

## **A Comparative Study of Isosorbide Mononitrate and Dinoprostone Gel for Cervical Ripening At Term**

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### **Original Research Article**

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#### **Article History**

*Received: 10.04.2018*

*Accepted: 25.04.2018*

*Published: 30.05.2018*

#### **DOI:**

10.21276/sjams.2018.6.5.18



**Abstract:** The aim of the study is to compare Isosorbide Mononitrate and Dinoprostone gel for cervical ripening in terms of efficacy and safety. In this study 220 pregnant women attending the antenatal clinics were evaluated and were selected for the study after applying inclusion and exclusion criteria and divided in 2 groups with 110 patients in each group. In group A 40 mg Isosorbide Mononitrate (IMN) was used for cervical ripening whereas in group B Dinoprostone gel (PGE2) was used. Both the groups were compared in term of efficacy and safety. In our study significant change in Bishop's score, fewer requirements of oxytocin, and short induction delivery interval was found in PGE2 group as compared to IMN group, whereas adverse effects like Tachysystole, Hyperstimulation and admission to NICU were less in IMN group. IMN is cheaper and effective alternative to dinoprostone for cervical ripening and induction of labour at term despite its shortcomings and those women who do not respond to IMN must be given a trial with intracervical PGE2 gel for which further studies are required.

**Keywords:** Dinoprostone gel, for cervical ripening, Tachysystole, Hyperstimulation.

### **INTRODUCTION**

Induction of labour involves methods to initiate uterine contractions in pregnant women to bring about cervical dilatation, with the aim of vaginal delivery. Indicated inductions are common and essential elements of contemporary obstetric practice. Rate of labour inductions have increased gradually [1]. It is indicated only when it is agreed that mother and fetus will benefit from higher probability of healthy outcome, than if birth is delayed.

It involves complex set of interventions and poses challenges to both mother and clinicians. In order to be successful, induction of labour must fulfill three objectives. First, it should result in labour namely adequate uterine contractions and progressive dilatation of cervix. Second, this labour should result in vaginal delivery and third, a good foetal outcome. These objectives must be achieved with a minimum discomfort to both mother and fetus. It has been known that achievement of these goals is largely dependent on the condition of the cervix. A ripe soft yielding cervix requires a lower quantum of uterine work than an unripe, hard and rigid cervix. An unripe cervix fails to dilate well in response to myometrial contractions [2].

Induction of labour when cervix is unripe is associated with maternal complications & high rates of induction failure [3]. Variety of cervical scoring systems is described but Bishops pelvic score is most commonly used for cervical assessment prior to induction [4]. Cervix is considered unfavourable if the

derived score is  $< 6$  & cervical ripening is indicated prior to artificial rupture of membranes & oxytocin to reduce the incidence of failed induction & caesarean delivery [5].

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.

The nitric oxide system relaxes the myometrium and have been proposed as tocolytic agents in the management of preterm labor and effectively been used in treating intrapartum fetal distress caused by uterine hypertonus[6].

Main effect of NO is rearrangement of collagen therapy allowing NO to soften cervix without uterus contraction. NO directly and also through stimulation of prostaglandin and cyclooxygenase 2, (COX-2) release of cytokines and inhibition of thromboxane A2 (TαA2) facilitates cervical ripening without causing complication such as fetal distress, hypertonicity.

There are limited studies on Nitric oxide donors for cervical ripening; in this context, Isosorbide mononitrate is one such agent which has been studied but there are conflicting results. More studies are required to prove its usefulness for cervical priming, especially in low resource setups where cost does matter. The present study was a comparative study of Isosorbide Mononitrate and Dinoprostone gel for cervical ripening at term.

**MATERIAL & METHODS**

The study was a prospective study conducted in Department of Obstetrics & Gynecology, SMS Medical College, Jaipur.

220 Pregnant women attending the antenatal clinics were evaluated and were selected for the study after applying inclusion and exclusion criteria.

