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Efficacy of oral and vaginal misoprostol for pre-induction cervical ripening in term primigravida undergoing induction of labor: a prospective study

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ABSTRACT

Background: Induction of labor, traditionally used for fetal demise, now utilizes various mechanical and pharmacological methods like Misoprostol for cervical ripening, crucial for successful induction. This study compares oral and vaginal Misoprostol (25µg) for pre-induction cervical ripening at term, evaluating their efficacy, safety, and associated maternal and neonatal outcomes.
Methods: This study assesses and compares the effectiveness of oral and vaginal misoprostol for pre-induction cervical ripening in full-term primigravida women undergoing labor induction. It primarily evaluates the improvement in the Modified Bishop's score, aiming for a score above 6, and secondarily examines induction-to-delivery interval and required misoprostol dosage. Conducted at tertiary care in Pune, this prospective comparative observational study spans from August 2021 to July 2022. Eligible women, divided into two groups based on the obstetrician's preference, receive either oral or vaginal misoprostol, with labor management and outcomes closely monitored and analyzed using IBM SPSS Statistics 26.0.
Results: Both oral and vaginal Misoprostol groups, comprising exclusively primigravida patients, had similar mean gestational ages and induction to delivery intervals (21 hours). The oral group achieved a favourable Bishop score (>6) faster (8 hours) than the vaginal group (12 hours), despite requiring more frequent dosing, and both groups showed comparable modes of delivery and indications for Caesarean sections.
Conclusion: This study found oral and vaginal Misoprostol equally effective for preinduction cervical ripening, with both showing similar delivery times and modes, despite more frequent dosing in the oral group.

Keywords: Misoprostol, Cervical ripening, Labor induction, Primigravida

INTRODUCTION

Induction of labor is a routine obstetric procedure performed to initiate labor artificially. This intervention is recommended when the advantages of proceeding with labor induction outweigh the risks associated with continuing the pregnancy, benefiting either the mother or the fetus.[1] Insufficient cervical ripening is a considered as barrier to achieving a successful labor induction and a timely delivery.[2-4]

Historically, induction was mainly performed in cases of fetal death. Today, various mechanical and pharmacological methods exist for induction, with pre-induction cervical ripening being crucial for success. Common cervical ripening methods include PGE1 and PGE2 analogues, intracervical foley's insertion, and amniotomy.[5] One relatively new option is misoprostol, a prostaglandin E1 analogue, known for its cervical ripening and uterotonic properties. Although initially FDA-approved for peptic ulcer treatment, its use in pregnancy was approved in 2002. Misoprostol is cost-effective, stable, and can be administered orally, sublingually,

vaginally, buccally, or rectally.[6,7] Comparing oral and vaginal administration, oral misoprostol reaches maximum plasma concentration faster but is eliminated quicker than vaginal misoprostol. Vaginal application has been validated but comes with potential drawbacks like repeated digital examinations and increased infection risk. Given these considerations, this study aims to compare the efficacy and safety of oral vs. vaginal misoprostol (25µg) for pre-induction cervical ripening at term, as well as assess maternal and neonatal complications and side effects in both groups.[8]

METHODS

The aim of this study is to assess and compare the effectiveness of oral and vaginal misoprostol in achieving pre-induction cervical ripening among full-term primigravida women who are undergoing labor induction. The primary objective is to evaluate the efficacy of oral and vaginal misoprostol in terms of improving the modified Bishop's score, with the desired outcome being a score greater than 6.

Additionally, there are secondary objectives, including the assessment of the induction-to-delivery interval and the dosage of misoprostol required in each group. This research aims to provide valuable insights into the most effective method for pre-induction cervical ripening in this specific population.

Study site

The research will take place at a tertiary care Hospital and Research Centre in Pune, spanning from August 2021 to July 2022.

Study design

This study adopts a prospective comparative observational approach within a hospital setting.

Inclusion criteria

Inclusion criteria for this study include several key parameters like participants must be primigravida, indicating first-time pregnant women. The pregnancy should involve a single live foetus positioned cephalically, and patients must be at term, specifically beyond 37 weeks of gestation. Clinical assessment must confirm the presence of an adequate pelvis, and a reactive Non-Stress Test (NST) result is mandatory for inclusion.

