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# INCIDENCE OF MECONIUM STAINED LIQUOR AND FETAL OUTCOME IN LABOUR INDUCED WITH MISOPROSTOL

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**ABSTRACT** Indication for induction is that terminating pregnancy would benefit the mother or her unborn fetus or both vis a vis continuing it.However, induction of labour is not completely free of risks. One has to keep in mind the potential risks such as failure of induction ending in caesarean section, possibilities of preterm delivery and risks of hyperstimulation leading to fetal hypoxia, uterine rupture and even death. Prostaglandins have advantage of ripening the cervix before the onset of labour pains. This study was aimed at finding out the induction and delivery interval and incidence of meconium stained liquor and its significance on the neonatal outcome with prostaglandin ($PGE_1$).

**KEYWORDS :**

## INTRODUCTION

Ideally a pregnancy should reach till completion of term or atleast 37 weeks for the baby to survive outside mother's womb.

Induced labour is one in which pregnancy is terminated artificially, any time after fetal viability is attained, by a method that aims to secure vaginal delivery.

## AIM OF THE STUDY:

To evaluate the incidence of meconium stained liquor and fetal outcome in labours induced with misoprostol vaginally.

## OBJECTIVES:

1. To study duration of labour namely induction – delivery intervals in patients induced with misoprostol.
2. To evaluate fetal prognosis and well being after induction with misoprostol.
3. To compare the incidence of meconium stained liquor and fetal outcome between labour induced with misoprostol with that of those who delivered spontaneously without induction.

## REVIEW OF LITERATURE

### Misoprostol as a Cervical Priming Agent in Gynaecological Procedures:

Misoprostol has been demonstrated to have significant cervical priming effect both in the pregnant and non-pregnant cervix. In gynaecological procedures such as hysteroscopy, misoprostol has successfully ripened the cervix.

### Misoprostol for Induction

Misoprostol was administered orally as 400mcg every 4 hrs until delivery occurs. Pregnancy was successfully terminated in all cases with a mean induction delivery interval of 9 hours 12 minutes.

- The optimal regimen for intravaginal misoprostol has not been firmly established, most clinical trials 25 to 100mcg inserted intravaginally.
- Misoprostol is available as 200mcg tablets, the desired dose is inserted into posterior fornix of vagina. The common dose is 50mcginserted either once or every 4-6 hrs. However inserting 25mcg every 6 hrs is associated with fewer side effects.
- ACOG recommendations (2003)[7] to minimize the risk of hyperstimulation and rupture in patient undergoing cervical ripening or induction in 3rd trimester.

## MATERIAL AND METHODS

This study was conducted at SVS Institute of Medical Sciences from June 2014 to May 2015.

## STUDY DESIGN – PROSPECTIVE STUDY

- It consists of 150 women who were randomly selected and with gestational age of 37-42 wks. These women were divided into 3 groups, with 50 women in each group.
- Group I consist of women who were admitted for induction of labour with uncomplicated pregnancy.
- Group II consists of women who were admitted for induction of labour with complicated pregnancies.
- Group III consists of women who delivered spontaneously without any induction.

## INCLUSION CRITERIA

- Women with 37 completed weeks of gestation.
- Singleton pregnancy with live fetus.
- Vertex presentation
- No contraindication for vaginal delivery
- Clinically and biophysical – normal fetus

## EXCLUSION CRITERIA

- Presence of abruptio placenta, chorioamnionitis
- Fetal distress
- H/o Asthama, glaucoma where prostaglandins are contraindicated
- Fetal malformation & malpresentation

## METHODS:

Women who were taken as part of the study were subjected to basic pelvic assessment to rule out contracted pelvis.

Each woman was assigned a Bishop's Score based on cervical status. 25 mcg (every 4hrs) Misoprostol was placed in the posterior fornix of vagina of each woman.

Fetal heart rate is monitored every 30 minutes along with nature of uterine contractions to detect any uterine tachysystole or hyperstimulation. Pelvic examination is done every 4 hours to note the progress of labour and 25 mg misoprostol is repeated if required.

At about 3-4 cm of cervical dilatation if the membranes have not been ruptured spontaneously an artificial rupture of membranes was done to note the colour of liquor and its correlation with fetal heart rate. Depending on colour of amniotic fluid and fetal heart rate pattern she was either taken for caesarean section or allowed to continue for vaginal delivery.

