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MISOPROSTOL: AN EFFECTIVE AGENT FOR LABOUR INDUCTION IN FULL TERM PAROUS WOMEN.

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ABSTRACT

OBJECTIVES: *To assess the ability of misoprostol vaginal insert for inducing labour using a dose reservoir of 50 mcg.*
DESIGN: *Descriptive cross sectional study.*
SETTING: *Sir Syed Trust Hospital – a private teaching hospital.*
SUBJECTS AND METHODS: *100 eligible women with unfavorable Bishop score were selected for induction of labour (10L). They were given 50 mcg of misoprostol every 6 hours up to a total of 3 doses.*
MAIN OUTCOME MEASURE: *Vaginal delivery within 24 hours of induction of labour.*
RESULTS: *66% of women received a single dose while 28% and 6% received second and third dose respectively. The main induction to vaginal delivery interval was 8 hours 35 minutes. After misoprostol, 96% patients went into labour and 42% did not require oxytocin augmentation. 12% had operative delivery. Neonatal outcome was acceptable as there were no perinatal deaths or birth trauma.*
CONCLUSION: *Misoprostol vaginal insert effectively induced labour in parous women at term.*

KEY WORDS: Labour induction, misoprostol, full term, parous women.

INTRODUCTION:

Misoprostol a synthetic prostaglandin E, analogue has anti-secretory and protective properties promoting gastric and duodenal ulcer healing. It is also used orally or vaginally for the induction of labour (unlicensed indication)[1,2].

Misoprostol has become an important drug in obstetric and gynecologic practice because of its uterotonic and cervical ripening activity and good safety profile. It is useful in the management of medical and surgical abortion, miscarriage, induction of labour and post partum hemorrhage.

Compared to other prostaglandin preparations, misoprostol is inexpensive. It does not require parenteral administration or refrigeration and has few systemic side effects. It can help save maternal life by preventing or treating post partum hemorrhage where other safe alternatives do not exist[3]. Cochrane pregnancy and childbirth group analyzing 45 randomized trails including >5400 women have found vaginal misoprostol to be more effective than oxytocin or vaginal prostaglandin E2 at affective delivery within 24 hours[3,4].

Though misoprostol is also in use for induction of labour for quite some time, its use is not encouraged by the manufacturers who have never sought to license (US FDA) misoprostol for labour induction[5]. Little incentive exists for a pharmaceutical company to engage in the expensive process required to add an indication to the label of misoprostol. It seems that the use of misoprostol for induction of labour is still controversial. The aim of this study was to test the ability of misoprostol as an agent to effectively induce labour. Misoprostol insertion to delivery interval was taken as the primary end point. Caesarean section, uterine hyperstimulation, post partum hemorrhage, low apgar score of the baby were duly noted and taken as matters of concern.

PATIENTS AND METHODS:

This study was conducted at the Sir Syed Medical College Hospital, Karachi over a period of one year (January 1, 2006 – Dec 31, 2006). One hundred parous women with informed consent were included in the study.

Inclusion criteria:

- o Parous Patient
- o Singleton pregnancy
- o Cephalic presentation
- o Gestational age 37 completed weeks
- o Bishop score = or <5
- o Reactive non-stress test

Exclusion criteria:

- o Previous Caesarean section or other uterine scar (as disruption of uterine scar with Misoprostol has been reported[3,6]).
- o Placenta previa
- o Patient's refusal to give consent
- o Known hypersensitivity or any contraindication to the use of prostaglandin
- o Any antenatal complication necessitating caesarean section.

Different indications for induction of labour are given in Table I.

Patient's characteristics are given in Table II.

Written informed consent was obtained from all the patients before insertion of 50mcg vaginal tablet. The dose was repeated after every 6 hours of previous dose. Once the labour was established, patients were continuously monitored through cardiotocograph and a partogram was plotted.

DEFINITIONS[7]:

- o Uterine hyper stimulation: exaggerated uterine response with non reassuring fetal heart rate tracing.
- o Hypertonus: a uterine contraction with duration of >120 seconds.
- o Tachysystole (polysystole): abnormally frequent contractions >5 per 10 minutes.
- o Non-reassuring fetal heart rate patterns: persistent or recurring episodes of severe variable decelerations, late decelerations, prolonged fetal bradycardia or a combination of decreased beat to beat variability and a deceleration pattern.

