

Assessing the Rate of Successful Induction of labor Following Intra-Vaginal Administration of Misoprostol

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Abstract

Introduction: The use of prostaglandin preparations with or without oxytocin infusion is widely recognized and accepted as a standard method of induction of labor. It has been shown to reduce induction time and the risk of failed induction. But the use of prostaglandin E2 is quite expensive and is not available in many developing countries. In such cases, misoprostol can also be used as an induction agent. The aim of the study was to assess the rate of successful induction of labor following intra-vaginal administration of misoprostol. **Methods:** This open clinical trial study was conducted at the Department of Obstetrics and Gynaecology, North East Medical College Hospital, Sylhet, Bangladesh. The study duration was 1 year and was conducted with a total of 100 patients who were admitted with term pregnancy and unfavorable cervix in the study hospital, fulfilling the inclusion and exclusion criteria. **Result:** Bishop's score was significantly raised after 6 hours vaginal misoprostol [4.63 (SD ± 1.17) VS 5.82 (SD ± 1.60); p<0.001]. The mean induction to vaginal delivery time was 14.6 (SD ± 4.6) hours (range 6 to 23 hours); the induction to vaginal delivery time was <12 hours in 44.3% and 12-24 hours in 55.7% cases. The mode of delivery was vaginal in most of the cases (70.0%) and cesarean section was in 30.0% of cases. Fetal distress was the most frequent indication of cesarean section (63.3%), followed by arrested labor (20.0%) and failed induction (16.7%). The maternal obstetric complication was postpartum hemorrhage (3.0%) without any ruptured uterus, tachysystole, hypertonus uterus, or hyperstimulation. The maternal side-effects were nausea or vomiting (5.0%), diarrhea (2.0%), and fever (1.0%). Fetal outcomes were, normal baby (65.0%), APGAR score <7 at 1 min (27.0%), resuscitation needed (27.0%), neonatal unit admission (13.0%), meconium passage (8.0%) and intrauterine Fetal death (diagnosed before induction) (8.0%). **Conclusion:** Vaginal misoprostol seems to be a promising drug for labor induction with a high rate of success. Possible advantages of misoprostol may be the availability, ease of administration, well tolerability, and most notably its dual action in cervical ripening and labor induction. However, future studies focusing on dosing regimens and routes of application are needed.

Keywords: Induction, Misoprostol, Intravaginal.

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INTRODUCTION

Induction of labor may be necessary if the mother or fetus is at risk if the pregnancy is allowed to continue. The decision between Cesarean Section and induction of labor is influenced by maternal condition, Fetal condition and gestational period, cervical ripening, and bony pelvic dimension. The success of induction is heavily reliant on the cervix's consistency, compliance, and arrangement. In approximately ten percent of all pregnancies, women have an unfavorable cervix and require labor to be induced. When labor is induced in an unripe cervix it is associated with a

higher-than-normal incidence of failure of induction, prolonged labor, instrumental delivery, and cesarean section [1]. Labor induction in the presence of an unfavorable cervix is often prolonged, tedious, and remains a well-recognized impediment to the success of induction of labor [2]. A simple efficient method of ripening the cervix before induction is, therefore, clearly of use. Various methods have been used to ripen the cervix before induction at labor to increase the success rate [1]. It is generally understood that induction of labor can be difficult and often failed in situations of an immature cervix. The use of medications to ripen the cervix before typical induction

procedures is an increasingly common practice. Prostaglandin E2 gel is used for cervical ripening and labor induction. These are, however, costly and need to be stored in a refrigerator at a temperature of 2–80C and its half-life is 18 months. Moreover, the tablet form of prostaglandin E2 is not available in many developing countries, including Bangladesh [3]. Oxytocin and prostaglandins (PGs) are the agents most frequently used for the induction of labor. Although oxytocin is commonly acknowledged as a safe and efficient uterine contraction initiator, its success is reliant on the state of the cervix at the start of induction. In a woman with an unfavorable cervix, cervical ripening agents are often applied before oxytocin therapy is initiated [4]. Numerous studies have shown locally applied prostaglandin's (PG), principally PGE 2 and PGE 1, to increase cervical compliance and dilatation [5]. But risks associated with the use of prostaglandins often include uterine hyperstimulation accompanying Fetal heart rate (FHR) changes [6-8]. Misoprostol use also has its own risk. Major complications after high doses of misoprostol include uterine hyperstimulation and uterine rupture [9]. Misoprostol is a synthetic PGE1 analog that is a safe and inexpensive agent for cervical ripening [10-12]. Misoprostol has a number of advantages for clinical obstetric and gynecologic use. It costs approximately 100 times less than other prostaglandins, has a long shelf life, is easy to administer, and does not require refrigeration. Furthermore, it is registered in more than 80 countries including Bangladesh, and is therefore widely available [1, 13]. The objective of this study is to determine the efficacy and safety of intra-vaginal administration of misoprostol in the induction of labor by observing successful induction cases after intra-vaginal administration of misoprostol.

