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Isosorbide Mononitrate as Cervical Ripening at Term

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Abstract **Original Research Article**

Background: The aim of the study is to find Isosorbide Mononitrate as cervical ripening in terms of efficacy and safety. ***Method:*** In this study 100 pregnant women attending the antenatal clinics were evaluated and were selected for the study after applying inclusion and exclusion criteria.Women were counselled about the procedure, after taking consent. 40mg of isosorbidemononitrate inserted in the posterior fornix and second dose repeated after 6 hours. After insertion, the patients were monitored for uterine contractions, fetal heart rate. Monitoring of Maternal pulse rate, blood pressure. Oxytocin was started after 12hours, at the dose of 2 mu / min with increments of 2 mu/min every 30 minutes. Membranes were ruptured, when the cervix was fully effaced with a cervical dilatation of more than 3 cms. If bishop score is not changed after 24 hours of insertion, it was considered as induction failure.Patients were taken for caesarean section if signs of fetal distress appeared. ***Result:*** In our study significant change in Bishop's score, fewer requirements of oxytocin, and short induction delivery interval was found in IMN group, whereas adverse effects like Tachysystole, Hyperstimulation and admission to NICU were less in IMN group. ***Conclusion:*** 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: Isosorbide Mononitrate**,** Cervical Ripening.

INTRODUCTION

Induction of labour involves methods to initiate uterine contractions in pregnant women to bring about cervical dilatation, with the aim of vaginal delivery. Rate of labour inductions have increased gradually [1, 2]. Induction of labour when cervix is unripe is associated with maternal complications & high rates of induction failure [3]. Bishops pelvic score is most commonly used for cervical assessment prior to induction.

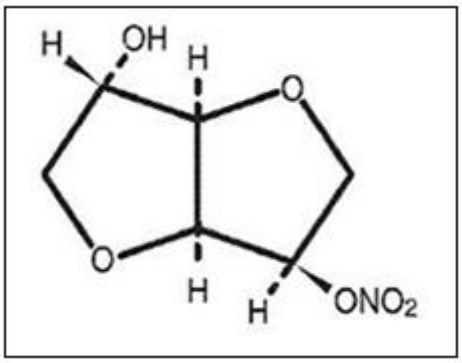
Now a day cervical status is a most accepted predictor of successful induction of labour and main cause of induction failure is unripe cervix [4, 5]. The use of prostaglandins for outpatient cervical ripening has been declared unsafe by many authorities because of their potential for uterine contractions to cause fetal hypoxia which would remain undiagnosed in the outpatient environment [6, 7].

The main effect o NO is rearrangement of collagen, herby allowing NO to soften the cervix without causing uterine contractions [8]. It has also been seen that a reduction of NO in the cervix may be cause of post-term pregnancy [9].

In the contrast to prostaglandins, nitric oxides donors inhibit rather stimulate uterine contractions, and promote rather than restrict uterine flow. Thus oxide donors such as IMN appear to be the ideal cervical ripening agent prior to labour induction [10]. Isosorbide mono nitrate (IMN) is a nitric oxide (NO) donor that can be used for cervical ripening without causing uterine contractions and the need for fetal monitoring and therefore be safety administered at home[11,12]. Vaginal IMN has no clinically significant adverse effects on either maternal or fetal haemodynamics[13].

Isosorbide Mononitrate- Ideal Ripening agent should make the cervix soft, compliant and moderately

dilated without stimulating uterine contractions and with no clinically important side effect in mother or baby.



Isosorbide Mononitrate an organic nitrate is a vasodilator with effects on both arteries and veins. The empirical formula is $C_6H_9NO_6$ and the molecular weight is 191.14. The chemical name for this is 1, 4:3, 6-Dianhydro-D-glucitol 5-nitrate and the compound has the following structural.

It is available in 10 mg and 20 mg tablets. Each tablet also contains as inactive ingredients: lactose, talc, colloidal silicon dioxide, starch, microcrystalline cellulose and aluminum stearate.

INDICATIONS

- Indicated for the prevention and treatment of angina pectoris.
- For induction of labour at term especially in post-dated pregnancy.

Isosorbide Mononitrate is the active metabolite of isosorbidedinitrate, and most of the clinical activity of the dinitrate is attributable to the mononitrate.

Side Effects

Headache, Dizziness, Nausea, Vomiting, Light headedness, Allergic reactions.

