

# Isosorbide Mononitrate versus Dinoprostone gel for Cervical Ripening at Term: Maternal and Fetal outcome

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## ABSTRACT

**Objective:** To evaluate the efficacy of Isosorbide mononitrate versus dinoprostone gel in cervical ripening at term and compare the maternal and fetal outcome.

**Methodology:** Sixty women with term pregnancies referred for induction of labor with Bishop scores of 6 or less were randomly assigned to receive a 40 mg of Isosorbide mononitrate tablet vaginally (n = 30) or Dinoprostone gel intracervically (n = 30), every 6 hours for maximum of three doses. Subjects were sent to the labor ward for amniotomy or oxytocin if their Bishop scores were more than 6 or their cervixes were not ripe 24 hours after treatment. Adverse effects, changes in the Bishop scores, progress and outcomes of labor were assessed.

**Results:** The median Bishop score after 12 hours was lower in women given Isosorbide monitrate as compared with those given dinoprostone. Adverse effects like headache was more frequent with Isosorbide monitrate than with dinoprostone. The cesarean rate was significantly lower in the Isosorbide mononitrate group than the dinoprostone group.

**Conclusion:** Isosorbide mononitrate can be used as a cervical ripening agent at term in normal pregnancies without any other complicating factors with minimal maternal neonatal side effects.

**Key words:** Cervical ripening, Isosorbide mononitrate , Dinoprostone gel

## Introduction

Although most of the patients have a spontaneous onset of labor at term, on occasions , the natural course of labor may have to be induced for various reasons. Induction of labour is now an integral part of modern day obstetrics. The aim of induction of labor is to achieve a successful vaginal delivery. The baby should be born in a good condition within acceptable time frame and with minimal maternal side effects.

Several factors influence the outcome of induced labor. Unfavorable cervix is one of the main causes of failed induction. In order to over come this, cervix needs to be ripened. The physical and biological changes in the uterine cervix resulting in its softening and dilation are recognized as cervical ripening. Cervical ripening is associated with decreased collagen fibre alignment , decreased collagen fibre strength, diminished tensile strength of the extracellular matrix and under the effect of myometrial contractions, the cervix passively dilates and is pulled over the presenting part.

Induction of labor in an unripe cervix is associated with frequent maternal complications and high rates of induction failure. Even when vaginal delivery is achieved in these patients, often they have a prolonged labor with increased incidence of instrumental delivery and birth asphyxia.

Over the years a variety of pharmacological and physical ripening agents have been evaluated to convert a firm, rigid, long cervix to a soft , effaced and slightly dilated cervix. Among these are amniotomy, oxytocin infusion, breast stimulation, estrogen gel, mechanical and electrical devices, local and systemic prostoglandins and nitrous oxide donors.

An ideal agent for cervical ripening would induce adequate cervical ripening without adverse maternal and fetal effects. Dinoprostone has been used for cervical ripening for decades. It is costly and has problems with storage, adverse maternal and fetal effects , mainly because of its stimulatory effects on uterine contractions.

Local application of nitric oxide donors effectly induce cervical ripening by rearranging the cervical colloagen and ground substance which soften the cervix and does not have severe adverse effects as dinoprostone. The present study is designed to compare the effects of isosorbide mononitrate versus dinoprostone gel for cervical ripening at term and its outcome.

## Materials and Methodology

This is a prospective study of 60 cases at Lady Goschen Government Hospital, Mangalore, India.

Inclusion Criteria are unfavourable cervix ( Bishop Score < 6 ) , Singleton pregnancy, Indicated labor induction, gestational age  $\geq$  37 weeks, vertex presentation.

Exclusion criteria are Grand multipara, previous scarred uterus, medical disorders like impaired renal or hepatic function, cardiac diseases, fetal malpresentations, known hypersensitivity to prostaglandins or Isosorbide mononitrate, History of severe asthma, hypotension, palpitation and migraine.

**Study Group :** Women attending the antenatal clinic who have met the inclusion criteria are examined to determine the Bishop score. After an informed consent 40mg of Isosorbide mononitrate was administered in the posterior vaginal fornix. The Bishop score was reviewed regularly at 6, 12 and 24 hrs after the medication. Uterine contractions and fetal heart rate was checked every 30 mins. Symptoms and vitals were checked every 4 hrs. the second and the third doses were given if Bishop score < 6 at 6 and 12 hrs. If the patient did not go into labor after 24 hrs of the first medication and Bishop score was < 6, these patients were then induced with dinoprostone gel. Even after 6 hrs if the Bishop score was < 6 then it was considered failed induction and the patient was taken for LSCS. If Bishop score > 6 then labor was augmented with oxytocin.

**Control Group :** Women attending antenatal clinic who have met the inclusion criteria and whose Bishop score is < 6 was administered dinoprostone gel in the endocervical canal. The patients were reviewed at 6, 12 and 24 hrs after administration of dinoprostone gel. The second and the third doses were administered if Bishop score < 6 at 6 and 12 hrs. Uterine contractions and fetal heart were monitored every 30 mins. If the patient did not go into labor after 24hrs after the first medication and Bishop score < 6 then this was considered as failed induction and the patient was delivered by caesarean section.

