients is complicated by their altered hemodynamic status, as they don't have the expected expansion volume of normal pregnancy and will show symptoms earlier than normal patients. Also, patients with severe preeclampsia have hypoproteinemia and hypoalbuminemia, so the use of intra-venous crystalloids can trigger pulmonary and cerebral edema ***(Khan et al., 2006).***

Aim of the Work

The aim is to compare the hemodynamic changes following administration of oxytocin, carbetocin and misoprostol for the routine prevention of atonic postpartum hemorrhage in patients with severe preeclampsia undergoing cesarean section.

Chapter (1)
Postpartum Hemorrhage

Postpartum hemorrhage is an obstetrical emergency which follow vaginal or cesarean delivery. It is one of the top three causes of maternal mortality. Furthermore, hemorrhage is the most preventable cause of maternal mortality ***(Mousa et al., 2003).*** It is the second leading cause of maternal mortality after preeclampsia/eclampsia ***(Kochanek et al., 2007)***.

Incidence

Postpartum hemorrhage (PPH) is the leading cause of maternal mortality. The condition is responsible for 25% of cases of peripartum mortality, and this figure is as high as 60% in some countries ***(WHO, 2008)***. It accounts for only 8% of maternal deaths in developed countries. The World Health Organization (WHO) estimates that 20 million morbidities every year result from postpartum hemorrhage ***(WHO, 2009).***

Definition

PPH is defined as excessive bleeding that makes the patient symptomatic. The most common definition of PPH uses estimated blood loss ≥500 mL after vaginal birth or ≥1000 mL after cesarean delivery ***(Andolina et al., 1999)***. Another classic definition of PPH is a 10 % decline in postpartum hemoglobin concentration from antepartum levels ***(Stafford et al., 2008)***.

Classification

PPH is primary or secondary. Primary PPH occurs within 24 hours after delivery (also called early PPH). Secondary PPH occurs 24 hours to 12 weeks after delivery (also called late PPH). Most cases of postpartum hemorrhage,greater than 99%, are early postpartum hemorrhage ***(Murphy et al., 2007*)**.

Risk factors

The risk factors of PPH are classified into antenatal risk factors and intrapartum risk factors. The antenatal risk factors are abruptio placenta, placenta previa, multible pregnancy, pre-eclampsia, previous PPH, Asian ethnicity, obesity (BMI more than 35), pre-eclampsia, and anemia (less than 9g/dl) (maternal mortality is four times higher in severely anemic women than in those who are not anemic) ***(Brabin et al., 2003)***.

The intrapartum risk factors are retained placenta, mediolateral episiotomy, operative vaginal delivery, prolonged labour, big baby (more than 4kg), pyrexia in labour, age (more than 40) (not multiparity), delivery by cesarean section and induction of labour ***(Sheiner et al., 2005).***

Etiology

A- <u>Atony</u>

Uterine atony is the most common cause of PPH, which complicates one in twenty births and is responsible for at least 80% of cases of PPH. It may have many causes including retained placental fragments. It is associated with prolonged labor, multiple pregnancies, polyhydraminos,