After the baby is delivered, birth Apgar of 1 minute, 5 minutes and 10 minutes were recorded. Babies with meconium stained liquor and other complications were shifted to NICU for observation of condition till the time of discharge.

All of these women were advised follow up at the outpatient after 1 month of delivery along with the baby.

## CRITERIA FOR SUCCESS

Induction was considered to have succeeded when there is improved Bishop's score resulting in successful vaginal delivery within 24 hrs with healthy fetus capable of surviving exutero.

## FAILED INDUCTION

- If there is no advancement in Bishop's score even after 24 hrs.
- If there is fetal distress
- If there is tachysystole or hyperstimulation

- Latent phase of labour beyond 12-18 hrs.

## RESULTS

This comparative study was conducted from June 2014 to May 2015 during which a total number of 150 term women were studied. Of these 100 women received 25 mcg Misoprostol, 4hrly and the number of doses of misoprostol was decided depending upon the progress of labour and cervical status. The other 50 women were taken as controls.

### Demographic Characteristics

### PARITY

### TABLE – 1

**Group I (n = 50 cases)**

| Parity | Number of cases | Percentage |
|---|---|---|
| Primi | 23 | 46 |
| 2nd Gravida | 20 | 40 |
| 3rd Gravida | 6 | 12 |
| 4th Gravida & above | 1 | 2 |

**Group II (n = 50 cases)**

| Parity | Number of cases | Percentage |
|---|---|---|
| Primi | 25 | 50 |
| 2nd Gravida | 12 | 24 |
| 3rd Gravida | 9 | 18 |
| 4th Gravida & above | 4 | 8 |

**Group III (n = 50 cases)**

| Parity | Number of cases | Percentage |
|---|---|---|
| Primi | 18 | 36 |
| 2nd Gravida | 24 | 48 |
| 3rd Gravida | 5 | 10 |
| 4th Gravida & above | 3 | 6 |

In all three groups multigravida constitute the majority with 278 cases in Group I, 25 cases in Group II and 32 cases in Group III.

### TABLE – 2
### INDICATION FOR USAGE OF MISOPROSTOL

**Group II (n = 50 cases)**

| | Number of cases | Percentage |
|---|---|---|
| PIH | 33 | 66 |
| Post Dates | 13 | 26 |
| PROM | 3 | 6 |
| Oligohydramnios | 1 | 2 |

The most common cause for induction was pregnancy induced hypertension (66%) followed by post dated pregnancy (26%)

### TABLE – 3

Comparison of Bishop's Score based on parity

**Group I (n = 50 cases)**

| Bishop's Score | Primigravida n (percentage) | Multigravida n (percentage) |
|---|---|---|
| Unripe Cervix ≤ 4 | 15 (69.6%) | 5 (15.5%) |
| Ripe Cervix > 4 | 7 (30.4%) | 22 (81.5%) |

$X^2$ – 13.29 P = (0.00026) Significant

- Statistical analysis has been done for this comparative study and the P value obtained is < 0.05 which shows the significance of values.
- Of the total 50 cases 21(42%) were having unripe cervix at the start of induction

- **Group II (n = 50 cases)**

| Bishop's Score | Primigravida n (percentage) | Multigravida n (percentage) |
|---|---|---|
| Unripe Cervix ≤ 4 | 12 (48%) | 4 (16%) |
| Ripe Cervix > 4 | 13 (52%) | 21 (84%) |

$X^2$ – 5.88 P = 0.01529 Significant

Among 50 cases, 16 (32%) were having unripe cervix at the start of induction.

### TABLE – 4

Comparison of Bishop score after 6 hours of inductions based on parity

**Group I**

| Bishop's Score after 6 hrs. | Primigravida n (percentage) | Multigravida n (percentage) |
|---|---|---|
| ≤ 4 | 5 (21.7%) | Nil |
| > 4 | 18 (78.3%) | 27 (100%) |

$X^2$ – 6.52 P = 0.01066 significant

Statistical analysis has been done for this comparative study and the P value obtained is < 0.05 which shows the significance of values.