Evaluation of labor, duration, obstetric and neonatal outcomes were compared amongst both the groups.

Statistical analysis was done by Chi square test, Student unpaired t test and Fishers exact test using SPSS Software and p value of < 0.05 was considered statistically significant.

## Result

Patients were distributed into 2 groups which contained 30 patients each for Isosorbide mononitrate ( Study group ) and Dinoprostone gel group ( Control group). The pattern of age distribution in both the groups were similar. Most of the women in both the groups were in the group which was not statistically significant. The parity index of both the groups were comparable. Primigravidas in IMN group were 56.7% and in Dinoprostone group were 53.3% which was statistically not significant. Distribution according to the period of gestation was 56.7% in IMN group and 53.3% in the dinoprostone group belonging to gestational age group of > 40 weeks.

Table 1. Distribution of change in Bishop score in both IMN and Dinoprostone groups

	IMN Group N ( mean)	PgE2 Group N ( mean)
BS - 0	30 ( 2.4 ± 1.25)	30 ( 2.5 ± 1.22)
BS - 6	30 ( 4.4 ± 1.07)	26 ( 4.4 ± 1.68 )
BS - 12	26 ( 5.1 ± 1.28 )	14 ( 4.4 ± 1.60 )
BS - 24	07 ( 4.4 ± 1.13 )	03 ( 3.7 ± 1.67)

IMN- Isosorbide mononitrate, Pg E2- Dinoprostone, BS – Bishop score

No deliveries occurred after single dose of IMN whereas 4 deliveries occurred following only a single dose of dinoprostone. The mean bishop score after 24 hrs was  $4.4 \pm 1.13$  and 19 patients had delivered with 3 doses of IMN. Whereas in the dinoprostone group the mean bishop score after 24 hrs was  $3.7 \pm 1.67$  and 11 patients had delivered with 3 doses of dinoprostone.

Table 2 – Induction delivery interval

Group	Duration in Hrs.	Std. deviation
IMN	25.2	18.37
PgE2	16.0	11.21

Pvalue = 0.024

The induction delivery interval was 25.2 hrs in the IMN group and 16 hrs in the PgE2 group. The induction delivery interval was significantly longer in the IMN group as the p value was 0.024.

There was an increase in the number of failed induction in the IMN group of 23.3% as compared to only 10% in PgE2 group which is not statistically significant as the p value was 1.66.

About 26.7 % of women in the IMN group complained of headache as compared to none in the PgE2 group which was statistically significant. 24.1% of the women in PgE2 group complained of nausea as compared to none in IMN group which was statistically significant.

All women in the IMN group delivered vaginally whereas 80% of the women in PgE2 group delivered vaginally with p value of 0.024 which was statistically significant. There was a significant ( p value 0.024) increase in the caesarean section in PgE2 group as compared to the IMN group.

Table 3. Neonatal outcome

APGAR	IMN	PgE2
< 7 at 1 min	0	2 ( 6.7%)
> 7 at 5 min	0	1 ( 3.3%)

10% of patients in the PgE2 group had their babies admitted to NICU for observation while none of the babies of IMN group were admitted to NICU.

## DISCUSSION

	PRIM Study	Chanrachakul et al	Present Study
Mean gestational age	40 weeks + 6 days	40 weeks + 1 day	40 weeks+1 day
Mode of Delivery			
Vaginal	36%	63%	100%
LSCS	33%	36.4%	Nil
Induction to delivery interval	39.7 hrs	25.6 hrs	25.2 hrs
Failed Induction	44.7%	40%	23.3%
Maternal side effect	88.2%	7.3%	26.7%
1) Headache	21.9%	0%	0%
2) Hot flushes			
Neonatal Effects			
1) APGAR < 7	11.7%	1.8%	0%
2) NICU admissions	6.6%	0%	0%

The mean gestational age in the PRIM study was 40weeks + 6 days while in the study done by Chanrachakul et al and the present study was 40 weeks+ 1 day which was comparable.

The mean induction delivery interval was 39.7 hrs in the PRIM study while it was only 25.6hrs in the study done by chanrachakul et al and 25.2 hrs in the present study which was comparable.

In the PRIM study only 36% of the patients had a vaginal delivery and 33% had LSCS while in Chanrachakul et al 63% had a vaginal delivery and 36.4% had undergone LSCS. Whereas in the present study 100% of the women induced with Isosorbide mononitrate had vaginal delivery. In PRIM study the failed induction rate was 44.7% , In Chanrachakul et al it was about 40% and in the present study it was only 23.3%. About 88.2% women in PRIM study headache as major side effect while only 7.3% had headache in Charanchakul study and 26.7% in the present study.

The babies with APGAR < 7 was 11.7% in PRIM study, 1.8% in Chanrachakul et al and none in the present study. About 6.6% of the babies were admitted in the NICU in the PRIM study and none of the babies were admitted in the NICU in Charanchakul et al and the present study.

**CONCLUSION**

Isosorbide mononitrate can be used as a cervical ripening agent at term in normal pregnancies without any other complicating with minimal maternal neonatal side effects but more studies are required to prove its efficacy in high risk pregnancies like pre-eclampsia, bronchial asthma, previously scarred uterus etc.

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