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Postpartum rectal Misoprostol in addition to intra-operative IV Oxytocin Vs Intra-operative IV Oxytocin alone to reduce intra-operative & post-operative blood loss

Thesis *Submitted for partial fulfillment of Master Degree (M.sc) in Obstetrics and Gynecology.*

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Abbreviations

ACOG	American College of Obstetricians and Gynecologists
AFE	Amniotic fluid embolism
AMTSL	Active Management of Third Stage of Labor
APH	AntePartum Hemorrhage
AUC0-∞	Antibiotics Area under the concentration time-curves from time zero to infinity
BP	Blood pressure
CCT	Controlled Cord Traction
Cmax	maximum Concentration
CS	Cesarean Section
CTG	Cardiotocography
DAG	Diacylglycerol
DIC	Disseminated Intravascular Coagulopathy
DVT/ PE	Deep Vein Thrombosis/Pulmonary Embolism
ED90	The dose of a therapeutic agent that eradicates 90% of the target pathogen
FDA	Food and Drug Administration
FFP	Fresh Frozen Plasma
HCV	Hepatitis C Virus
HELLP	Hemolysis, Elevated Liver enzymes, Low Platelets
HIV	Human Immunodeficiency Virus
HPLC	High performance liquid chromatography
IM	Intramuscular
IP3	inositol tri-phosphate
ITP	Idiopathic Thrombocytopenic Purpura
IUD	Intrauterine death

IV	Intravenous
MAP	Mean arterial pressure
mg	Milligram
mL	milliliter
NO	Nitric Oxide
NSAIDs	Non Steroidal Anti-Inflammatory Drugs
PET	Preeclampsia Toxaemia
PGE1	Prostaglandins E1
PGE2	Prostaglandins E2
PGF2α	Prostaglandins F2 α
PPH	Postpartum Hemorrhage
RCOG	Royal College of Obstetricians and Gynecologists
RIA	Radioimmunoassay
SAE	Selective Arterial Embolization
SOGC	Society of Obstetricians and Gynecologists of Canada
SROM	Spontaneous Rupture Of Membranes
TOP	Termination of pregnancy
UI	Urinary incontinence
UK	United Kingdom
USA	United States of America
VBAC	Vaginal Birth After Cesarean
vWD	von Wilebrand's Disease
WCC	White Cell Count
WHO	World Health Organization

Abstract

Objective: The current study is designed to compare the efficacy of post-partum rectal misoprostol in addition to intra-operative IV oxytocin to intra-operative IV oxytocin alone during cesarean delivery to reduce intra-operative and post-operative blood loss.

Study design: This is an interventional prospective controlled study assessing the use of postpartum rectal misoprostol in addition to intraoperative IV oxytocin during cesarean delivery to reduce intra-operative and postoperative blood loss in comparison with routinely used intra operative intravenous oxytocin injection alone. The Study is composed of 150 women undergoing elective or emergency cesarean delivery under general or spinal anaesthesia, subjects included in the study will be randomized into 2 groups:

•First group (75 women): will receive post-partum misoprostol 800 ug, administered rectally in addition to intra-operative 5 IU of IV Oxytocin.

•Second group (75 women): will receive intra-operative 5 IU of Oxytocin after the delivery of the neonate as slow IV dose.

Results: In our study, differences in the age, parity and gestational age were statistically insignificant among the two groups. In our study, 32 % among the first group patients needed further uterotonic agents compared to 26 % of the patients in the other group, also 14.7 % out of the first group needed blood transfusion, compared to 12 % of the second group, which is statistically insignificant. According to our study, no statistical significance was found between IV Oxytocin alone and post-operative rectal misoprostol in addition to Intra-operative IV Oxytocin in the estimated mean operative blood loss, hemoglobin and hematocrit values preoperatively and postoperatively and pulse and mean arterial pressure measured both pre-operatively & post-operatively.

Conclusion: To date Oxytocin is the drug of choice in the management of the third stage of labour.

Keywords: Misoprostol, Oxytocin, postpartum hemorrhage.

Abstract

Introduction

Postpartum hemorrhage (PPH) is the leading cause of maternal death worldwide, with an estimated mortality rate of 140 000 women per year, or 1 maternal death every 4 minutes **(Leduc et al.,2009)**.