**Group II**

| Bishop's Score after 6 hrs. | Primigravida n (percentage) | Multigravida n (percentage) |
|---|---|---|
| ≤ 4 | 6 (24%) | 1 (4%) |
| > 4 | 19 (76%) | 24 (96%) |

$X^2$ – 4.15 P = 0.04157 significant

In group I after 6 hrs of induction, out of 16 cases of primigravida with unripe cervix, II cases had better cervical score. Whereas in Group II after 6 hrs of induction out of 12 cases of nullipara 6 had better cervical score.

### TABLE – 5 INDUCTION TO DELIVERY INTERVAL

**Group I**

| Time in Hours | Primigravida n (%) | Multigravida n (%) |
|---|---|---|
| < 4 | 1 (5.3%) | Nil |
| 4 – 8 | 2 (10.5%) | 19 (73.1%) |
| 9 – 13 | 8 (42.1%) | 6 (23.1%) |
| 14 – 17 | 6 (31.6%) | Nil |
| > 17 | 2 (10.5%) | 1 (3.8%) |

$X^2$ – 20.8 P – 0.0003477 Significant

Statistical analysis has been done for this comparative study and the P value obtained is < 0.05 which shows the significance of values.

The average time from induction to vaginal delivery was 11.7 hours in primigravida and 7.4 hours in multigravida.

### INDUCTION TO DELIVERY INTERVAL

**Group II**

| Time in Hours | Primigravida n (%) | Multigravida n (%) |
|---|---|---|
| < 4 | 1 (5.3%) | Nil |
| 4 – 8 | 5 (26.3%) | 14 (63.6%) |
| 9 – 13 | 8 (42.1%) | 8 (36.4%) |
| 14 – 17 | 4 (21%) | Nil |
| > 17 | 1 (5.3%) | Nil |

$X^2$ – 10.1 P – 0.03881 Significant

Statistical analysis has been done for this comparative study and the P value obtained is < 0.05 which shows the significance of values.

The average time from induction to delivery was 10.1 hours in primigravida and 7.5 hours in multigravida.

### TABLE – 6 MODE OF DELIVERY Group I

| Mode of Delivery | Primigravida n (%) | Multigravida n (%) |
|---|---|---|
| SPVD | 18 (78.3%) | 25 (92.6%) |
| Outlet Forceps | 1 (4.3%) | Nil |
| Caesarean Section | 4 (17.4%) | 2 (7.4%) |

(SPVD – Spontaneous Vaginal Delivery)
$X^2$ – 1.346 P – 0.2466, Not significant

The most common indication for caesarean section was failure to progress and thick meconium stained liquor found in 5 cases. One underwent caesarean section for fetal distress and baby was born with good Apgar.

**Group II**

| Mode of Delivery | Primigravida n (%) | Multigravida n (%) |
|---|---|---|
| SPVD | 17 (68%) | 21 (84%) |
| Outlet Forceps | 2 (8%) | 1 (4%) |
| Caesarean Section | 6 (24%) | 3 (12%) |

$X^2$ – 1.754 P – 0.4159, Not significant

The most common indication for caesarean section was failure to progress found in 4 cases. Whereas in other 5 cases, fetal distress (3 cases) and thick meconium stained liquor were indications for caesarean section.

**TABLE – 7 NUMBER OF DOSES OF MISOPROSTOL (25 mcg)**

**Group I**

| Number of Doses | Primigravida n (%) | Multigravida n (%) |
|---|---|---|
| 1 Dose | 2 (10.5%) | 8 (32%) |
| 2 Doses | 7 (36.9%) | 17 (68%) |
| 3 Doses | 10 (52.6%) | Nil |
| ≥ 4 Doses | Nil | Nil |

$X^2$ – 17.27 P – 0.001 Significant

The average number of doses required for vaginal delivery in case of primigravida is 2.4, whereas in case of multigravida it is 1.7 doses.

**Group II**

| Number of Doses | Primigravida n (%) | Multigravida n (%) |
|---|---|---|
| 1 Dose | 3 (15.8%) | 8 (36.4%) |
| 2 Doses | 10 (52.6%) | 9 (40.9%) |
| 3 Doses | 6 (31.6%) | 5 (22.7%) |
| ≥ 4 Doses | Nil | Nil |

$X^2$ – 2.209 P – 0.3314 Not Significant

The average number of doses required for vaginal delivery in case of primigravida is 2.1, whereas in case of multigravida it is 1.4.

