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Induction of Labour At Term with Isosorbide Mononitrate

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Abstract: *Induction of labor involves methods to initiate uterine contractions in pregnant woman to bring about progressive cervical dilatation with the aim of vaginal delivery with good maternal and fetal outcome.Various methods like mechanical, surgical and drugs like PGE1,PGF2alfa are available today. But study on isosorbide mononitrate is conducted as it has very minimal side effects and good maternal and fetal outcome.*

Methods: *This is an interventional study conducted over 100 pregnant woman at Gandhi hospital for one year period with isosorbide mononitrate -40mg-2 doses with 12hrs apart for induction of labour.*

Results: *Results were studied in terms of various parameters like mode of delivery, induction -delivery interval, side effects, neonatal and maternal outcome.90-delivered vaginally,10 had cesarean section, 20 had headache, 3 neonates admitted into NICU. The induction delivery time was 22hrs.*

Conclusions: *ISMN for induction of labour is safe, effective ,easily available, can be stored at room temperature, minimal side effects ,and good maternal and neonatal outcomes.*

Keywords: *Ismn,Tg,Nvd,Induction,Lscs, Weeks, Gestational Age.*

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I. 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 out come. 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 are 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].Various methods for ripening of unfavourable cervix and induction of labour are being used by many obstetricians, intravenous infusion of oxytocin, intracervical foleys balloon catheter insertion,intravaginal or intracervical administration of PGE_1 andPGE_2 as the standard methods of induction. A variety of more economical mechanical methods are also used for cervical ripening like extraamniotic saline infusion and hygroscopic laminaria tents.

IsosorbideMononitrate (ISMN), a NOD(Nitric oxide donors),induces cyclo-oxygenase-2 which leads

to production of endogenous prostaglandins in human cervix and causes ultra structural rearrangement in the cervix similar to spontaneous onset of labour[6]. In addition, NODs have a relative relaxant effect on the uterine myometrium. Thus, these are not expected to cause uterine hyper stimulation in contrast to prostaglandins. There have been trials comparing different doses of ISMN alone or in the combination with prostaglandins showing different efficacy[7]. One double blind trial has been done on the use of combination of misoprostol and ISMN which demonstrated that combination of misoprostol and ISMN is more effective than misoprostol alone and shows a shorter latent phase of labour and shorter induction to vaginal delivery time[7]. A randomized placebo-controlled trial compared ISMN 40mg tablet vaginally with placebo tablet vaginally for outpatient cervical ripening and concluded that ISMN self-administered vaginally at home does not shorten induction to delivery

Interval despite a significant effect on cervical ripeness assessed using Bishop score[8]. Collingham et al. used ISMN vaginally and misoprostol orally for labour induction and this concurrent use of ISMN and misoprostol did not reduce time to vaginal delivery and was associated with a greater incidence of headache[9].

A recent double blind randomized controlled trial compared the efficacy of two different doses of vaginal isosorbidemononitrate (40mg and 60mg sustained release) with placebo and the result shown greater cervical ripening with ISMN as compared to placebo and also found that ISMN 60mg sustained release is a better cervical ripening agent as compared to 40mg tablet without significant difference in adverse effects profile[10].

II. Aims And Objectives

1.To find out the efficacy of Isosorbide Mononitrate in induction of labour in inpatients admitted in Gandhi Hospital.
2.To study the induction to delivery interval after administration of Isosorbide mononitrate.

Induction Of Labour

Ian Donald: stated that induction of labour is the one in which pregnancy is terminated artificially any time after the period of viability by a method which aims to secure delivery via naturalis.
Arul Kumaran: stated that induction of labour is the non-spontaneous initiation of uterine contractions that results in progressive cervical effacement and dilatation, descent of presenting part to achieve vaginal delivery when continuation of pregnancy presents a threat to the life or well being of the mother or her unborn fetus.
Williams: stated that induction of labour implies stimulation of uterine contractions before spontaneous onset of labour with or without ruptured membranes.

Cervical ripening refers to a pre labour phase when cervix changes the characteristics such as consistency, position, effacement and dilatation. Induction of labour refers primarily to produce regular uterine contractions along with cervical changes to begin active phase of labour. In clinical practices however the two have many overlapping features and the ultimate outcome of successful vaginal delivery without fetal or maternal compromise.