OBJECTIVE

General Objective

- To assess the rate of successful induction of labor following intra-vaginal administration of misoprostol.

Specific Objectives

- To assess the safety and efficacy of misoprostol in the induction of labor

METHODS

This open clinical trial study was conducted at the Department of Obstetrics and Gynaecology, North East Medical College Hospital, Sylhet, Bangladesh. The study duration was 1 year, from 1st January 2011 to the 31st of December, 2011. The sample size for this study was determined to be 96 by using Cochran's formula considering a 5% level of significance, but in this study, 100 patients with term pregnancy and unfavorable cervix and fulfilled the inclusion and exclusion criteria were enrolled. All patients admitted with term pregnancy and unfavorable cervix in the study hospital,

fulfilling the inclusion and exclusion criteria were enrolled as the study population in this study. A consecutive, convenient and purposive sampling technique was applied to collect the sample. After admission of the patients, history was taken and clinical examination was done. Informed written consent was obtained from each of the patients, and ethical approval was obtained from the ethical review committee of the study hospital. One hundred women were assigned to receive 50µgm intra-vaginal misoprostol intravaginally. Assessment of cervix was done before application of medication and documented. For women who were selected for vaginal misoprostol, an initial dose of 50µgm was applied in the posterior vaginal fornix. If labor did not establish within 6 hours subsequent doses of 50µgm were applied 6 hourly maximum up to 4 doses. After delivery, both the mother and neonate were followed for 48 hours or until hospital discharge, whichever came sooner. All relevant necessary information and clinical data were recorded in a pre-designed datasheet.

Inclusion Criteria

- Patients with term pregnancy with single-tone baby without labor pain
- Patients who had given consent to participate in the study.
- Cephalic presentation
- Adequate pelvis
- Bishop score < 6
- Patients with IUFD, GDM (Size baby 2.5 – 3.5 kg, estimated by USG), Post-dated pregnancy, Pre-eclampsia, eclampsia, Rh-negative mother.

Exclusion Criteria

- Pregnancy less than 37 weeks
- Cephalopelvic disproportion
 - Previous cesarean section or myomectomy or hysterotomy
- Antepartum hemorrhage
- Grand multipara (≥ 4)
- Vaginal infection
- Known hypersensitivity to prostaglandin
- Unable to answer the criteria question.
- Exclude those affected with other chronic diseases etc.

RESULTS

The age of the participants ranged from 18 to 32 years, with the mean age being 22.4 (SD \pm 2.9) years. Bishop's score was significantly raised after 6 hours vaginal misoprostol [4.63 (SD \pm 1.17) VS 5.82 (SD \pm 1.60); $p < 0.001$]. The mean induction to vaginal delivery time was 14.6 (SD \pm 4.6) hours (range 6 to 23 hours); the induction to vaginal delivery time was <12 hours in 44.3% and 12-24 hours in 55.7% cases. The mode of delivery was vaginal in most of the cases (70.0%) and cesarean section was in 30.0% of cases. Fetal distress was the most frequent indication of

cesarean section (63.3%), followed by arrested labor (20.0%) and failed induction (16.7%). The maternal obstetric complication was postpartum hemorrhage (3.0%) without any ruptured uterus, tachysystole, hypertonus uterus, or hyperstimulation. The maternal side-effects were nausea or vomiting (5.0%), diarrhea

(2.0%), and fever (1.0%). Fetal outcomes were, normal baby (65.0%), APGAR score <7 at 1 min (27.0%), resuscitation needed (27.0%), neonatal unit admission (13.0%), meconium passage (8.0%) and intrauterine Fetal death (diagnosed before induction) (8.0%).

