REDUCTION OF BLOOD LOSS AT CESAREAN SECTION: EFFICIENCY OF SUBLINGUAL MISOPROSTOL VERSUS OXYTOCIN INFUSION

Thesis

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Nesrin Salah Ismail El-Katsha

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LIST OF ABBREVIATIONS

µg:	Microgram.
AC:	After Century.
BC:	Before Century.
CCT:	Controlled cord traction.
CD:	Cesarean delivery.
cm:	Centimeter.
CNS:	Central nervous system.
CS:	Cesarean Section.
D and E:	Dilatation and evacuation.
DIC:	Disseminated Intravascular Coagulopathy.
gm:	Gram.
Hbs Ag:	Hepatitis B surface antigen.
HIV:	Human immunodeficiency virus.
ICU:	Intensive Care Unit.
IM:	Intramuscular.
IU:	International unit.

IV: Intravenous.

Kg: Kilogram.

L/S ratio: Lecithin Sphyngomyelin ratio.

L: Litre.

mcg: Microgram.

mg / dl: Milligram per decilitre.

mg: milligram.

min: minute.

mIU / min: Milli international unit per minute.

mIU: milli international unit.

ml / dl: Millilitre per decilitre.

ml / kg: Millilitre per kilogram.

ml / min: Millilitre per minute.

ML : Millilitre.

mm: Millimeter.

mmol / l: Milli molecule per litre.

mu / min: Milli unit per minute.

No: Number.

NSAIDs : Non steroidal anti-inflammatory drugs.

PG: Prostaglandin.

PGE: Prostaglandin E.

PPH: Postpartum hemorrhage.

RBC: Red blood cell.

RCTs: Randomized controlled trials.

VBAC: Vaginal birth after cesarean delivery.

WHO: World Health Organization.

INTRODUCTION

Postpartum hemorrhage (PPH) continues to be the leading cause of maternal morbidity and mortality worldwide and that is according to the estimates of the World Health Organization in ١٩٩٨. Average blood loss during delivery progressively increases with the mode of delivery, vaginal delivery (٥٠٠ ml), cesarean section (١٠٠٠ ml) and emergency hysterectomy (٣٥٠٠ ml) of blood ***(Pritchard et al., 1962).***

Excessive blood loss as estimated by a ١٠% drop in hematocrit postdelivery or by need for blood transfusion, occurs in approximately ٤% of vaginal deliveries and ٦% of cesarean births ***(Combs et al., 1991).***

A reduction of operative blood loss at cesarean section is beneficial to the patients in terms of decreased postoperative morbidity and a decrease in risks associated with blood transfusions. The routine use of oxytocin is associated with a significant reduction in the occurrence of postpartum hemorrhage ***(Prendiville et al., 1989).***

Although many delivery units use oxytocin as first line agent to prevent uterine atony at cesarean section, it may not be the ideal agent for prevention of PPH especially in compromised patients with preeclampsia, cardiac disease or prolonged labor. Oxytocin and specifically its preservative chlorobutanol increases the heart rate and has

negative inotropic, antiplatelet and antidiuretic effects ***(Barrigon et al., 1984).***

Misoprostol, a PGE١ analogue, has been shown in several studies to be an effective myometrial stimulant of the pregnant uterus, selectively binds to EP-٢/EP-٣ prostanoid receptors ***(Senior et al., 1993).***

Misoprostol administration either by oral or rectal route has been shown to be effective in prevention of PPH and is considered as an effective alternative to other conventional oxytocics especially in developing countries as it is cheap and thermostable ***(El-Refaey et al., 1997).***

Recent pharmacokinetic study suggested that the bioavailability of misoprostol after sublingual administration was higher than those after oral or vaginal administration ***(Trag et al., 2002).***

A few studies are now available for the use of sublingual misoprostol in the prevention of PPH following vaginal delivery and have reported it to be an effective and convenient route of administration ***(Vimala et al., 2004).***

However, none of the studies conducted so far have evaluated the response of sublingual misoprostol for prevention of PPH during cesarean section ***(Lam et al., 2004).***

Sublingual misoprostol appears to be effective in reducing postpartum blood loss during cesarean section. In addition, misoprostol offers several advantages over oxytocin including long shelf life, stability at room temperature and oral administration which make it as a suitable alternative for routine management of third stage of labor particularly in low resource countries ***(Vimala et al., 2006).***

AIM OF THE WORK

To evaluate the efficiency of sublingual misoprostol versus oxytocin infusion to reduce blood loss at cesarean section.

Chapter (١)

MISOPROSTOL

Description:

Misoprostol is a synthetic prostaglandin E١ analogue (١٥-deoxy-١٦-hydroxy-methyl PGE١) manufactured by (Searle pharmaceutical, Skokle, Illinos, USA). Misoprostol was originally developed in the early ١٩٧٠s for the treatment of peptic ulcer disease, and inhibitor of gastric acid secretion. It was marketed under the trade name Cytotec, or when combined with diclofenac, Anthrotec. Its safety when used for this indication has been established over the past ١٥ years ***(Topozzada et al ., ١٩٩٥).***

Recent studies have explored the effectiveness and safety of misoprostol for cervical ripening and induction of labor. This prostaglandin E١ analogue is less expensive, more stable, and easier to store than dinoprostone preparation. However, the U.S.Food and Drug Administration (FDA) in ١٩٨٨ approve misoprostol currently for the treatment of peptic ulcer disease and not for induction of labor ***(ACOG, ١٩٩٩)***. Moreover, the manufacturer does not plan to pursue approval for this indication ***(Bauer et al., ١٩٩٧)***.

It is currently available as a ١٠٠ µg or ٢٠٠ µg tablet, and can be broken to provide ٢٥ µg or ٥٠ µg doses but recently a

tablet of only ٢٥ µg has been released in the market, Vagiprost ***(Tang et al., ٢٠٠٢)***.

Historical review:

In the early ١٩٧٠ there was a chemical program to synthesize analogues of PGE١ with the objective of improving its pharmacological profile. The specific goals of the program were oral activity, longer duration of action and selectivity of biological action. So there were investigations done by which achieved oral activity by blocking the oxidation of the hydroxyl group in C-١٥. With placement of either a methyl group at C-١٦ or two methyl groups at C-١٦, the resulting compounds were potent, but the selectivity of these compounds was not improved ***(Southern, ١٩٧٢).***

At the end of ١٩٧٠, there were other investigations decided to synthesize a derivative of PGE١ in which the lower side chain hydroxyl group is located at the adjacent C-١٦, instead at C-١٥. This analogue possessed gastric antisecretory potency equivalent to PGE١, but the typical prostaglandin side effects were minimally diminished, and this compound was weakly active by oral administration, with its duration of action was quite short. So, in view of dramatic increase in oral potency and duration of action achieved by placement of methyl group at C-١٦, this structural change produce misoprostol which was approximately ٣٥ times more active than ١٦-hydroxy compound by intravenous administration, possessed good oral activity and increased duration of action ***(Collins et al., ١٩٩٣).***