

**A COMPARATIVE STUDY BETWEEN THE EFFECTS
AND SIDE EFFECTS OF 400 AND 600 MICROGRAMS
OF MISOPROSTOL GIVEN RECTALLY FOR THE
PREVENTION OF POSTPARTUM HEMORRHAGE**

**Thesis submitted for
Partial fulfillment of
The Master Degree
In
Obstetrics and Gynecology**

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List of abbreviations

aPTT	Activated Partial Thrombin Time
AUC	Area Under Serum Concentration
BUN	Blood Urea Nitrogen
C.S	Cesarean Section
cAMP	Cyclic Adenosine MonoPhosphate
CBC	Complete Blood Count
Cmax	Peak concentration
COX	Cyclooxygenase
CT	Computed Tomography
DIC	Disseminated Intravascular Coagulopathy
ELISA	Enzyme- Linked ImmunoSorbent Assay
FIGO	International Federation of Gynecology and Obstetrics
Gr-1	Group 1
Gr-2	Group 2
INR	International Normalized Ratio
ITP	Idiopathic Thrombocytopenic Purpura
IU	International Unit
IUD	Intrauterine Device
LFT's	Liver Function Tests
LRS	Lactated Ringer's Saline
M:W	Molecular Weight
MLCK	Myosine Light Chain Kinase
MPA	Misoprostol Acid
MPS	Making Pregnancy Safer
MRI	Magnetic Resonance Imaging
NS	Normal Saline
NSAIDs	Non Steroidal AntiInflammatory Drugs
NVD	Normal Vaginal Delivery
PG	Prostaglandins
PKA	Protein Kinase A
PPH	Postpartum Hemorrhage
PT	Prothrombin Time
RBC's	Red Blood Cells
SGPT	Serum Glutamic Pyrovic Transaminase
Tmax	Peak time concentration
VBAC	Vaginal Birth After Cesarean section
WHO	World Health Organization

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INTRODUCTION

Maternal death is a major challenge that usually occurs as a result of pregnancy and child birth, it occurs in about one in six in the poor parts of the world, compared with one in 30,000 in north Europe. This poses a huge challenge to reduce maternal mortality by 75% between 1995 and 2015. Maternal deaths are clustered around labor, delivery and immediate postpartum period, with postpartum hemorrhage being the main medical cause of death, (*Ronsmans, Graham, 2006*).

Considered as the main cause of death, postpartum hemorrhage is defined as the loss of 500 mL of blood or more within the first 24 hours after delivery. It accounts for at least 150,000 maternal deaths and 20 million morbidities every year, 28% of these deaths are in developing countries. So, there is a need for oxytocics that are stable, inexpensive and safe to be used with simple route of administration when parenteral uterotonics are not available, such as misoprostol, (*Joyce Primo Carpenter, 2001*).

Misoprostol is a prostaglandin E1 analogue that is not only has a strong uterotonic activity, but unlike other prostaglandins, it is inexpensive and is stable at room temperature. These two properties have attracted great

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interest in the drug as an affordable method for preventing and treating postpartum hemorrhage in both low and middle income countries (*WHO statement 2009*), and it also showed promising results in reducing blood loss after delivery (*Gülmezoglu; et al., 2007*). But it is less effective than injectable uterotonics. (*Gülmezoglu; et al., 2002*). On the other hand, when it is added sublingually to injectable oxytocin after cesarean section, it shows more effectiveness than oxytocin alone, (*Fekih; et al., 2009*).

As a review of pharmacological, physiological, and clinical evidence surrounding the use of misoprostol for the treatment of postpartum hemorrhage, *G. Justus Hofmeyr; et al., (2009)* found that:

- The oral route of administration is the fastest but also the one associated with the shortest duration of action.
- The rectal route has slow uptake but prolonged duration of action.
- The buccal and sublingual route has rapid onset and prolonged duration of action with the greatest bioavailability.

So the sublingual route is considered the most promising route.

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However some other researchers have found that the postpartum use of Misoprostol by sublingual route has a comparable effect in reducing postpartum hemorrhage as that of rectal use, (*Abdelrahman Al-Harazi, Kaima Frass, 2009*).

In a recent placebo controlled trial where deliveries take place by nurses or midwives at home, a significant reduction of postpartum hemorrhage and complications was obtained with the use of misoprostol 600 micrograms orally, (*G. Justus Hofmeyr; et al., 2009*). Also the WHO guidelines support the use of 10 IU oxytocin parenterally or misoprostol in a dose between 200 and 800 micrograms orally or sublingually, (*WHO statement, 2009*).

In addition to its uterotonic action, misoprostol has some known pharmacological effects as it (*Davis; et al., 2001*):

- Inhibits platelet-activating factor and leukocyte adherence.
- Protects against gut irradiation injury.
- Improves nutrient absorption in cystic fibrosis patients.
- Lowers cholesterol level.
- Lessens the severity of peripheral vascular disease.
- Can be used to treat trigeminal neuralgia pain.

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However, the use of misoprostol has been associated with some side effects, as it significantly increases the postpartum shivering and fever with no effect on the newborn, (*Shobhana S. Patted; et al., 2009*). In this regard, it was noticed that fever may reach above 40 degrees Celsius and may be associated with altered consciousness with the use of 800 micrograms or more misoprostol, (*WHO statement, 2009*).

Despite of these side effects mentioned above, (*Shobhana S. Patted; et al., 2009*) see that the benefits of misoprostol use are greater than the associated risk.

In the light of the above discussion, it was noticed that there is no enough researches regarding the least effective dose of misoprostol whether it is 400 or 600 micrograms with the least side effects.

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AIM OF WORK

The aim of this study is to compare between the efficacy and side effects of 400 and 600 micrograms of misoprostol given via rectal route for prevention of postpartum hemorrhage.