PPH occurs in 5% of all deliveries and is responsible for a major part of maternal mortality (**Reynders et al.,2006).**

The majority of these deaths occur within 4 hours of delivery, which indicates that they are a consequence of the third stage of labour **(Ramanathan et al.,2006).** Non fatal PPH results in further interventions, iron deficiency anemia, pituitary infarction (Sheehan's syndrome) with associated poor lactation, exposure to blood products, coagulopathy, and organ damage with associated hypotension and shock **(Leduc et al.,2009).**

Since all parturient women are at risk for PPH, care providers need to possess the knowledge and skills to practice active management of the third stage of labour, to prevent PPH and to recognize, assess, and treat excessive blood loss **(Leduc et al.,2009).** Caesarean section is a recognized risk factor for PPH and the worldwide caesarean delivery rate is increasing **(viler et al.,2006).**

Systematic reviews have concluded that active management of third stage of labour, particularly the prophylactic use of uterotonic agents can significantly decrease the incidence of postpartum haemorrhage compared with that of expectant management. An ideal uterotonic agent should promote prompt, strong and sustained uterine contractions after intramuscular (IM) injection without any significant adverse effects **(Leung et al.,2006).**

The administration of oxytocics after the delivery of the neonate reduces the likelihood of PPH and 5 IU oxytocin by slow intravenous injection is currently recommended for all caesarean sections**(NICE, 2007).** However, the use of additional oxytocic medication is common **(Wedisinghe et al.,2008)**, to arrest bleeding, or prophylactically if there are risk factors for PPH.

Carbetocin is a synthetic analogue of human oxytocin with structural modifications that increase its half life thereby prolonging its pharmacological effects. Two double- blind randomised trials compared 100 microgramg carbetocin (the licensed dose) with different combinations of oxytocin, bolus and infusion, following caesarean section. The first trial found that significantly more women needed additional oxytocic interventions in the oxytocin group. The second trial found no significant differences in the intraoperative blood loss **(Leduc et al.,2009)**.

Misoprostol is a synthetic prostaglandin E1 analogue that has been found to be as effective as dinoprostone and oxytocin in inducing labor and as a uterotonic agent **(Elhassan et al.,2007)** .

Aim of work

1- To compare the efficacy of post-partum rectal misoprostol in addition to intra-operative IV oxytocin to intra-operative IV oxytocin alone during cesarean delivery to reduce intra-operative and post-operative blood loss.

2- Subsequent need of additional uterotonic drugs.

3- To document safety and evaluate adverse events recorded during the study either maternal or fetal.

Chapter 1

Management of third stage of labor

The third stage of labor is the stage of separation and expulsion of the placenta **(Cunningham et al., 2010).** It is perhaps the most dangerous part of labor for the mother, the main danger is post partum hemorrhage (PPH) **(McDonald et al., 1993).**

Primary PPH is one of the top five causes of maternal mortality in both developed and developing countries found that the most important risk factors for severe PPH were related to an abnormal third stage of labor. The most common abnormalities being third stage more than or equals 30 minutes and retained placenta **(Mousa and Alfirevic, 2007).**

A recently published study concluded that a third stage longer than 18 minutes is associated with a significant risk of PPH. After 30 minutes ,the odds of having PPH are 6 times higher than before 30 minutes **(Magann and Lanneau, 2005).**

Several complications encountered in the third stage of labor may lead to maternal morbidity. PPH may cause anemia or lead to poor iron reserves, ultimately contributing to anemia. Anemia may cause weakness and fatigue. Hospitalization may be prolonged, and the establishment of breastfeeding may be affected. A blood transfusion may ameliorate the anemia and shorten the hospital stay, but it carries risks of transfusion reaction and infection. Access to safe blood is not universal, and PPH can sometimes strain the resources of the best blood bank. Severe PPH ,retained placenta, and uterine inversion may require emergency anesthetic services. Any exploration or instrumentation of the uterus increases the risk of sepsis **(AbouZahr, 1998).**

Expectant Versus Active Management

The controversy surrounding third-stage management exists between authorities who advocate the physiological or expectant approach and those who advocate the active approach. The basic components of the two management strategies are outlined in table (1).

- **Expectant management**