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A Comparative Study Between Rectal Misoprostol and Standard Ecbolic Therapy for Prevention of postpartum Hemorrhage

Thesis

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M.Sc. Degree in
Obstetrics and Gynecology

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PROTOCOL

- ***Introduction***

Postpartum hemorrhage has been traditionally defined as loss of 500 ml or more of blood after completion of the third stage of labor. Nonetheless, nearly a half of all women who are delivered vaginally shed that amount of blood or more when measured quantitatively ***(Cunningham et al, 2001).*** Blood loss during operative delivery is even more; for example it was estimated that women shed about 1000 ml blood during cesarean section, 1400 ml during elective cesarean hysterectomy and 3000 to3500 ml during emergency cesarean hysterectomy ***(Clark et al, 1984; Chestnut et al, 1985).*** Alternatively postpartum hemorrhage was defined as excessive blood loss sufficient to affect the general condition of the mother with an incidence of 0.3% in low parity and 2% in high parity ***(Babinszki et al, 1999).***

Postpartum hemorrhage may be due to bleeding from placental implantation site (caused by uterine atony or retained placental parts), trauma to the genital tract or coagulation defects ***(Cunningham et al, 2001).*** According to ***Bonnar (2000),*** postpartum hemorrhage is responsible for half of the maternal deaths in the United Kingdom. Also, postpartum hemorrhage is still the leading cause of maternal deaths in the developing countries accounting for 28% of maternal deaths ***(Bukowski and Silver, 2000).*** In Egypt, maternal mortality rate was reported to decline from 174 to 66/100,000 livebirths with postpartum hemorrhage accounting alone for 50% of maternal deaths ***(National Maternal Study, 2000).***

According to evidence based results, routine active management was found to be superior to expectant management. Therefore, active management should be the routine management of choice for women expecting to deliver a baby by vaginal delivery in a maternity hospital Active management is, however, associated with an increased risk of unpleasant side effects (eg nausea and vomiting), and hypertension, where ergometrine is used ***(Prendiville, 2001)***

Drugs used for prophylaxis against postpartum hemorrhage include oxytocin (Syntocinon 5 and 10 IU ampoules, Sandoz), methyl ergometrine maleate (Methergine 0.2 mg ampoule, Sandoz). Randomized trials and their meta-analysis confirmed that these agents can reduce the incidence of postpartum hemorrhage by about 30% to 40% compared with placebo, when given parenterally following delivery of the baby ***(Prendiville and Elbourne, 1989; Keirse et al, 1995).*** There are strong suggestions of benefit for oxytocin in terms of postpartum haemorrhage,

and the need for therapeutic oxytocics.There seems little evidence in favour of ergot alkaloids alone compared to either oxytocin alone, or to combined oxytocin and methergine (Syntometrine), but the data are sparse ***(Elbourne, 2002).***

Misoprostol (Cytotec; Searle, UK; Misotac, Sigma, Egypt) is a prostaglandin E_1 synthetic analogue, The only Food and Drug Administration approved indication in misoprostol labeling is the treatment and prevention of intestinal ulcer disease resulting from non-steroidal antiinflammatory use ***(Wing, 1999).***This medication is inexpensive, easy to store, and stable at room temperature ***(Sanchez et al, 1993).*** It has been shown to be a useful agent for termination of pregnancy in the first, second and third trimesters ***(Webster et al, 1996).*** Misoprostol is a potent uterotonic agent and is therefore acquiring clinical applications in induction of abortion, cervical ripening and induction of labor with or without pre-treatment with mifepristone (RU 486) ***(El-Refaey et al, 1995).***

Misoprostol is rapidly absorbed after oral, vaginal or rectal adminstration, being detected in the circulation within two minutes of its oral ingestion ***(Karim, 1987).*** Its effect on the post partum uterus has also been shown to be rapid ***(Choo et al, 1998).*** It was suggested as an alternative to conventional standard oxytocic drugs for the prevention of atonic postpartum hemorrhage in low risk women ***(El-Refaey et al, 1996).***

- ***Aim of the work***

The aim of this work is to evaluate the effectiveness of the rectally administered PGE_1 synthetic analogue (misoprostol) compared to standard ecbolic therapy in the prevention of postpartum hemorrhage in women at risk of developing this condition.

- ***Patients and Methods***

This study will be carried out in the Maternity Hospital of Ain Shams University. It will include 100 women delivered vaginally at high risk of developing postpartum hemmorrhage. They will be randomized into two groups according to a computer generated randomization sheet to receive either :

Group A. Standard ecbolic therapy in the form of 10 IU oxytocin intravenous infusion and 1 ampoule methergine intramuscular injection after delivery of the baby and before delivery of the placenta.

Group B. Misoprostol (Misotac, Sigma) two tablets each 200 ug. Adminstered rectally after delivery of the baby and before placental delivery.

Inclusion criteria

- **Risk factors of postparum hemorrhage**
  1. Age > 35 years
  2. High parity > 3
  3. Uterine overdistension (multifetal pregnancy, polyhydramnios, etc...)
  4. History of previous postpartum hemorrhage
  5. Antepartum hemorrhage during this labor.

Exclusion criteria:

1. Previous cesarean deliveries or hysterotomies.
2. Hypertensive disorders with pregnancy.
3. Operative deliveries.

An informed written consent will be taken from every woman participating in this study. In all cases, information sheet will be completed including age, parity, gestational age at delivery, special habits, and previous scar or maternal diseases. Also, temperature, systolic & diastolic blood pressure, Hb%, hematocrite value, fetal presentation and placental localization before delivery will be recorded. Other partogram data will be completed. Including augmentation or induction and course and duration of labor, length of the third stage, and blood transfusion.

- ***Statistical methods***

Data will be summarized using percentages, means and standard deviation. Comparison of means will be done using a single-tail student's t-test. Comparison of percentages will be done using the chi-square test with continuity correction for small frequencies whenever applicable. The threshold of significance will be fixed at 5% level.

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