Applied Physiology - Cervical Ripening

Cervical ripening refers to the prelabor change in the physical and biochemical configuration of collagen fibres in the uterine cervix ,The process of prelabor cervical softening ,shortening and eventual dilatation is part of a continuum that cumulates in spontaneous labour .The success of any method of induction in a particular circumstance ,depends largely on the point in this continuum at which the effort of induction starts. However, the distinction between cervical priming and induction of labour is artificial as it attempts to compartmentalize the latent prelabor phase, from the active acceleratory phase.

Cervical Assessment

The success of any method of induction depends largely on the parity and favourability of cervix at the beginning of induction. Cervical ripening is prerequisite for successful labour, spontaneous or induced. When cervix is unripe, labour often fails leading to increase in a overall incidence of caesarean deliveries (keirse MJ 1993)[11] Cervical ripening can be quantified by cervical scoring system.

This provides

1. A degree of objectivity to assessment, a factor which is vital for comparative studies pertaining to cervical ripening and induction.
2. Predictor of type of labour and outcome.

At present the best guide to this prognosis is an assessment to the state of the cervix, by using a scoring system devised by BISHOP in 1964[12].BISHOP score ranged from 0 to 13. Successful induction is seen with score greater than or equal to 9.

Bishop Pelvic Scoring System (1964)

Point value	0	1		2	3
Dilatation[cm]	0	1-2		3-4	5-6
Effacement[%]	0-30%	40-50%		60-70%	80%
Station	-3	-2		-1/0	+1/+2
Consistency	Firm	Medium		Soft	_
Position	Posterior	Middle		Anterior	_
Total Value=13, Favourable Score = 6-13,				Unfavourable = 0-5	

Cervical score of calder modified bishop score (1974)[13].

	0	1	2	3
Dilatation(cm)	<1	1-2	2-4	>4
Length(cm)	>4	2-4	1-2	<1
Station	-3	-2	-1,0	+1,+2
Consistency	Firm	Medium	Soft	_
Position	Posterior	Mid/Anterior	_	_

Total score -12 (<5- unfavourable, 5 -12 favourable)

Factors for successful induction:-

1. Period of gestation: - pregnancy near term or post-term.
2. Pre-induction score: - Bishops score >6 is favourable.
3. Sensitivity of Uterus: - Positive Oxytocin sensitivity test.
4. Cervical ripening: - Favourable in parous women & in case of PROM, less responsive in elderly primi or cases with prolonged retention of dead fetus.
5. Presence of Fetal Fibronectin in vaginal swab more than 50mg/ml favourable for induction of labour.
6. Low bishops score ≤5 is unripe & unfavourable.

Prerequisites For Induction

1. Assessment of fetal maturity / confirmation of gestational age
2. Cervical assessment
3. Assessment of pelvis and fetal size/ presentation
4. Membrane status
5. Fetal well being and non - stress test

Methods of induction of labour & common clinical conditions

1) Medical methods:-

- IUD
- PROM
- In combination with surgical induction (Amniotomy)

2) Surgical methods:-
Abruption placenta
Chr. Hydramnios
Severe pre-eclampsia
Eclampsia
In combination with medical induction
To place scalp electrode for electronic fetal monitoring

3) Combined methods:-
To shorten the induction delivery interval
Medical methods followed by surgical or surgical methods followed by medical

INDICATIONS FOR INDUCTION (ACOG PRACTICE Bulletin 107, 2009) [14].

1. Gestational Hypertension
2. Preeclampsia, Eclampsia
3. Premature Rupture of membranes
4. Abruptio placentae
5. Chorioamnionitis
6. Suspected fetal well – being IUGR
7. Iso immunization
8. Maternal medical problems

- Diabetes
- Renal disease
- Chronic pulmonary disease
- Cardiac disease

8. Fetal demise
9. Post-dated pregnancy

Various Methods For Cervical Ripening And Labour Induction[15].

PHARMACOLOGICAL METHODS				
	METHOD	DOSE AND ROUTE OF ADMINISTRATION	ADVANTAGES	DISADVANTAGES
1	Oxytocin	IV infusion as low Or high dose Regimen. Max. 42 Mau/min	Safe and effective To initiate Contractions. Physiological effect safe for VBAC	Less effective for poor cervical score Risk of failed inductions Water intoxication Neonatal Hyperbilirubinemia
2	Dinoprostone	Intracervical gel 0.5mg 6 hrly, max 1.5 mg in 24 hrs Vaginal insert in post.fornix, 10mg for 12 hrs	Effective in cases with poor cervical Score Safe for VBAC No systemic Effects	No decrease in Caesarean rates. Risk of hyper stimulation, needs refrigeration
3	Misoprostol	Vaginal tablet 25µg 4 hrly, max 6 Doses	Inexpensive, stable at room temperature	Hyper stimulation, Risk of uterine rupture and PPH

