Obstetric and Neonatal Outcome of Induction of Labour at term with Sublingual Misoprostol as Compared to Intravaginal Misoprostol

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Abstract
Background: Misoprostol, a synthetic prostaglandin E1 analog, has been given both orally and vaginally for induction of labor at term. Due to the difference in pharmacokinetics of sublingual as compared to vaginally administered misoprostol, hence this study.
Aim: To study Obstetric and Neonatal outcome of induction of labour with sublingual misoprostol as compared to intravaginal misoprostol.
Method: 120 women with singleton pregnancy with no Cephalo-pelvic disproportion were randomized to receive Tab. Misoprostol 25mcg at 4 hour interval by vaginal route (60 patients) and sublingual route (60 patients).
Results: With sublingual route of administration the number of doses of misoprostol used was significantly lower [p<0.05], reduced induction delivery interval [p<0.05], reduced pelvic examinations [p<0.05] when compared to vaginal route of administration. No difference in maternal and foetal complications.

Introduction
Induction is defined as stimulation of contractions before the spontaneous onset of labor, with or without ruptured membranes. When the cervix is closed and uneffaced, labor induction commences with cervical ripening, a process that generally employs prostaglandins to soften and open the cervix. Some centuries ago, fetal death was the only indication for labor induction. Now, in modern obstetrics, induction of labor at term in a live foetus with successful outcome is a challenge to obstetrician. Now-a-days the rate of labor induction varies in different centers. Despite a large body of literature, the optimal mode of induction for this purpose has yet to be established.
There is no preferred method for induction and it depends on institute protocol. There is increased risk of failed induction and caesarean section in presence of unfavorable cervix and hence cervical ripening is needed.

**Aim of the Study**
To study obstetric and neonatal outcome of induction of labor at term with sublingual misoprostols compared to intravaginal misoprostol.

**Objective of the Study**
To determine efficacy and safety of sublingual administration of misoprostol compared with vaginal misoprostol at or after term pregnancy in a women with a live foetus.

**Materials and Methods**
This study was conducted in Great Eastern Medical School and Hospital, Ragolu, Srikakulam, Andhra Pradesh in the department of obstetrics and Gynaecology during the period of December 2018 to June 2019 (6 months). 120 antenatal women admitted in the ward were included in this study.

**Inclusion Criteria**
1. Singleton pregnancy
2. Live foetus
3. Term gestation - 37 completed weeks or more with a medical or obstetric indication for induction including gestational age >/ 41 weeks (post dated pregnancy), prelabour rupture of membranes (PROM) ,gestational hypertension, mild pre eclampsia ,gestational diabetes mellitus (GDM) .
4. Primigravida and multiparous women
5. Cephalic presentation
6. An unfavourable cervix (bishop score <5 )
7. Reassuring foetal heart tracing.

**Exclusion Criteria**
1. Multiple gestation
2. Malpresentation ( other than cephalic)
3. Previous uterine surgery (hysterotomy, myomectomy, caesarean section)
4. Contraindications for the use of prostaglandins like asthma
5. Grand multipara ( >5)
6. Need for immediate delivery
7. Chorioamnionitis
8. Active Vaginal bleeding
9. Ultrasonically confirmed severe oligohydramnios, placenta praevia and macrosomia.
10. Abnormal doppler velocimetry

**Methodology**
**Group A:** Sublingual misoprostol [S]
60 patients for labour induction were randomly allocated for 25 microgram sublingual misoprostol administration every 4th hourly for maximum of 6 doses.

**Group B:** vaginal misoprostol [V]
60 patients for labour induction were randomly allocated for 25 microgram vaginal misoprostol administration every 4th hourly for maximum of 6 doses.

Further induction is withheld if women had regular contractions (3-4 contractions, lasting for more than 40 seconds in 10 minute duration,goes into active labor (4 cms) or cervix is favourable for amniotomy (bishop score >/8). Oxytocin was administerd by diluting inringer lactate solution and started as IV drip ,not earlier than four hours of last dose of misoprostol.

Continuous fetal cardiotocography was used throughout the study.
All episodes of hyperstimulation were noted and included in study. Recognised episodes were managed by maternal repositioning, stopping the oxytocin infusion, maternal hydration and oxygenation. Women were advised to spit out the medication in sublingual group and in vaginal group tablet was removed from vagina if possible.
Failure of induction is considered if women fails to enter active phase of labor following six doses of misoprostol through any route and it is considered as an indication for section.
Results and Analysis

Table 1 - Comparison of age (in years) and parity

|                  | Group A [S]     | Group B [V]     |
|------------------|-----------------|-----------------|
| Age [years]      | 25.07 ± 3.97    | 25.08 ± 3.70    |
| Primi gravida    | 42[70]          | 43[71]          |
| Multigravida     | 18[30]          | 17[29]          |

Table 1 shows mean and standard deviation of age and parity in both groups. Primigravida and multigravida were shown in number [percentage]. No significant difference found in both groups.

