CONTENTS

Page No.

* List of tables.		Ш
** List of figures.		П
*** Abbreviations.		Ш
**** Acknowledgement.		IV
1-Introduction.		V
2-Aim of the study.	,	VII
3-Review of literature:		1
-Chapter I (MISOPROSTOL):	1	
*Historical hint.	1	-
*Pharmacological properties		
*Adverse effects		
*Early off-label use.	7	
-Chapter II (CERVIX):	8	
*Anatomy	. 8	
*Cervical changes during pregnancy	. 12	
-Chapter III (LABOR):	15	
*Parturition	15	
*Cervical ripening.	. 20	
-Chapter IV (LABOR INDUCTION):	25	
*Definition	. 25	
*Introduction		
*Indications of induction		
*Mean Methods of induction.	31	
4-Subjects and methods:		39
-Inclusion criteria.	. 39	
-Exclusion criteria	40	
-Study design	41	
-Data of concern	42	
-Cases' data extraction sheet	44	
-Statistical analysis		
5-Results.	-	47
6-Discussion.		60
7-Summary.		67
8-Conclusion and recommendations.		69
9-References.		
10-Arabic summary.		90

LIST OF TABLES

Page No.

Table A:	Modified Bishop Score.	23
Table B:	Apgar Score.	45
Table 1:	Maternal basic characters.	47
Table 2:	Distribution of primi and multi-gravida.	47
Table 3:	Indications for induction of labor.	48
Table 4:	Mode of delivery.	49
Table 5:	Means ± SD of I-D interval.	51
Table 6:	No. of misoprostol doses.	52
Table 7:	The use of OT.	53
Table 8:	Rate of side effects.	54
Table 9:	Rate of uterine hyperstimulation.	54
Table 10:	Pattern of uterine action and its fate.	55
Table 11:	Indications of CS.	57
Table 12:	1 and 5 Apgar Score.	58
Table 13:	The need for NICU admission.	58

LIST OF FIGURES

Page No.

Fig. 1:	Mode of delivery in the three groups.	50
Fig. 2:	Mean ID interval in each group.	51
Fig. 3:	OT administration in each group.	53
Fig. 4:	Hyperstimulation rates in the three groups.	55
Fig. 5:	NICU admission in each group.	59

ABBREVIATIONS

1	ACOG:	American College of Obstetricians and Gynecologists.
2	ARM:	Artificial rupture of membranes.
3	APH:	Antepartum hemorrhage.
4	CI:	Confident interval.
5	CTG:	Cardiotocography.
6	CS:	Cesarean section.
7	DM:	Diabetes mellitus.
8	FDA:	Food and Drug Administration.
9	FHR:	Fetal heart rate.
10	GA:	Gestational age.
11	GIT:	Gastrointestinal tract.
12	Hs:	Hours.
13	I-D:	Induction-to-delivery interval.
14	IGF-1:	Insulin-like growth factor 1.
15	IL-8:	Interleukin 8.
16	IOL:	Induction of labor.
17	IUFD:	Intrauterine fetal demise.
18	LGA:	Large for gestational age.
19	LMP:	Last menstrual period.
20	Mcg:	Microgram.
21	Min:	Minute.
22	mRNA:	Messenger ribonucleic acid.
23	MRI:	Magnetic resonance imaging.
24	Mg:	Milligram.
25	NSAIDs:	Non-steroidal antiinflammatory drugs.
26	OT:	Oxytocin.
27	PAF:	Platelet activating factor.
28	PGs:	Prostaglandins.
29	PGE1:	Prostaglandin E one.
30	PGE2:	Prostaglandin E two.
31	PGF2α:	Prostaglandin F two alpha.
32	PROM:	Pre-labor rupture of membranes.
33	RR:	Relative risk.
34	SGA:	Small for gestational age.
35	SD:	Standard deviation.
36	ug:	Microgram.
37	Wk:	Week.
38	Ys:	Years.

ACKNOWLEDGEMENT

(In The Name of {Allah} Most Gracious Most Merciful)

This work is dedicated to {Allah}, who helped me to finish this research, hoping for his satisfaction.

Then I'd like to thank my supervisors: **Dr. Ahmed Mohamed Elsaeed** (Professor of Ob. and Gyn., faculty of medicine, Benha University), **Dr. Nour Eldin Ibraheem Ashmawy** (Professor of Ob. and Gyn., faculty of medicine, Benha University), and **Dr. Emad Mahmoud Abdelmagid** (Assistant Professor of Ob. and Gyn., faculty of medicine, Benha University) for their great advices and helpful efforts leading to finish this work by a good way.

I think that **the ninety women** who participate in this trial, are also must be thanked.

Much credit also goes to **my mother** who is always praying for me, and for her sincere guidance and continuous support through this work.

Mohamed Abdelmonim Salim

MB, BCH

Cairo, in June, 2009

INTRODUCTION

Labor induction, when performed on a patient with an unripened cervix, is often prolonged and difficult. Failed induction requiring cesarean delivery is common in this setting (Adair, et al. 1998). Prostaglandin preparations and intravenous oxytocin are the most frequent pharmacologic choices used today for induction (Hofmeyr. 1999). Oxytocin, which acts purely by stimulating uterine activity, is widely accepted as safe and effective, but its success is highly dependent on the condition of the cervix at the onset of induction (Ngai, et al. 1996).

Misoprostol, a synthetic analogue of prostaglandin E1, has been widely studied in a variety of dosages and routes of administration as an alternative to oxytocin. Misoprostol offers the advantage of promoting both cervical ripening and myometrial contractility (**Tang, et al. 2002**).

More than **100** randomized, controlled trials have shown misoprostol to be a safe and effective agent for cervical ripening and labor induction in patients with viable pregnancies. The majority of participants in these trials have received repeated doses of 25 ug to 50 ug of intravaginally administered misoprostol (**Chong, et al. 2003**). Several studies assessing orally administered misoprostol for cervical ripening and labor induction have been published. The majority of participants included in these latter studies have received 50 ug orally every 4 hours. This dose administered orally seems to be as effective as the same dose administered vaginally (**Toppozada, et al. 1997**). Vaginal administration of misoprostol seems to be more effective than oral route, although there

is more liability of uterine hyperstimulation with vaginal doses of 50 ug or more (Shetty, et al. 2001).

The pharmacokinetics of misoprostol suggests that it is more bioavailable when given vaginally than orally, its plasma concentration peak of its metabolite (misoprostolic acid) is reached after 1: 2 hs from vaginal administration, compared with about 30 min. after oral administration (**Zieman, et al. 1997**). Although peak levels are lower with the vaginal route, they are sustained longer and overall exposure to the drug is increased. This may be an explanation for its greater efficacy along with its possible direct effect on the cervix (**Danielson, et al. 1999**).

The sublingual route would have the higher efficacy than the oral route by avoiding the 1st pass effect of the gastric and hepatic systems, while having lower hyperstimulation rates by avoiding the direct effect on the cervix on the contrary with the vaginal route. Thus, the sublingual route has a better effect as compared with oral and vaginal routes with no increase in uterine hypercontractility rates (**Shetty, et al. 2002**).

AIM OF THE STUDY

To compare the **efficacy** (as regard labor and neonatal outcome) **and safety** (as regard complications and side effects) of 50 ug misoprostol; between three routes of administration; orally, vaginally and sublingually; for cervical ripening and labor induction at term.