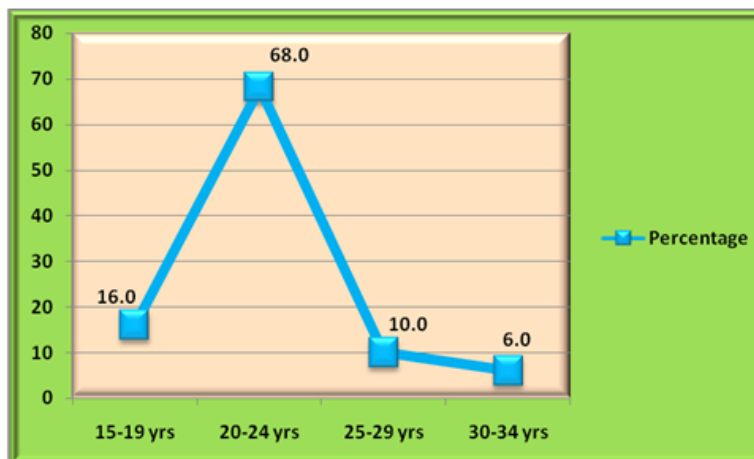


Fig-1: Distribution of the patients by age group (n=100)

The age of the patients ranged from 18 to 32 years with a mean age of 22.4 (SD \pm 2.9) years. Figure 1 showed the distribution of the patients based on age group. There were 68 (68.0%) patients in the age group

of 20-24 years, 16 (16.0%) patients in the age group of 15-19 years, 10 (10.0%) patients in the age group of 25-29 years, and 6 (6.0%) patients in the age group of 30-34 years.

Table-1: Distribution of the patients by causes of induction (n=100)

Indication of induction	Frequency	Percentage
Postdated pregnancy	63	63.0
Pregnancy Induced Hypertension	24	24.0
Gestational Diabetes Mellitus	5	5.0
Intrauterine Fetal Death (diagnosed before induction)	8	8.0
Total	100	100.0

Distribution of the patients on the basis of causes of induction was shown in table-3.1. Post-dated pregnancy was the most frequent indication of induction (63.0%), followed by pregnancy-induced

hypertension (24.0%), intrauterine Fetal death (diagnosed before induction) (8.0%), and gestational diabetes mellitus (5.0%).

Table-2: Distribution of the patients by Bishop's score before and 6 hours after induction (n=100)

Bishop score	Before induction	6 hours after induction	p-value
Mean	3.32	5.82	*p<0.001)
Standard deviation	0.96	1.60	
Range	2-5	2-8	

*Paired t-test was done to find out the level of significance.

Bishop's score before induction (vaginal misoprostol) ranged from 2 to 5 with the mean of 3.32 (SD \pm 0.96) and Bishop's score 6 hours after induction (vaginal misoprostol) ranged from 2 to 8 with the mean of 5.82 (SD \pm 1.60). Bishop's score was significantly

raised 6 hours after vaginal administration of misoprostol (p<0.001). Table-3.2 showed the distribution of the patients by Bisop score before and 6 hours after induction.

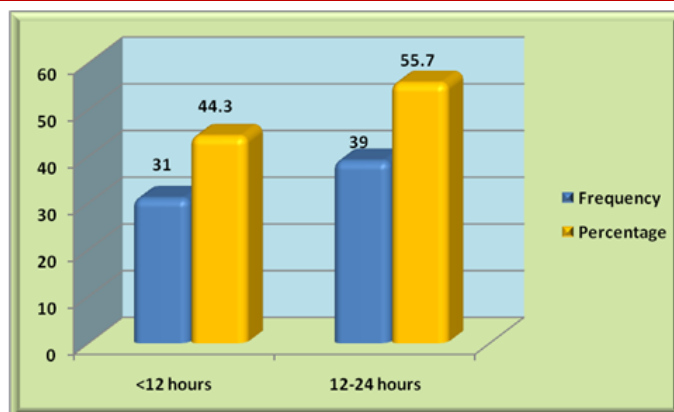


Fig-2: Distribution of the patients by induction to vaginal delivery time (n=70)

The induction to vaginal delivery time ranged from 6 to 23 hours with the mean of 14.6 (SD ± 4.6) hours. Figure 2 showed the distribution of the patients

by induction-vaginal delivery time. Induction-vaginal delivery time <12 hours was in 31 patients (44.3%) and 12-24 hours in 39 patients (55.7%).