Investigational Pharmacological Methods

	Method	Dose And Route OF Administration	Advantages	Disadvantages
1	Mifepristone	200mg Orally×2days	Effective,Safe In Cases With Previous LSCS	Preliminary Data Available, Further Research Required
2	Relaxin	1-4mg Gel Vaginally	Porcine Derived Effective , Reduces LSCS Rate, No Risk Of Hyper Stimulation	Recombinant Human Relaxin Not Effective. Role Not Clearly Established
3	Isosorbide Nitrate	40mg Oral	Improves Cervical Dispensibility	Preliminary Data Available, Further Research Required

Surgical Methods

SURGICAL METHODS				
	METHOD	DOSE AND ROUTE OF ADMINISTRATION	ADVANTAGES	DISADVANTAGES
1	Amniotomy	Rupture of fore bag membranes surgically, oxytocin to be started after 4hrs if no contractions	Effective when used with oxytocin, Inexpensive	Can be performed in ripe cervix, Risk of infection, cord prolapsed, bleeding in cases of vasaprevia
2	Membrane Stripping	Digital separation of membranes from lower uterine segment, daily or weekly	Increases spontaneous labour, decreases need for formal induction for post Term	Discomfort, needs minimal cervical dilatation, accidental rupture of membranes, only for non urgent Induction

MECHANICAL METHODS				
	METHOD	DOSE AND ROUTE OF ADMINISTRATION	ADVANTAGES	DISADVANTAGES
1	Hygroscopic Dilators	Intracervical insertion, laminaria tent ×12-16 hrs, synthetic dilators ×6hrs	low cost, effective, No risk of hyper stimulation	Risk of infection
2	Foley's Catheter	Catheter introduced through cervix in extraamniotic space and bulb inflated	Low cost, very effective more than other methods including PGE1, no hyper stimulation risk	Risk of infections
3	Extra Amniotic Saline Infusion	Normal saline infused through catheter	No hyper stimulation	Risk of infections

Contraindications for induction:[16].

Absolute

1. Previous classical or inverted T-shaped or unknown uterine incision
2. Previous hysterotomy/ myomectomy of the uterine corpus involving entry of the uterine cavity or extensive myometrial dissection
3. Previous uterine rupture
4. Placenta previa or Vasa previa
5. Abnormal fetal lie
6. Active genital herpes infection
7. Major degree of cephalopelvic disproportion and contracted pelvis

Relative:

1. Grand multipara
2. Malpresentation
3. Over distension of uterus like polyhydramnios or multiple pregnancy
4. Invasive carcinoma cervix
5. Pregnancy following repair for vesicovaginal fistula

III. Risks Of Induction

Maternal:

- Psychologically upset
- Need for emergency caesarean delivery oDue to fetal distress / failed induction

- Placental abruption
- Precipitated labour
- Abnormal uterine action- Hypertonicity

1. incoordinated uterine action
2. Uterine rupture

- Postpartum haemorrhage due to uterine atony due to paralysis myometrial fibrils due to hyper stimulation syndrome
- Water intoxication and electrolyte imbalance Infection
- Amniotic fluid embolism.

Fetal:

- Iatrogenic prematurity
- Fetal hypoxia due to uterine hypotony
- Placental site retraction
- Cord complications
- Neonatal jaundice in association with oxytocin

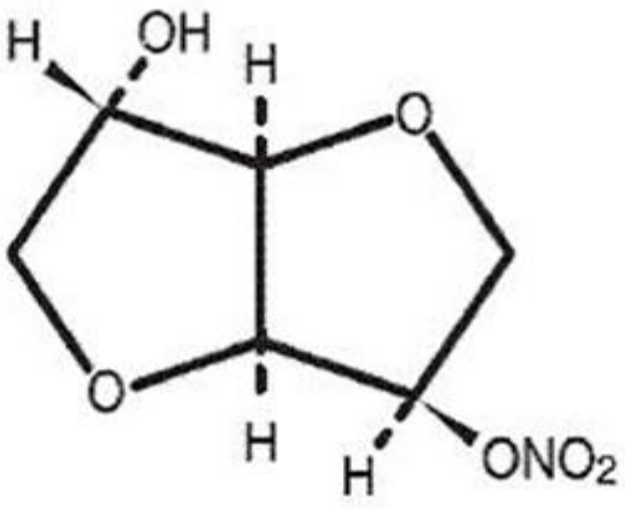
Factors To Be Considered Before Induction

1. Consent
2. Patient counselling
3. Estimation of fetal pulmonary maturity
4. Estimation of fetal maturity and gestational age
5. Pelvic assessment / Evaluation
6. Readiness of cervix by modified Bishop‘s score system(Calder, 1974)

Isosorbide Mononitrate

Drug Description

Isosorbidemononitrate 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 formula:



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

1.Indicated for the prevention and treatment of angina pectoris due to coronary artery disease. The onset of action of oral isosorbidemononitrate is not sufficiently rapid for this product to be useful in aborting an acute anginal episode.