**TABLE – 8 MATERNAL COMPLICATIONS**

| Complication | Group I n (Percentage) | Group II n (Percentage) | Group III n (Percentage) |
|---|---|---|---|
| Hyperstimulation | 1 (2%) | 1 (2%) | 1 (2%) |
| Tachysystole | 2 (4%) | 3 (6%) | 1 (2%) |
| Diarrhoea | 3 (6%) | 4 (8%) | 1 (2%) |
| Vomitings | Nil | 1 (2%) | Nil |
| Hyperpyrexia | 1 (2%) | 2 (4%) | Nil |

Prostaglandin related side effects were noted in 4 cases of Group I and 7 Cases of Group II. In case of control group hyperstimulation is noted in one case and tachysystole in one case.

**TABLE – 9**
**INCIDENCE OF MECONIUM STAINED LIQUOR**

| MSL | Group I n (%) | Group II n (%) | Group III n (%) |
|---|---|---|---|
| Light | 5 (10%) | 8 (16%) | 2 (4%) |
| Thick | 2 (4%) | 7 (14%) | 2 (4%) |

$X^2$ – 2.748 P – 0.2531 Not Significant

Statistical analysis has been done for the comparative study and the P value obtained is > 0.05 which shows there is no significance of values.

The total incidence of meconium stained liquor was about 14% in case of Group I and all these babies are born with good Apgar Scores. In case of Group II the total incidence of meconium stained liquor is 30% and out of these 7 babies had low Apgar.

In Group III, meconium stained liquor was found in 4 cases (8%) and out of these 3 babies had low Apgar scores.

**TABLE – 10**

**NEONATAL COMPLICATIONS**

| | Group I n (%) | Group II n (%) | Group III n (%) |
|---|---|---|---|
| Birth weight < 2 kg | Nil | 3 (6%) | 1 (2%) |
| 2 – 2.5 Kg | 19 (38%) | 18 (36%) | 14 (28%) |
| 2.6 – 3 Kg | 22 (44%) | 28 (56%) | 30 (60%) |
| > 3 Kg | 9 (18%) | 1 (1%) | 4 (8%) |
| Apgar Scores <7 | 3 (6%) | 8 (16%) | 3 (6%) |
| > 7 | 47 (94%) | 42 (84%) | 47 (94%) |
| Admission to NICU | 8 (16%) | 14 (28%) | 3 (6%) |

Majority of babies were admitted to NICU in view of meconium stained liquor and the other reasons being low Apgar, low birth weight and delayed cry.

**DISCUSSION**

Prostaglandins have dual advantage of ripening the cervix as well as inducing myometrial contractility.

25 mcg of Misoprostol kept intravaginally was found to be safe, efficacious and with low incidence of side effects.

**TABLE 1 (PARITY)**

| AUTHORS | NULLIPARA | MULTIPARA |
|---|---|---|
| Tan et al(2005) | 55.2% | 44.8% |
| Calder et al (2008) | 56% | 44% |
| Current study | 44% | 56% |

**TABLE 2**
**INDICATION FOR USAGE OF MISOPROSTOL**

| | Tan et al (2005) | Calder et al (2008) | Current study |
|---|---|---|---|
| PIH | 10.3% | 9% | 66% |
| Post Dates | 32.8% | 75% | 26% |
| PROM | - | - | 6% |
| Oligohydramnios | 19% | - | 2% |
| IUGR | 12.1% | 2% | - |
| Others (GDM, APH, social) | 25.8% | 14% | - |

**TABLE 3 & 4**

In the current study of the total 100 cases in whom induction was done unripe cervix was present in 37 cases (37%) before induction and in 12 cases (12%) after 6hrs of induction.