Table 2: Comparison of bishop score

| Bishop score     | Group A [S]  | Group B [V]  | P value |
|------------------|--------------|--------------|---------|
|                  | 4.03±0.81    | 4.05±0.59    | 1.00    |

Table 2 shows mean and standard deviation of Bishop score in both groups. No significant difference among the groups.
Table 3: Comparison of indication for induction

| Group | Post term (>41 weeks) | Prelabour rupture of membrane | Mild preeclampsia | Gestational diabetes mellitus |
|-------|------------------------|-------------------------------|-------------------|-----------------------------|
| A     | 28 [46.7]              | 17 [28.3]                    | 11 [18.3]         | 4 [6.7]                     |
| B     | 25 [41.7]              | 18 [30]                      | 14 [23.3]         | 3 [5]                       |

Table 5: Comparison of total doses of misoprostol

| Group | Total doses of misoprostol | P value |
|-------|---------------------------|---------|
| A     | 1.85±1.02                 | <0.05   |
| B     | 2.3±1.2                   |         |

Table 5 shows mean and standard deviation of total doses of misoprostol in both groups. Misoprostol used was significantly lower in sublingual route than vaginal route [p<0.05].

Table 6: Comparison of number of vaginal examination

| Group | Number of pelvic examination | P value |
|-------|------------------------------|---------|
| A     | 5.75±2.05                    | <0.05   |
| B     | 8.22±2.04                    |         |

Table 7 shows mean and standard deviation of number of pelvic examination in both groups. Pelvic examination was significantly lower in sublingual route misoprostol than vaginal route of administration [p<0.05].
Table 8: Comparison of induction delivery interval [minutes]

|                      | Group A [SLM] | Group B [VM] | P value |
|----------------------|---------------|--------------|---------|
| Induction delivery   | 650.98±250.83 | 779.7±269.97 | <0.05   |
| interval (min)       |               |              |         |
| Induction vaginal    | 597.42±186.47 | 720±195.47   | <0.005  |
| delivery interval (min)|            |              |         |

Table 8 shows mean and standard deviation of induction delivery interval including caesarean section [minutes] and induction vaginal delivery interval [minutes] in both groups. Induction delivery interval including caesarean section and induction vaginal delivery interval was significantly lower in sublingual route misoprostol than vaginal route of administration [p<0.05]

Table 9: Comparison of mode of delivery

|                      | Group A [SLM] | Group B [VM] | RR [CI 95%] |
|----------------------|---------------|--------------|-------------|
| Spontaneous vaginal delivery | 49[81.7] | 45[75] | 1.09 [ 0.90 – 1.32] |
| Instrumental vaginal delivery | 3[5] | 5[8.3] | 0.6 [ 0.15 – 2.40] |
| Caesarean section     | 8[13.3] | 10[16.7] | 0.8 [ 0.34 - 1.89] |

Table 9 shows number [percentage] of mode of delivery in both groups. There was no significant difference among the groups.
Table 10 Comparison of indication for caesarean section

| Indication                        | Group A [SLM] | Group B [VM] | RR [CI 95%] |
|-----------------------------------|---------------|--------------|-------------|
| Fetal distress                    | 2[25]         | 3[30]        | 0.83 [0.18 – 3.84] |
| Non progress of labour / arrest of labour | 4[50]       | 4[40]        | 1.25 [0.45 – 3.49] |
| Failed induction                  | 2[25]         | 3[30]        | 0.83 [0.18 – 3.84] |

Table 10 shows number [percentage] of indication for caesarean section in both groups. There was no significant difference in fetal distress, non progress of labour / arrest of labour and failed induction among the groups.

Chart 10 Comparision for indication for induction

Table 12 shows number [percentage] of maternal uterine complication in both groups. There was no significant difference among the groups.
Table 4 shows number [percentage] of indication for induction in both groups. There was no significant difference among the group.

Chart 4 shows percentage of indication of induction.

Table 12 Comparison of birth weight of baby [kilograms]

| Baby birth weight [kgs] | Group A [SLM] | Group B [VM] | P value |
|------------------------|---------------|--------------|--------|
| 2.89±0.23              | 2.90±0.19     | 0.83         |

Table 12 shows mean and standard deviation of baby birth weight [kilograms] in both groups. There was no significant difference among the groups.
Table 7: Comparison of number of pelvic delivery in < 24 hours of induction

| Vaginal delivery < 24 hours | Group A [SLM] | Group B [VM] | RR [CI 95%] |
|-----------------------------|---------------|---------------|-------------|
|                             | 52 [86.7]     | 50 [83.3]     | 1.04 [0.89 - 1.20] |

Table 6 shows number [percentage] of vaginal delivery in <24 hours in both groups. There was no significant difference among the groups.