- Inclusion criteria are term Nulliparous/Multiparous women with singleton pregnancy and intact membranes, postdated pregnancy, vertex presentation, pregnancy induced hypertension, gestational diabetes, Rh-negative pregnancy and cholestasis of pregnancy.
- Exclusion criteria are premature rupture of membrane (PROM), multiple pregnancy, cephalo pelvic disproportion (CPD), and non-cephalic presentation, history of previous uterine scar, antepartum hemorrhage, fetal distress, and preterm pregnancy.

- A written informed consent was taken from all the patients. All patients were evaluated thoroughly with complete history, parity, menstrual history, general examination, per abdomen examination, and pelvic examination. All routine blood investigation, ultrasound and non-stress test were done.
- Patients were divided in two groups with 110 in each arm using the chit method.
- In group A patients were laid in lithotomy position and under all aseptic condition cervix was assessed for Bishop’s score. When Bishop’s score was <6 then 40 mg of Isosorbide mononitrate was administered in posterior vaginal fornix. Bishop’s score was reviewed again at 6 and 12 hours. After 6 hours if Bishop’s score was <6 then 40 mg of Isosorbide mononitrate was again administered. If the Bishop’s score was >6 at 12 hours then labour was augmented with oxytocin and if the Bishop’s score was <6 at 12 hours then it was considered as failed induction and patient was taken for caesarean section.
- In group B patients were laid in lithotomy position and under all aseptic condition cervix was assessed for Bishop’s score. When Bishop’s score was <6 then dinoprostone gel was administered in endocervical canal. Bishop’s score was reviewed again at 6 and 12 hours. After 6 hours if Bishop’s score was <6 then second dose of dinoprostone gel was administered. If the Bishop’s score was >6 at 12 hours then labour was augmented with oxytocin and if the Bishop’s score was <6 at 12 hours then it was considered as failed induction and patient was taken for caesarean section.
- Maternal pulse rate, and blood pressure were checked every 30 minutes and following parameters were recorded: induction delivery interval, need of amniotomy, requirement of oxytocin augmentation, mode of delivery, maternal and fetal complications.
- Statistical analysis was done by chi square test, and unpaired student’s t-test and p-value was calculated.

**RESULTS**

**Table-1: Maternal Characteristics**

Variables	IMN	PGE2	P value
Mean age (years)	24.91 ± 3.2	25.26 ± 3.4	0.34
Gestational age (weeks)	41.35 ± 1.41	41.29 ± 1.44	1.00
Parity	Nulliparous	70 %	68 %
	Multiparous	30 %	32 %

The patterns of age distribution in both the groups were similar. The parity indexes of both the groups were comparable. Nulliparous in IMN group were 70 % and in dinoprostone group were 68 %

which were statistically not significant. Most common indication of induction in both the groups was post datism.

**Table-2: Induction Delivery Interval**

Induction-Delivery Interval (in hrs)				
Gr	No.	Mean	Std. Deviation	P Value LS
IMN	110	13.82	3.793	<0.001s
PGE2	110	10.73	5.393	

Induction delivery interval was 13.82 hours in IMN group and 10.73 hours in PGE2 group. The

induction delivery interval was significantly longer in IMN group as p value was <0.001.

**Table-3: number of tablets required**

No. Of Tablets	IMN		PGE <sub>2</sub>	
	NO.	%	NO.	%
I	35	31.82	64	58.18
ii	75	68.18	46	41.82
Total	110	100	110	100
Mean±SD	1.68	.468(1to2)	1.42	.496(1to2)

Chi-square = 14.399 with 1 degree of freedom; P <0.001S

68.18 % patients required 2 tablets in IMN group as compared to 41.82 % in PGE2 group.

**Table-4: mode of delivery**

Mode of Delivery	IMN(N=110)		PGE <sub>2</sub> (N=110)	
	NO.	%	NO.	%
Delivery	70	63.64	77	70
Fetal Distress	6	5.45	15	13.64
NPOL	10	9.09	6	5.45
Failed.Induction	24	21.81	12	10.91
L.s.c.s	40	36.36	33	30

63.64 % patients in IMN group deliver vaginally whereas 70 % patients in PGE2 group

delivered vaginally. There was a slightly increased rate of caesarean section in IMN group compared to PGE2.