2. for induction of labour at term especially in post-dated pregnancy

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

Pharmacokinetic Data

It is not subjected to first pass metabolism in the liver.

Bio availability	- 100%
Plasma protein binding	- <5%
Peak plasma concentration	- about 30-60 minutes
Volume of distribution	- 0.6lit/kg
Overall elimination half life is	- 5hours
Excretion	- 93% excreted in urine in 48 hours
Fecal excretion	-1%

Clinical Application In Obstetrics

During the recent years, Nitric oxide donors (NODs), like isosorbidemononitrate (ISMN), has been studied as an agent for pre induction cervical ripening with less adverse effects compared to other pharmacological agents. Isosorbidemononitrate causes increase in cyclo-oxygenase-2 which induces endogenous prostaglandin production in the cervix and also leads to cervical ultra structural rearrangement that is similar to spontaneous onset of labour.

Side Effects

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

Contraindications

Isosorbidemononitrate is contraindicated in patients who are allergic to it. Do not use this in patients who are taking certain drugs for severe pulmonary hypertension (phosphodiesterase inhibitors), such as sildenafil, tadalafil, or vardenafil. Concomitant use can cause severe hypotension, syncope, or myocardial ischemia. Do not use this in patients who are taking the soluble guanylatecyclase stimulator riociguat. Concomitant use can cause hypotension. Vidanagamage et al. performed a study comparing two doses of ISMN i.e. ISMN 40mg compared with ISMN 6omg sustained release tablet and concluded that ISMN sustained release dose has a longer duration of action[10]. ISMN-SR 60 mg has a longer duration of action about 12 hours[17,18]. Vaginal administration of ISMN has been shown to result in lower plasma levels with peak levels being achieved only after 6 hours or more [17]. However, vaginal ISMN is thought to have its effects on the cervix much earlier due to the direct transport of the ISMN from the vagina to the cervix [17, 19, 20].

Storage

Store at room temperature away from light and moisture. Do not store in the bathroom. Keep all medications away from children and pets.

IV. Patients And Methods

Study Design

Interventional study, conducting in 100 cases undergoing induction of labour after 34 weeks of

pregnancy. Cases for the present study were taken from Gandhi Hospital attached to Gandhi Medical College,Secunderabad, from the period 2015 to 2016.

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

Protocol

Women requiring induction of labour for different indications, who met the inclusion criteria were evaluated for study entry .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 recruited for induction, 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 active phase to delivery
- 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

- Cbp,cue,urine culture and sensitivity report,rbs,blood urea,serum creatinine,lft.

V. 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.

VI. Results

The study was performed on 100 cases, which fulfilled the inclusion criteria with various indications, admitted in Gandhi hospital.

Table -1: Age

AGE	No of Patients
18-24	74
25 -30	26
TOTAL	100

There are 74 cases in the age group of 18-24 years, and 26 cases in the age group of 25-30 years.

Table - 2: Parity

PARITY	No of Patients
PRIMI	81
MULTI	19
TOTAL	100

In the present study 81 were primigravidas 19 were multigravidas.

Table -3: Gestational Age

GESTATIONAL AGE IN WKS	No of patients	PERCENTAGE
35 - 37	14	14%
37 - 42	56	56%
>42 wks	30	30%
TOTAL	100	100%

There are 14 cases in 35 - 37 weeks of GA, 56 cases in 37 - 42 weeks of GA and 30 cases in> 42 weeks of gestation.

Table - 4: Indications For Induction

INDICATIONS FOR INDUCTION		No. of Patients
PRIMI	Post dates	22
	Severe pre eclampsia	11
	Bishop score<or=6	32
	Intra uterine death	05
	Intrauterine growth retardation	05
	Rh isoimmunisation	05
	Congenital anomalies to fetus	01
MULTI	Post dates	08
	Severe pre eclampsia	04
	Bishop score<or=6	05
	Intrauterine growth retardation	02
	Rh isoimmunisation	00
	Intra uterine death	00
	Congenital anomalies to fetus	00

Table - 5 : Modified Bishop's Score Prior To Induction

Bishops score	No of Patients	PERCENTAGE
1	10	10%
2	43	43%
3	26	26%
4	10	10%
5	11	11%
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 43%.