Contraindications

- Who are allergic to it?
- Who are taking certain drugs for sildenafil, tadalafil. Or vardenafil.

MATERIAL AND METHOD

Study was prospective study conducting in 100 cases. Cases for the present study were taken from SMS Medical College-Jaipur (2016-2017).

Inclusion Criteria

- Bishop score < or = 6
- pregnancy induced hypertension
- intra uterine growth restriction
- Rh–isoimmunisation
- fetus with major congenital anomaly
- intra uterine death of fetus
- Singleton pregnancy
- 35 or more completed weeks of gestation

Exclusion Criteria

Contraindications for induction of labour

- Placenta previa
- Prelabour rupture of membranes
- Previous LSCS
- Malpresentations
- Major degree of CPD
- Established fetal distress
- Heart disease complicating Pregnancy
- Liver disease complicating Pregnancy
- Anemia complicating Pregnancy

Women requiring induction of labour for different indications, who met the inclusion criteria were evaluated for study .After taking informed consent, detailed history was taken regarding relevant medical, surgical and obstetric conditions. Obstetric examination was performed for height of uterus, presentation, position, fetal heart and liquor. Vaginal examination was performed to rule out cephalopelvic disproportion. Bishops score was assessed by 2 independent observers. Gestational age was confirmed by date of last menstrual period and earlier ultrasound scan reports. Ultrasound was done for assessing gestational age, liquor content and estimated fetal weight. CST was done to assess fetal condition. Baseline investigations were sent.

Women were counselled about the procedure, after taking consent. 40mg of isosorbidemononitrate inserted in the posterior fornix and second dose repeated after 6 hours. NST was performed before insertion of isosorbidemononitrate. After insertion, the patients were monitored for uterine contractions, fetal heart rate. Monitoring of Maternal pulse rate, blood pressure for every 30 minutes during induction period, during delivery, postpartum for 6 hours done, NST was repeated with interval of 6 hours. Monitoring of fetal heart was done by intermittent auscultation and uterine action by number of contractions, duration and intensity in ten minutes. Oxytocin was started after 12hours, at the dose of 2 mu/min with increments of 2 mu/min every 30 minutes. Membranes were ruptured, when the cervix was fully effaced with a cervical dilatation of more than 3 cms. If bishop score is not changed after 24 hours of insertion, it was considered as induction failure.

Patients were taken for caesarean section if signs of fetal distress appeared.

Outcome measures

- Duration and frequency of contractions
- Interval between administration of first dose to active phase
- Interval between induction to delivery

Obstetric outcome

- Spontaneous Vaginal Delivery
- Outlet Forceps Delivery
- Caesarian section
- Postpartum Hemorrhage

Neonatal outcome

- Apgar Score
- Birth Weight
- Colour Of Liquor
- Nicu Admission

Investigations Required

Cbc, urine culture and sensitivity report, rbs, blood urea, serum creatinine, lft.

STATISTICAL ANALYSIS

Data analysis- observations were tabulated on a sheet by using Microsoft excel. Statistical analysis of the patients was carried out with CHI SQUARE TEST. A "p" value <0.05 was considered statistically significant.

RESULTS

The study was performed on 100 cases, which fulfilled the inclusion criteria with various indications, admitted in SMS medical college-jaipur.

Table-1: Modifies Bishop's Score Prior to Induction

BISHOPS SCORE	No of Patients	PERCENTAGE
1	10	10%
2	40	40%
3	20	20%
4	10	10%
5	20	20%
TOTAL	100	100%

The above table shows modified bishops score prior to induction. In the present study more cases are with Bishop score 2 with 40%.

Table-2: Modifies Bishop's Score After 12Hrs

BISHOPS SCORE	No. of Patients		TOTAL
	Primi	Multi	
1-4	3	3	6
5-8	60	10	70
>8	15	9	24
TOTAL	78	22	100

The above table and graph shows modified bishops score after induction. In the present study more cases are with Bishop Score in between 5-8.

Table-3: Induction- Delivery Interval

	No. Of Patients	PERCENTAGE
12-24 hrs	34	34%
24-36 hrs	60	60%
36-48 hrs	6	6%
TOTAL	100	100%

In the present study 34 cases were delivered in 12 to 24 hrs, 60 cases were delivered in 24 to 36 hrs, 6 cases were delivered in 36 to 48 hrs.