RESULTS:

One hundred women were included in this study spanning over a period of one year. In 96 women, induction was successful. Induction to delivery time ranged between 5 hours 10 minutes to 16 hours 40 minutes mean being 8 hours and 35 minutes.

66% of the women delivered with a single insertion of misoprostol, 28% were given a second dose while 6% required a third dose. Augmentation of labour with Oxytocin infusion was done in 58% of women.

Vaginal delivery was achieved in 88 women and 12 women had to undergo Caesarean section, indications for caesarean section were:

- Non-reassuring cardiotocograph – 5
- Failed induction – 4
- Non progress of labour – 2
- Cephalopelvic disproportion – 1

Post partum haemorrhage, a known complication of induction of labour, occurred in 5 women. Uterine hyperstimulation occurred in 8 women which was managed medically. None of the cases were found to have hypertonus or tachysystole.

Obstetric outcome details and number of doses required can be seen in Table III.

Details of mode of delivery, and blood loss

Indications for induction of labour:

TABLE I

Indications for induction	No	%
Post date Pregnancy (41 - 43)	54	54
Hypertension	8	8
Diabetes Mallitus	3	3
Intrauterine growth restriction	5	5
Psychological	2	2
PROM	12	12
IUD	4	4
Oligohydramnios	4	4
Congenital Malformation	2	2
Others	6	6

Characteristics of the women selected for the study:

TABLE II

Maternal Characteristics	Median	Range
Maternal Age	25	20-37
Parity	2	1-4
Gestational age	40	37 - 43
Initial Bishop score	4	3-5

Obstetrical outcome and number of doses used:

TABLE III

OBSTETRICAL OUTCOME	N=100
No of pt went into labour	96%
Failed induction	4%
Mean induction to delivery time	8 hrs 35 mins
Delivery < 12	57%
Delivery < 24	88%
NUMBER OF DOSES	
Single dose	66%
Second dose	28%
Third dose	6%
Required oxytocin augmentation	58%
Meconium staind liquor	12%
Spontaneous rupture of membrane	52%
Uterine hyperstimulation	8%

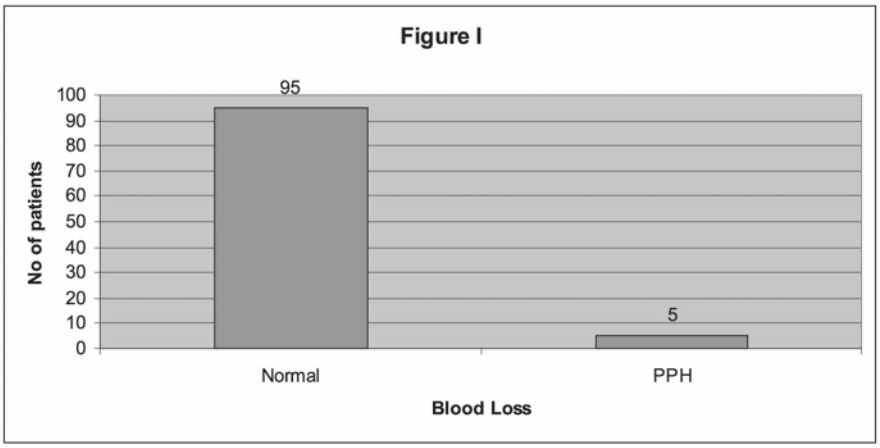
Neonatal outcome:

TABLE IV

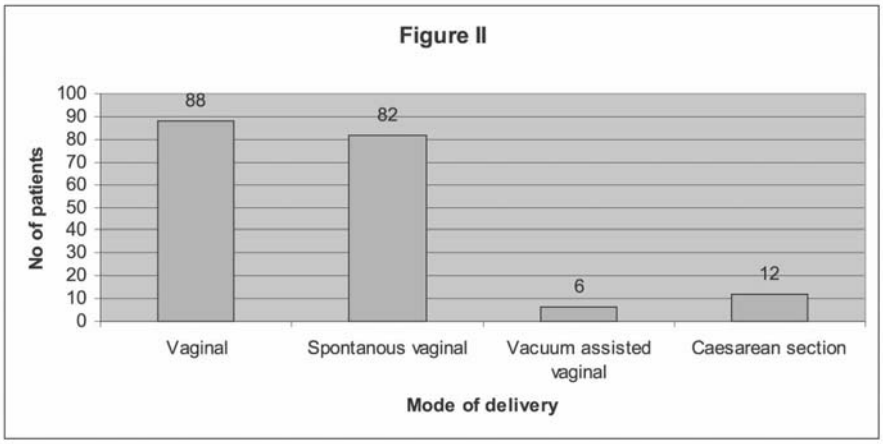
NEONATAL OUTCOME	N=100 (%)
Average birth weight (g)	2890
Prenatal death	0
O2 supplementation	10
Apgar score < 7	7
Birth trauma	0

at the time of delivery are presented in histograms I and II respectively.
There was no peri-natal death. 93 babies were born with an Apgar score >7. Oxygen supplementation was required in 10 babies. 3 babies were admitted to neonatal intensive care unit (NICU) which was anticipated due to antepartum or intrapartum fetal condition. Eventually all the babies did well.
Neonatal outcome is presented in Table IV.

BLOOD LOSS AT THE TIME OF DELIVERY:



MODE OF DELIVERY:



DISCUSSION:
Induction of labour is a common procedure on the labour ward. It is performed for a variety of conditions, some being relevant to maternal health while in others the fetal health and well being after birth is the main consideration. With an unripe cervix induction of labour may be difficult and unsuccessful. The use of agents to ripen the cervix prior to conventional methods of induction is the standard practice. Prostaglandins (E2 and E1) are most frequently used for ripening the cervix and induction of labour. Oxytocin is seldom used for induction though it is used widely for augmentation of labour. Prostaglandin E2 vaginal pessaries are currently the agents of choice. These are costly and not easily affordable. A more affordable alternative is to use misoprostol for the induction of labour. Misoprostol is a synthetic analogue of naturally occurring prostaglandin E1 originally manufactured for the treatment of gastric and duodenal ulcer. It is an effective drug for ripening the cervix and induction of labour. It is less expensive, easy to handle and is stored at room temperature. Although it is not approved by FDA for this indication, the American College of Obstetricians and Gynecologist advocates misoprostol and it is on the WHO essential drug list for labour induction. WHO guidelines[8] address induction of labour with misoprostol in:

o Selected populations such as women with pre-eclampsia and eclampsia and with unfavorable cervix if a caesarean is unsafe.

o Women who have had in-utero fetal death, who have decreasing platelets, and spontaneous labour is not imminent.

Other agencies await more evidence to its safety including organizations in Britain, Canada and Scandinavia[9]. However, generic forms of misoprostol have become available, and it is now licensed for labour induction in Egypt and Brazil, and a licensed induction product was expected in UK sometime in 2008[5]. In fact Mariani Neto et al, in 1987, in Brazil presented their first report on misoprostol induced vaginal delivery[10]. Since then many studies have suggested that per vaginal use of misoprostol is helpful for labour induction in unfavorable cervix. Cochrane database systemic review cites 45 randomized trials including more than 5400 women. Similarly Li XM et al presented a meta – analysis of 124 articles including 19,287 cases (published data from English and Chinese literatures) and found misoprostol a superior agent over oxytocin on the induction of term labour, the dosages and regimens of the agents needing further investigation[11]. Different studies have been published in the local Pakistan literature describing the efficacy and the ease of use of misoprostol though with a word of caution for interpretation of results as larger studies are needed to establish the facts [14, 15]. As appropriately stated by Loto OM et al and endorsed by Ekele BA et al, misoprostol can be used safely for induction of labour in less endowed hospital settings such as in developing countries especially in low resource settings using basic clinical tools for monitoring[12,13].

CONCLUSION:
The study found Misoprostol vaginal insert a safe and effective drug for induction of labour in term, parous women.

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