Table 13: Comparison of fetal complications

|                          | Group A [SLM] | Group B [VM] | RR [CI 95%] |
|--------------------------|---------------|---------------|-------------|
| Meconium passage         | 3 [5]         | 3 [5]         | 1 [0.21 – 4.76] |
| Apgar score < 7 at 5 minutes | 2 [3.3]      | 2 [3.3]      | 1 [0.15 – 6.87] |
| NICU admission           | 1 [1.6]       | 2 [3.3]       | 0.5 [0.05 – 5.37] |

Table 13 shows number [percentage] of fetal complication in both groups. There was no significant difference among the groups.
Discussion
In our study we had included 120 antenatal women by randomization technique. There was no difference in age, parity, gestational age, bishop score and indication of induction among the both groups in our study. The results had showed that 25μg of sublingual misoprostol administration resulted in significantly shorter induction to delivery interval \[p <0.005\], with a lower number of misoprostol doses required \[p<0.01\] and lesser number of pelvic examination \[p<0.05\] required as compared with those administered 25 μg of vaginal misoprostol.

In present study no statical significant difference was found in age group, parity, induction to delivery interval, which is similar in Jahroni bahia namavar et al\(^5\) study (2009-2011), Ayathi et al\(^6\) study (2007-2008).

In present study, there is no statistical significant difference in bishop score in both groups.Similar results were observed in jahroni study but In Ayathi etal study , bishop score was found higher in sublingual when compared to vaginal group.

In Tang et al.\(^7\) study, the sublingual route has been shown to produce significantly higher serum peak concentration of misoprostol than either oral or vaginal administration.

A recently published study evaluated the effects of misoprostol on uterine contractility following different routes of administration\(^10\). The sublingual application of misoprostol had rapid effect on uterine contractility as oral administration and the bioavailability was similar to vaginal administration. We had administered sublingual dosage every 4\(^{th}\) hourly. These findings may explain the significant reduction in induction delivery interval with sublingual misoprostol.

Our study had showed a significant reduction in number of pelvic examination before delivery. Patient would be comfortable when number of pelvic examination was reduced. We had not taken satisfaction parameter in our study as it was beyond our scope.

Nasser et al\(^11\) had studied on patient satisfaction criteria and concluded that sublingual misoprostol was convient and satisfactory route. This route of administration may reduce the chance of infection particularly in PROM cases because of less number of vaginal examinations required. On considering these facts and our observation on significant decrease in number of pelvic examination sublingual route may be a satisfactory route of administering misoprostol.

Conclusion
Sublingual dosing for labour induction is attractive because of ease of administration, less frequent need for vaginal examination, possibility of its use in case of vaginal bleeding or ruptured membranes and better patient acceptability. We believe further studies on safety with large number of women need to be conducted before we
advocate sublingual misoprostol as routine labour induction agent.

References
1. Gary, F. Williams Obstetrics. (25 ed.). United States Of America: ; c2014.
2. Dutta, D.C. Text book of obstetrics including contraception and perinatology. (7 th ed.). United States Of America: Hiralal konar; 2013.
3. Hofmeyr GJ. Induction of labour with an unfavourable cervix. Best Pract Res Clin Obstet Gynaecol 2003; 17:777–94.
4. Jahromi BN, Poorgholam F, Yousefi G, Salarian L. Sublingual versus Vaginal Misoprostol for the Induction of Labor at Term: A Randomized, Triple-Blind, Placebo-Controlled Clinical Trial. Iran J Med Sci. 2016;41(2):79–85.
5. Ayati S, Vahidroodsari F, Farshidi F, Shahabian M, Afzal Aghae M. Vaginal versus sublingual misoprostol for labor induction at term and post term: a randomized prospective study. Iran J Pharm Res. 2014;13(1):299–304.
6. Tang OS, Schweer H, Seyberth HW, Lee SW, Ho PC. Pharmacokinetics of different routes of administration of misoprostol. Human Reproduction 2002; 17:332–6.
7. Aronsson, M. Bygdeman and K. Gemzell- Danielsson. Human Reproduction 2004; Vol.19 No.1:81-84.
8. Nassar AH, Awwad J, Khalil AM, Abu-Musa A, Meho G, Usta IM. A randomized comparison of patient satisfaction with vaginal and sublingual misoprostol for induction of labour at term. BJOG 2007; 114:1215–21.