Table -6: Modified Bishops Score After 12 Hours

BISHOPS SCORE	No of Patients		TOTAL
	Primi	Multi	
1- 4	01	01	02
5- 8	63	13	76
>8	17	05	22
TOTAL	81	19	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 - 7- Induction - Delivery Interval

	No of Patients	PERCENTAGE
12-24 hours	43	43%
24-36 hours	52	52%
36-48 hours	05	5%
TOTAL	100	100%

In the present study43 cases were delivered in 12 to 24 hrs,52 cases were delivered in 24 to 36 hrs,5 cases were delivered in 36 to 48 hrs.

Table - 8- Delivery In 12-24 Hours

12-24 HRS	No of Patients
PRIMI	25
MULTI	18
TOTAL	43

In the present study 25 primi cases and 18 multi case were delivered in 12 to 24 hrs.

Table - 9 - delivery in 25- 36 hours.

25 - 36 HRS	No of Patients
PRIMI	42
MULTI	10
TOTAL	52

In 25 - 36hours,52 cases delivered.p <0.002 which is statistically significant,In that 52 cases 42 cases were primi,10 cases were multigravida was observed.

Table - 10 - Delivery In 36 - 48 Hours

36-48 HRS	No of Patients
PRIMI	4
MULTI	1
TOTAL	5

In 36-48hours, 5 cases delivered, In that 4 cases were primigravida,1 case was multigravida was observed.

Table - 11- Induction - Delivery Interval(Hours)

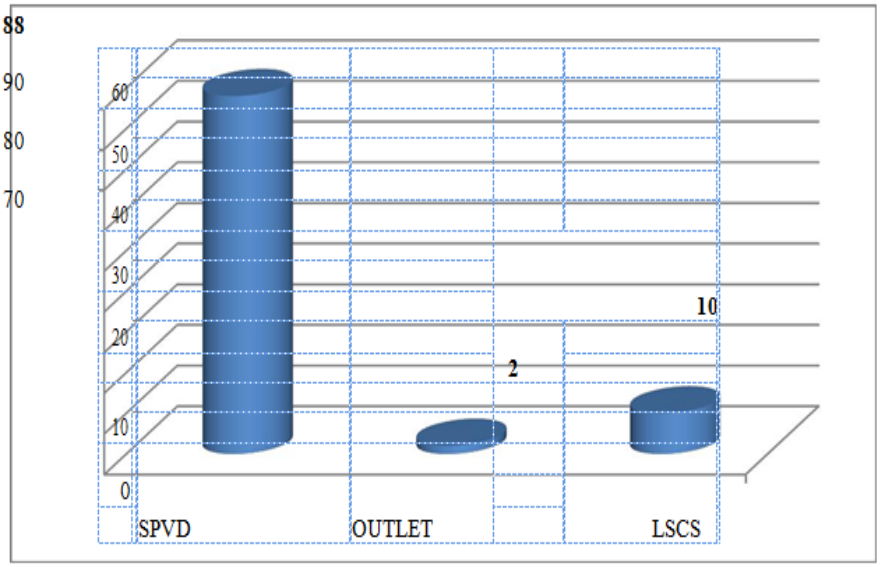
	Vaginal	LSCS
No of cases	90	10
IDI	22.23 ± 2.94	29.4 ± 4.23

The mean induction delivery interval in vaginal deliveries is 22.23, in LSCS it is 29.4, P value is < 0.0001 which is statistically significant.

Table - 12 - Mode Of Delivery

Mode Of Delivery	No Of Patients
Spvd	88
Outlet	2
Lscs	10
Total	100

GRAPH -11



90 cases were delivered vaginally, Out of these 2 cases delivered by outlet forceps, 10cases underwent for LSCS. Out of 100 cases 11 cases required second ripening agent in that 11 cases 5 cases were delivered viginally,6 cases were underwent for LSCS for various indications.

Table - 13 - Indications For Lscs

SL.No	INDICATIONS	No of Patients
1	Fetal distress	
	a) Meconium stained Liquor	6
	b)Fetal bradycardia due to hyper stimulation	0
2	Failure to progress	
	a)Deep transverse arrest	0
	b)Secondary arrest of dilatation	0
3	Failed induction	4

LSCS done for fetal distress in 6 cases (meconium stained liquor), and for failed induction in 4 cases. Out of 6 cases 3 were induced with second ripening agent that is PGE2 gel,3 were not required second ripening agent.