**Table-5: distribution of changes in Bishop's score**

Gr		Bishop's Score-At		
		At 0	At 6 Hrs	At 12 Hrs
IMN	N	110	107	75
	Mean	3.36	5.16	5.43
	SD	.885	1.899	1.526
	Minimum	2	2	2
	Maximum	5	9	9
PGE2	N	110	94	48
	Mean	3.36	6.06	6.27
	SD	.984	2.109	1.997
	Minimum	2	3	0
	Maximum	5	9	9
P Value LS		1.000s	.002s	0.009s

Mean Bishop's score after 12 hours was 5.43 ± 1.52 in IMN group, whereas 6.27 ± 1.99 in dinoprostone group.

**Table-6: maternal complications**

Maternal Complication	IMN		PGE <sub>2</sub>		P Value LS
	NO.	%	NO.	%	
Headache	32	29.09	6	5.45	<0.001S
Palpitation	13	11.8	0	0	<0.001S
Nausea/Vomiting	17	15.45	28	25.45	0.95NS
Shivering	0	0	9	8.18	0.006S
Tachysystole	0	0	11	10	0.002S
Hyperstimulation	0	0	3	2.73	0.245NS
None	48	43.65	53	48.2	0.58NS

About 29.1 % patients in IMN group complained of headache compared to 5.5 % in PGE2 group which was statistically significant. 25.45 %

patients in PGE2 group complained of nausea and vomiting compared to 15.45 % in IMN group.

**Table-7: fetal outcome**

Fetal Outcome	IMN		PGE <sub>2</sub>	
	NO.	%	NO.	%
Apgar<7in 1min	6	5.5	29	26.45
Apgar<7in 5min	0	0	4	3.65
NICU Admission.	0	0	7	6.4

6.4 % neonates of PGE2 group admitted to NICU while none of IMN group.

**DISCUSSION**

IMN and PGE2 both are effective for cervical ripening but significant improvement in mean Bishop’s score and less number of women with Bishop’s score <6 after initiation of treatment, higher change in Bishop’s score, less oxytocin requirement and shorter induction delivery interval in PGE2 group support that PGE2 is more effective than IMN.

In present study after initiation of treatment increase in mean Bishop’s score was higher in PGE2 group than in IMN group. Agrawal K *et al.* [7] also reported significantly higher changes in modified Bishop’s score in PGE2 group (p value < 0.002).

Oxytocin requirement was significantly less in PGE2 group (p value 0.001) compared to IMN group. Similar results were also noted by Agrawal K *et al.* [7].

In present study induction delivery interval was significantly shorter in PGE2 group than in IMN group (p value <0.001). Agrawal K *et al.* [7] also concluded that induction delivery interval was significantly shorter in PGE2 group (13.37 hours) than in IMN groups (30.78 hours).

The caesarean section rate was found to be slightly higher in IMN group compared to PGE2 group (36.36 % vs 33.20 %). Similar results were also noted by Agrawal K *et al.* [7].

Tachysystole was seen in significant number of patients in PGE2 group in present study. There were three cases of Hyperstimulation in PGE2 group whereas no cases of Tachysystole and Hyperstimulation in IMN group. Agrawal K *et al.* [7] also found that Tachysystole and Hyperstimulation were more commonly associated with PGE2 compared to IMN group. In present study incidence of headache and palpitation was higher in IMN group than in PGE2 group. Similar findings have also been reported in previous study. In present study 7 babies of PGE2 group admitted in NICU compared to none in IMN group.

**CONCLUSION**

To conclude, I would like to say that IMN is cheaper and effective alternative to dinoprostone for cervical ripening and induction of labour at term. Although induction delivery interval is prolonged compared to dinoprostone but it’s convenient to use and well tolerated. IMN does not cause uterine Hyperstimulation, side effects like nausea, vomiting, and palpitation occur but are mild and not clinically significant. IMN is cost effective but improvement in Bishops score is slow, the score being <6 after 24 hours of initiation of treatment. Oxytocin requirement is more and larger induction delivery interval. However, I feel that those women who do not respond to IMN must be given a trial with intracervical PGE2 gel for which further studies are required.

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