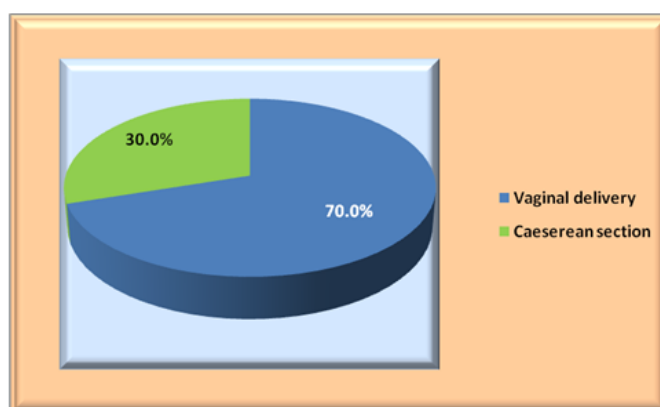


Fig-3: Distribution of patients according to mode of delivery (n=100)

Figure 3 showed the distribution of patients according to the mode of delivery. Mode of delivery

was vaginal in most of the cases [70 (70.0%) and caesarean section in 30 patients (30.0%)].

Table-3: Distribution of patients according to the indication of cesarean section (n=30)

Indication of cesarean section	Frequency	Percentage
Fetal distress	19	63.3
Failure to progress of labor	6	20.0
Failed induction of labor	5	16.7
Total	30	100.0

Fetal distress was the most frequent indication of cesarean section (63.3%), followed by arrested labor (20.0%) and failed induction (16.7%). The distribution

of patients according to the indication of cesarean section was shown in table-3.

Table-4: Distribution of patients by characteristics of labor and maternal outcome (n=100)

Variables	Frequency	Percentage
Labor		
Oxytocin augmentation	23	23.0
Tachysystole	0	0.0
Hypertonus uterus	0	0.0
Hyperstimulation	0	0.0
Maternal outcome		
Postpartum hemorrhage	3.0	3.0
Ruptured uterus	0	0.0

Distributions of patients by characteristics of labor and maternal outcome were shown in table 4. During labor, oxytocin augmentation was required in

23.0% cases and postpartum hemorrhage in 3.0% cases but no ruptured uterus, hyperstimulation, tachysystole, or hypertonus uterus.

Table-5: Distribution of patients by maternal side-effects (n=100).

Maternal side-effects	Frequency	Percentage
Nausea/vomiting	5	5.0
Diarrhoea	2	2.0
Fever	1	1.0

Maternal side-effects observed were nausea or vomiting in 5.0%, diarrhea in 2.0%, and fever in 1.0%.

Table-6: Distribution of patients according to Fetal outcome (n=100)

Fetal outcome	Frequency	Percentage
Normal baby	65	65.0
APGAR score <7 at 1 min	27	27.0
Resuscitation needed	27	27.0
Needed Neonatal unit admission	13	13.0
Meconium passage	8	8.0
Intrauterine Fetal death (diagnosed before induction)	8	8.0

65 baby were normal (65.0%), 27 baby's APGAR score <7 at 1 min (27.0%), resuscitation needed 27 (27.00%), needed neonatal unit admission 13 (13.0%), meconium passage 08 (8.0%) and intrauterine Fetal death 08 (8.0%) (diagnosed before induction).

DISCUSSION

In the 20th century, indications for labor induction have focused increasingly on preeclampsia (toxemia) and postdates [14]. Labor induction, also known as inducing labor, is the artificial stimulation of uterine contractions during pregnancy prior to the onset of labor in order to promote a vaginal delivery. A health care physician may propose labor induction for a variety of reasons, most notably when a mother's or baby's health is jeopardized. Cervical ripening, or how soft and swollen the cervix is, is one of the most critical markers in predicting the chance of successful labor induction [15]. Labor induction often becomes necessary for patients when they are 2 weeks or more behind their due date, in cases of the unripe cervix, or when there might be other risk factors for the children. The use of agents to ripen the cervix before conventional methods of induction is now standard practice. Here, various methods can be used for induction of labor, including the use of inducing agents like prostaglandins, misoprostol, mifepristone, oxytocin, and relaxin. The present study was based on a clinical trial conducted in the Department of the Obstetrics and Gynaecology, North East Medical College Hospital, Sylhet during the period from 1st January 2011 to 31st December 2011 with a view to finding out the efficacy and safety of intra-vaginal administration of misoprostol in cervical ripening and induction of labor in women with unfavorable cervix in term pregnancy. In this study, the age of the patients ranged from 18 to 32 years with a mean age of 22.4 (SD