Table-4: Delivery in 12-24 Hours

12-24 HRS	No of Patients
PRIMI	22
MULTI	12
TOTAL	34

In the present study 22 primi cases and 12 multi case were delivered in 12 to 24 hrs.

Table-5: Delivery in 25-36 Hours

25-36 HRS	No of Patients
PRIMI	50
MULTI	10
TOTAL	60

In 25 - 36hours, In that 60 cases 50 cases were primi,10 cases were multigravida was observed.

Table-6: Delivery In 36-48 Hours

36-48 HRS	No of Patients
PRIMI	5
MULTI	1
TOTAL	6

In 36-48hours, 6 cases delivered, In that 5 cases were primigravida,1 case was multigravida was observed.

Table-7: Induction - Delivery Interval (Hours)

	Vaginal	LSCS
No of cases	80	20
IDI	25.23+-3.2	33.4 +-4.2

The mean induction delivery interval in vaginal deliveries is 25.23, in LSCS it is 33.4, P value is <0.0001 which is statistically significant.

Table-8: Mode of Delivery

Mode of Delivery	No of Patients
Vaginal Delivary	80
Lscs	20
Total	100

80 cases were delivered vaginally, 10cases underwent for LSCS.

Table-9: Maternal Out Come

SL No	Complications	No of Patients
1	Nil	70
2	Tachysystole	0
3	Headache	25
4	Palpitations	2
5	Tachycardia	0
6	Hypotension	0
7	Post-partum Hemorrhage	3
	Atonic	0
	Traumatic	0

There are no maternal complications in 70 patients, 25 patients had headache,3 had postpartum hemorrhage.

Neonatal Out Come

Neonatal Complications	No of Patients
NIL	85
LOW APGAR	10
BIRTH ASPHYXIA	5
STILL BIRTH	0
SEPSIS	0
TOTAL	100

In the present study 15 cases were admitted in NICU in view of low APGAR and discharged healthy after 3 days.

DISCUSSION

In this study the efficacy of Isosorbide Mononitrate in induction of labour at term is assessed through the outcome measures in the form of change in bishop's score, induction to delivery interval, and mode of delivery, maternal and neonatal outcomes. Prostaglandins are most commonly used pharmacological cervical ripening agents, but these are associated with uterine Tachysystole which may lead to fetal distress.

INDUCTION – DELIVERY INTERVAL

The results of the present study showed has induction - delivery interval 25 hrs, P value <0.0001 which is statistically significant and is consistent with previous studies. The results of the study conducted by Hamideh showed induction to delivery interval 33.9 Hrs with P value of 0.032 which is statiscally significant. The results of the study conducted by Hana alani showed induction to delivery interval 32.1 Hrs with P value of 0.02 which is statiscally significant. The results of the study conducted by Kavithaagarwal showed induction to delivery interval 30.78 Hrs with P value of <0.001 which is statiscally significant. The results of the study conducted by Bollapragada showed induction to delivery interval 31.06 Hrs with P value of 0.02 which is statiscally significant.

Present study shows 20% LSCS With p value < 0.0001which is statistically significant and consistent with previous studies. The study by kavitha agarwal had incidence of 17% of LSCS with P value of 0.001. The present study is consistent with the study done by Pallavi RK et al with P value of <0.0001. Caesarean delivery rate in this study was 10%. The various indications were fetal distress & failure to progress.

MATERNAL OUTCOME

In the present study, 25 patients had headache out of these 5 members required analgesia. In the study conducted by Hamideh *et al*. 22 pregnant women had headache only 3 required analgesia? In study conducted by Kavithaagarwal *et al*. 46 pregnant women had headache only 6 women required analgesia.

NEONATAL OUTCOME

In the present study there are 15 cases were admitted in NICU in view of low APGAR. Study done by Ramyakrishnamurthy only 1 case admitted in NICU and discharged after 2 days shifted to mother side.

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. IMN does not cause uterine hyper stimulation, side effects like nausea, vomiting, and palpitation occur but are mild and not clinically significant. IMN is cost effective. It can also be safely used in previous LSCS cases, in asthamatic clients. Isosorbide mononitrate can be used for induction at term with minimal maternal and neonatal side effects, but more studies are required to prove its efficacy further. Further randomized trials

will give the final conclusion. 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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