Maternal Out Come

Table - 14

SL.No	Complications	No of Patients
1	Nil	80
2	Tachysystole	0
3	Headache	20
4	Palpitations	0
5	Tachycardia	00
6	Hypotension	0
7	Post partum Hemorrhage	--
	Atonic	0
	Traumatic	0

There are no maternal complications in 80 patients, 20 patients had headache, out of these 20 patients only 3 patients required analgesia in the present study.

Neonatal Out Come

Table - 15

Neonatal complications	No of Patients
NIL	97
LOW APGAR	03
BIRTH ASPHYXIA	0
STILL BIRTH	0
SEPSIS	0
TOTAL	100

In the present study 5 cases were admitted in NICU in view of low APGAR and discharged healthy after 3 days.

VII. Discussion

In this study the efficacy of isosorbidemononitrate in induction of labour at term is assessed through the outcome measures in the form of change in bishops 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. Nitric oxide donors like isosorbidemononitrate used for induction of labour with less adverse effects compared to other

pharmacological agents, it causes increase in cyclooxygenase 2 which induces endogenous prostaglandin production in the cervix and leads to cervical ultra structural rearrangement that is similar to spontaneous onset of labour.

The results of this study are discussed under following headings -

1. Induction- delivery interval
2. Maternal out come
3. Neonatal out come

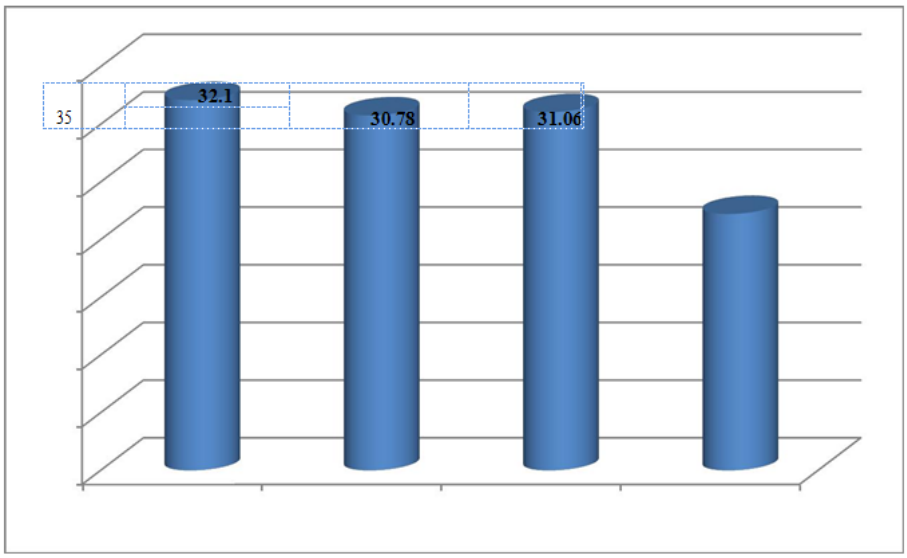
INDUCTION – DELIVERY INTERVAL

The purpose of this study is to assess the efficacy of isosorbidemononitrate in induction of labour Primary outcome measureis the induction to delivery interval in both primigravidasand multigravidas.Comparison of this primary outcome with other previous similar studies is as shown

TABLE- 16
INDUCTION - DELIVERY INTERVAL

	IDI in hrs	P VALUE
Hamideh	33.9	0.032
Hana Alani	32.1	0.02
Kavithaagarwal	30.78	< 0.001
Bollapragada	31.06	0.02
Present study	22.23	<0.0001