**TABLE 5**
**INDUCTION DELIVERY INTERVAL**

| Authors | Duration |
|---|---|
| Marguiles et al (1992)[9] | 6.7 ± 4.4 hrs |
| Sanchez Ramos (1993)[10] | 11 hrs |
| Kadanali et al (1996)[12] | 9.2 ± 2.4 hrs |
| Wing et al (1996)[17] | 15 ± 8 hrs |
| Chuck et al (1999)[19] | 11.4 ± 5.9 hrs |
| Kolderup et al (1999)[20] | 19.8 ± 11.5 hrs |
| Tan et al (2005)[99] 25 mcg single dose | 21.8 ± 1.5 hrs |
| Tan et al (2005)[99] 25 mcg 2 doses 6 hrly | 19.5 ± 1.3 |
| Khoury et al (2001)[98] | 21.3 |
| Calder et al (2008)[95] 25 mcg 5 hrly | 24.67 |
| Current study | 9.1 ± 2.2 hrs |

There is wide variation in induction delivery interval between different trials. Variations in the dose of drug used, dosing interval and oxytocin augmentation might have contributed to the difference.

Our study is comparable to that of Kadanali et al, Sanchez Ramos et al and Chuck et al with the induction delivery interval falling in between 8-12 hrs.

In our study out of 100 cases induced with Misoprostol almost 85 cases (85%) delivered by spontaneous vaginal delivery.

**TABLE 6**
**CAESAREAN SECTION RATES AMONG TRIALS**

| Authors | Caesarean Section Rate |
|---|---|
| Sanchez Ramos et al (1993)[10] | 21.9% |
| Tan et al (2005)[99] | 17.2% |
| Wing et al (1996)[17] | 14.7% |
| Moraes Filho et al (2005)[93] | 24.19% |
| Feitosa et al (2006)[92] | 30.6% |
| Bartusevicius et al (2006)[91] | 20% |
| Caliskan et al (2007)[90] | 17.5% |
| Nassar et al (2007)[94] | 28.2% |
| Calder et al (2008)[95] | 28% |
| Praget et al (2008)[96] | 28% |
| Current study | 15% |

The overall caesarean section rate was comparable to other studies and high proportion of these were done due to failure of progressive of labour.

Caesarean section rate was comparatively more in nulligravida explained by unfavorable cervix as well as undiagnosed pelvic abnormalities.

**TABLE 7 MULTIPLE DOSING REGIMEN**

| Authors | Misoprostol Dosing regimen (intravaginal) | Average number of doses |
|---|---|---|
| Sanchez Ramos (1993)[10] | 50 mcg, 4th hrly | 1.4 |
| Wing et al (1996)[17] | 50 mcg, 3rd hrly | 2.4 $\pm$ 1.3 |
| Wing et al (1996)[17] | 25 mcg, 3rd hrly | 2.6 $\pm$ 1.9 |
| Chuck et al (1999)[19] | 50 mcg, 4th hrly | 1.8 $\pm$ 1.1 |
| Kolderup et al (1999)[20] | 50 mcg, 4th hrly | 1.4 $\pm$ 1 |
| Caliskan et al (2005)[90] | 50 mcg, 4th hrly | Not stated |
| Feitosa et al (2006)[92] | 25 mcg, 6th hrly | 2.8 $\pm$ 1.8 |
| Nassar et al (2007)[94] | 50 mcg, 4th hrly | Not stated |
| Current study | 25 mcg, 4th hrly | 2.1 $\pm$ 1.1 |

Our study is comparable to Wing et al who had used 25 mcg Misoprostol intravaginally and the average number of doses required being 2.6 + 1.9 whereas in other studies the average number of doses required was lesser in comparison to our study. This can be explained by the higher dose (50 mcg) used by them.

**TABLE 8**
**INCIDENCE OF TACHYSYSTOLE AND HYPERSTI MULATION**

| Authors | Dose of Misoprostol | Tachysystole | Hyperstimulation |
|---|---|---|---|
| Marguiles et al (1992) | 50 mcg single dose | 17% | Nil |
| Wing et al (1996) | 50 mcg 3rd hrly | 37% | 7% |
| Wing et al (1996) | 25 mcg 3rd hrly | 17% | 6% |
| Caliskan et al (2005) | 50 mcg 4th hrly | 3.75% | 1.25% |
| Maracas Filho et al (2005) | 25 mcg 6th hrly | 4.8% | 3.2% |
| Fietosa et al (2006) | 25 mcg 6th hrly | 6.6% | 1.3% |
| Bartusevicius et al (2006) | 25 mcg 4th hrly | 4.2% | 7.14% |
| Nassar et al (2007) | 50 mcg 4th hrly | 14.1% | 9.4% |
| Calder et al (2008) | 25 mcg 4th hrly | 3% | 6% |
| Current study complicated | 25 mcg 4th hrly | 6% | 2% |
| Uncomplicated | 25 mcg 4th hrly | 4% | 2% |

Current definition of Tachysystole according to ACOG[97] is more than five contractions in 10 minutes averaged over 30 minute windows.