± 2.9) years. This was similar to the findings of Abbasi *et al.*, where the mean age was 22 (SD ± 5.2) years.^[16] In a few other similar studies, the mean age was similar but slightly higher [1, 17, 18]. We also observed that there were 68 (68.0%) patients in the age group of 20-24 years, 16 (16.0%) patients in the age group of 15-19 years, 10 (10.0%) patients in the age group of 25-29 years and 6 (6.0%) patients in the age group of 30-34 years. This study observed the gestational age of the patients ranging from 38 to 42 weeks with the mean gestational age of 40.5 (SD ± 1.3) weeks. This was similar to the findings of multiple other studies [17, 18]. While observing the indication of induction of labor among the 100 study participants, postdated pregnancy was the most frequent indication of induction, observed in 63.0% of cases. Hypertension was observed in 24%, intrauterine Fetal death (diagnosed before induction) was observed in 8.0%, and the remaining 5% had gestational diabetes mellitus. These findings were in line with the findings of Chowdhury *et al.*, who found similar indications of induction [17]. The Bishop's score, a medical system used to determine how long till possible labor, was measured for the patients before induction and 6 hours after induction. Bishop's score before induction (vaginal misoprostol) ranged from 2 to 5 with the mean of 3.32 (SD ± 0.96) and Bishop's score 6 hours after induction (vaginal misoprostol) ranged from 2 to 8 with the mean of 5.82 (SD ± 1.60). This elevation of the Bishop's Score was statistically significant. A similar significance was observed in a study by Agarwal [2]. Wing *et al.* observed a significant improvement of the Bishop's score at 3 hours after the intervention [19]. The mean score before and after the intervention was 2 and 4 respectively in their study. Similar to our study, Buser *et al.* also used 50 mg of intravaginal misoprostol and observed a mean improvement of 3.5 ± 2.1 from the pre-induction score

[20]. In our study, 70% of patients had a vaginal delivery, while 30% had a cesarean section. This result was supported by the findings of Shetty *et al.*, where the mode of delivery after induction with vaginal misoprostol was vaginal in 72% and cesarean section in 28%.^[21] Induction to the vaginal delivery time ranged from 6 to 23 hours with a mean of 14.6 (SD \pm 4.6) hours. Almost similar results were observed in multiple other studies [22, 23]. The induction to the vaginal delivery time of <12 hours were observed in 31 patients (44.3%), and 12-24 hours in 39 patients (55.7%). For the 30 patients who went through cesarean section, Fetal distress was the most frequent indication, present in 63.3% of cases. 20% had arrested labor and the remaining 5 patients (16.7%) had failed induction of labor. These indications were similar to the findings of Chowdhury *et al.* [17]. Observing the labor and maternal outcomes of the 100 participants of our study, oxytocin augmentation was required for 23.0% of cases, while postpartum hemorrhage was observed in 3.0% of the patients. No ruptured uterus, hyperstimulation, tachysystole, or hypertonus uterus was observed in our study. This was considerably better compared to some other studies where these problems were also recorded [12, 17] maternal side effects were observed in a total of 8% of patients in this study. 5% had experienced nausea or vomiting, 2% had a fever, and 1 patient had a fever. These ratios were much lower compared to other previous studies [12, 24]. Fetal outcome was normal for 65% of the cases of the present study. 27% had APGAR score <7 at 1 min of birth, and resuscitation was necessary for these children. Admission at the neonatal unit was necessary for 13%, Meconium passage was observed in 8 cases, and in another 8 cases, intrauterine Fetal death was observed, which was diagnosed before the induction, and the primary cause of induction.

Limitations of The Study

The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community. The study did not have a long-term follow-up plan to better observe possible complications.

CONCLUSION

Bishop's score was significantly raised after 6 hours vaginal misoprostol. The mean induction to vaginal delivery time ranged from 6 to 23 hours, and the mean delivery time was 14.6 (SD \pm 4.6) hours; the induction to vaginal delivery time was <12 hours in 44.3% and 12-24 hours in 55.7% cases. Vaginal delivery had the highest prevalence, and Fetal distress was the most common indication of cesarean section. Maternal obstetric complications were much lower compared to other similar studies. In conclusion, vaginal misoprostol seems to be a promising drug for labor induction. Possible advantages of misoprostol may be the availability, ease of administration, well tolerability, and most notably its dual action in cervical ripening and labor induction. However, future studies

focusing on dosing regimens and routes of application are needed.

RECOMMENDATION

Close monitoring of labor, intrapartum CTG, and maintenance of partogram is mandatory for using vaginal misoprostol preparations.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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