Graph -14

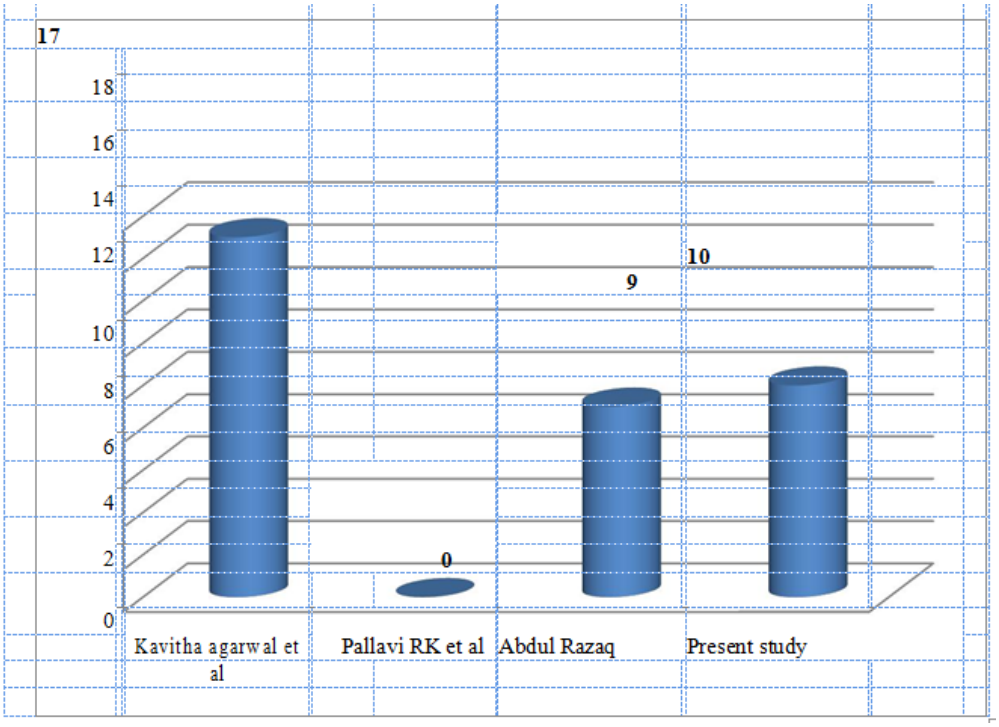


Hana Alani et alKavitha agarwal et al Bollapragada et al Present study The results of the present study showed has induction - delivery interval 23 hrs, P value <0.0001 which is statistically significant and is consistent with previous studies. The results of the study conducted by Hamideh showed induction 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.

Table-17

	LSCS in %	P VALUE
Kavithaagarwal	17%(17)	0.001
Pallavi RK	0%(0)	< 0.0001
Abdul Razaq	12%(9)	0.2
Present study	10%(10)	<0.0001

Lscs



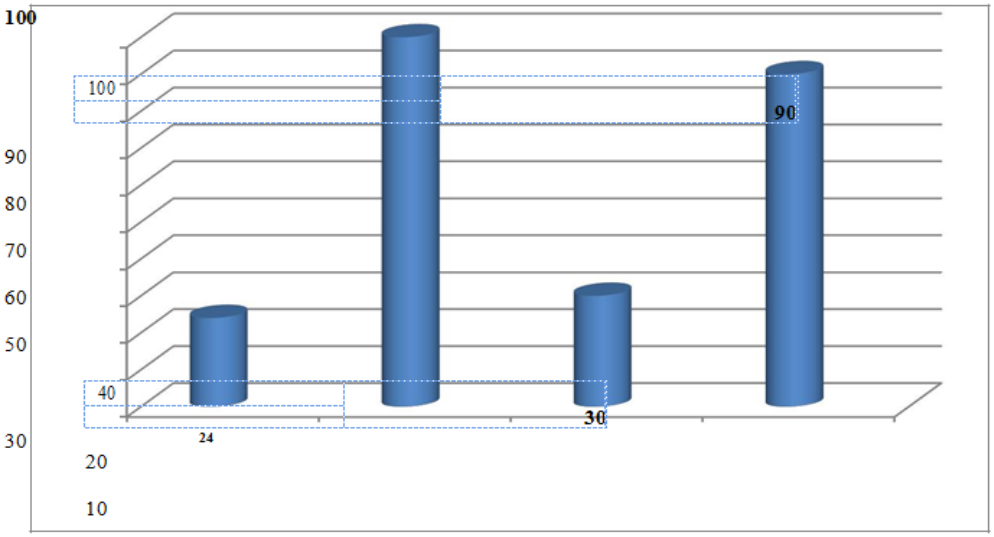
Present study shows 10%LSCS With p value < 0.0001which is statistically significant and consistent with previous studies. The study by kavitha agarwal had incidence of 17% of LSCS with P value of 0.001. The present study is consistent with the study done by Pallavi RK et al with P value of <0.0001. Caesarean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

Vaginal delivery:

Table-18

	Vaginal Delivery	Percentage (%)	P Value
Ramya Krishnamurthy	24	48%	0.025
Pallavi RK	100	100%	<0.0001
Abdul Razaq	30	40%	0.2
Present Study	90	90%	<0.0001

Graph-16



Krishnamurthy et al In the present study 90% of patients delivered vaginally(90patients) 2 patients out of 90 delivered after applying outlet forceps with P value of < 0.0001 consistent with the previous studies.