With exception of Wing et al study, there is low incidence of hyperstimulation and tachysystole.

The low incidence of tachysystole and hyperstimulation in our study can be explained by the low dosage (25 mcg) used for induction.

The following table compare the incidence of meconium stained liquor in various trails.

**TABLE 9**
**INCIDENCE OF MECONIUM STAINING**

| Authors | Incidence of MSL |
|---|---|
| Kadanali et al (1996) | 10.7% |
| Wing et al (1996) 50 mcg regimen | 27.9% |
| Wing et al (1996) 50 mcg regimen | 17.4% |
| Chuck et al (1999) | 8% |
| Tan et al (2005) 25 mcg single dose | 3.5% |
| Tan et al (2005) 25 mcg 2 doses 6 hrly | 10.4% |
| Prager et al (2008) | 26% |
| Current study | |
| Uncomplicated | 14% |
| Complicated | 30% |

In our study thick meconium was found in 2 cases and thin meconium is 5 cases. None of these neonates has meconium aspiration syndrome.

Wing et al reported a higher incidence of meconium with 50 mcg regimen.

In our study none of the infants had low Apgar scores but all of them were admitted in NICU as it was a policy to routinely admit neonates with meconium stained liquor in our hospital.

Previous reviews have shown a trend towards more meconium passage with misoprostol than with other agents. They have postulated that certain myometrial stimulants (Misoprostol) may cross the placenta to stimulate smooth muscle of fetal bowel and cause meconium passage. They also cause relaxation of sphincters of GIT.

Chuck F et al (1985)100 stated that it is unlikely that small amount of hydrogenated castor oil found in misoprostol tablets would have any pharmacological effect.

Matonhodze BB et al (2002)101 has shown invitro effect of misoprostol on isolated rat ileum as well as myometrium.

In Group II (complicated) thick meconium was found in 7 cases and thin meconium in 8 cases out of these 8 babies had low Apgar. This increased incidence can be explained by the inherited pathology of associated complications like PIH, post dates and others.

In Group III (without induction) the incidence of MSL was 8% with thick meconium in 2 cases and light meconium in 2 cases and out of these 3 had low Apgar. The main cause being cord around the neck and unknown chronic pathology.

The current study shows that incidence of meconium is higher in labour induced with misoprostol especially in complicate pregnancies.

Although it has been demonstrated that the passage of meconium is a very late phenomenon after hypoxia has occurred, it is far more common to note presence of meconium in absence of hypoxia.

It is often found that misoprostol tablet was still present in the vagina even after the drugs effect was clinically apparent. The explanation offered by Chuck et al is that cellulose matrix which is formulated to give misoprostol stability at room temperature gets left behind while drug is absorbed.

Ramsey et al (2000)[102] stated that vaginal pH does not appear to affect the efficacy of vaginally applied misoprostol tablets.

Sanchez-Ramos et al (2002)[103] in a study showed no benefit from moistening misoprostol prior to insertion with 3% acetic acid versus dry tablets.

Ghindi and Spong et al (2001)[104] Oyelese an Coworkers (2006)105 stated that the presence of meconium in amniotic fluid is relatively common and incidences range from 12-20%.

## CONCLUSION

It can be concluded from the study that misoprostol is an effective priming and labour inducing agent that fulfills all the criteria of an ideal inducing agent.

The higher incidence of meconium associated with misoprostol is due to the action of the drug on the gastrointestinal tract of the fetus and not due to hypoxia vagal stimulation by cord or head compression may be associated with in meconium passage in absence of fetal distress. It is also not significant compared to the control group.

The incidence of low Apgar scores of the neonate is similar in uncomplicated pregnancies induced with misoprostol and the control group. Hence the neonatal outcome is satisfactory with misoprostol.

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