Maternal Out Come

In the present study, 20 patients had headache out of these 3 members required analgesia. Out of 90 vaginal deliveries 2 patients required outlet forceps for poor maternal efforts. 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.

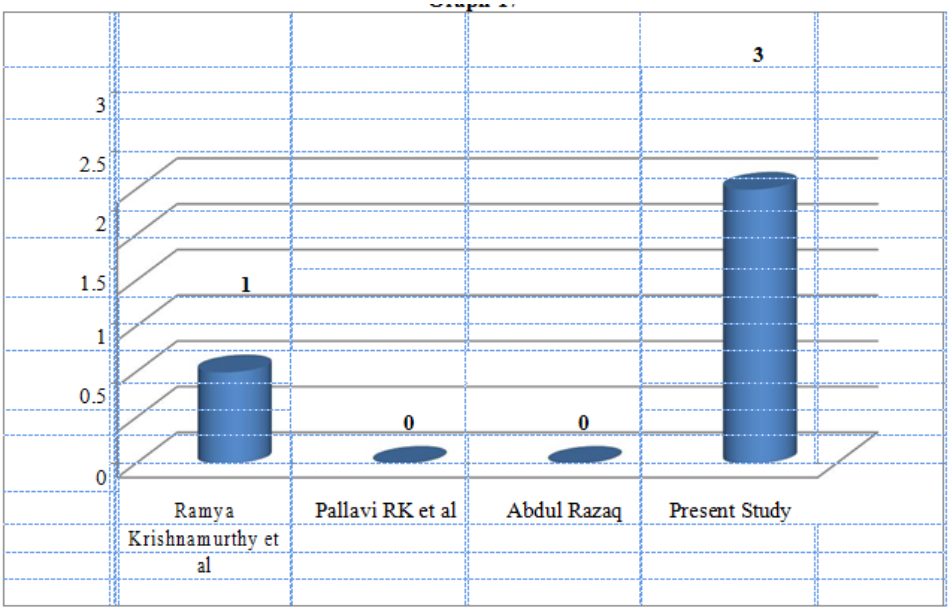
Neonatal Outcome

In the present study there are 3 cases were admitted in NICU in view of low APGAR, those 3 cases were discharged after 3 days and shifted to mother's side. Study done by Ramyakrishnamurthy only 1 case admitted in NICU and discharged after 2 days shifted to mother side.

Table-19

	NICU Admission	P Value
Ramya Krishnamurthy	1(2%)	< 0.05
Pallavi RK	0	< 0.05
Abdul Razaq	0	< 0.001
Present Study	3(3%)	< 0.001

Graph-17



VIII. Summary

100 pregnant women , who gave consent for study and in whom labour induction was indicated were evaluated for study participation. The selected women were induced with vaginal isosorbidemononitrate 40mg at 6th hour interval for 2 doses. Indication of induction were post dated pregnancy,preeclampsia,IUGR,Rh isoimmunisation, congenital anomalies,IUD. Primary outcome measured in the form of mode of delivery, induction to delivery interval, and 90% of vaginal delivery with 10% LSCS rate. The mean induction to delivery interval was 22.23 in vaginal delivery and in LSCS induction to delivery interval was 29.4. The most common indication for caesarean section was fetal distress and also the failed induction.Maternal outcome regarding headache 20 patients had headache only 3 patients required analgesia. Out of 90 vaginal deliveries 2 patients were delivered after applying outlet forceps because of poor maternal efforts. Neonatal outcome regarding NICU admission 3 babies admitted in NICU in view of low APGAR and discharged healthy after 3 days. Hence when compared to prostaglandins in induction of labour the complications like vomitings, diarhoea, fetal distress, tachycardia, bronchospasm, and sometimes unavoidable hypertonic uterine contractions are very minimal with isosorbide mononitrate.

IX. Conclusion

Induction of labour with isosorbidemononitrate is-safe, cost effective, easily available, stored at room temperature, as effective to prostaglandins, less side effects, no hyperstimalation, no abnormal fetal heart rate pattern and easily acceptable to clients and physicians. It can also be safely used in previous LSCS cases, in asthamatic clients. Isosorbidemononitrate 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.

Abbrevations: TG-Term gestation, GA-Gestational age, IUD-Intrauterine death, NVD-Normal vaginal delivery, LSCS-Lower uterine segment cesarean section, Wks-weeks, HRS-Hours, IUGR-Intra uterine growth retardation, ISMN-Isosorbide mononitrate, NOD-Nitric oxide donar.

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