Exclusion criteria

The exclusion criteria are defined as individuals with a scarred uterus, those experiencing antepartum haemorrhage, or displaying cervical dilation exceeding 2.5 cm will not be eligible. Additionally, any evidence of fetal distress or a non-reassuring NST, as well as patients with a contracted pelvis, will be excluded from participation in the study.

Study population

The patients who are admitted to the labor room for induction of labor, at Deenanath Mangeshkar Hospital and Research Centre, Pune.

Sample Size and justification

The formula for calculating the sample size (nB) is expressed as follows: $n= (1 + 1/\kappa) [\sigma(Z\alpha + Z1-\beta) / (\mu A - \mu B)]^2$, where, n is the required sample size (nB) for each group, σ is the SD of the outcome variable, the means (µA and µB) of the two study groups, the desired power (1−β) and level of significance (α) for the statistical analysis.

To detect a difference of 0.67 units in the improvement of Bishop's score at 6 hours between the two induction methods (oral misoprostol, mean 1.40, and vaginal misoprostol, mean 2.06 for cervical ripening) with a standard deviation of 1, 80% power, and a significance level of α=5%, a minimum sample size of 36 pregnant women at term in each group is required.

Statistical methods

Statistical analysis was done using IBM SPSS Statistics 26.0 software. Quantitative variables were presented as mean and standard deviation (SD), while qualitative variables were presented as frequency and percentage. Unpaired Student's t-test was used to assess the significance of differences between means for quantitative data. For the comparison of categorical variables, chi-square tests and Fisher's exact test was used. Significance will be considered for p values<0.05.

Methodology

The study was conducted at Deenanath Mangeshkar Hospital (from August 2021 to July 2022) and involves ANC registered patients meeting inclusion exclusion criteria. The eligible women are divided into Group A and B based on the obstetrician's preference. Group A receives oral misoprostol (25 mcg every 2 hours, max 8 doses), with the next dose deferred for optimal contractions or a Bishop score >6. Group B gets vaginal misoprostol (25 mcg every 4 hours, max 6 doses), with similar deferral criteria. Labor is managed with expectant methods, amniotomy, or oxytocin as needed.

The primary outcome, improvement in cervical status, is measured by the Modified Bishop’s score. Patient progress is monitored for Bishop’s score, uterine contractions, and fetal heart rate. If primary outcomes are not met after 8 misoprostol doses or due to fetal distress, interventions like LSCS or other labor augmentation methods are considered. Outcomes, including misoprostol dosage, time

to initiate contractions, and operative interventions, will be compared between groups.

RESULTS

In the study, the average gestational age (mean±SD) for Group A was 39.81±0.79 weeks and for Group B, it was 39.81±0.54 weeks. The range of gestational ages was 37.57-43.43 weeks in Group A and 37.71-40.43 weeks in Group B. No significant difference was observed in the mean gestational age among the two groups (p>0.984) (Table 1)

Table 1: Between group comparison of mean gestational age.

Group	n	Gestational age (weeks) (Mean±SD)	P value
A (Oral)	55	39.81±0.79	0.984
B (Vaginal)	55	39.81±0.54	

Among the 55 cases in Group A, 37 (67.3%) had a Bishop's score of less than 4, while 18 (32.7%) had a score greater than 4 at the time of induction of labor (IOL). In contrast, of the 55 cases in Group B, a significant majority of 53 (96.4%) had a Bishop's score less than 4, and only 2 (3.6%) had a score greater than 4 at IOL. This difference in the distribution of Bishop's scores at the time of IOL is statistically significant, with Group A having a higher proportion of cases with a favourable (higher) Bishop's score compared to Group B (Table 2).

At 8 hours post induction of labor (IOL), the Bishop's scores in group A were distributed as follows: 16 cases (29.1%) scored between 1 and 3, 23 cases (41.8%) scored between 4 and 6, 12 cases (21.8%) scored between 7 and 9, and 4 cases (7.3%) scored between 10 and 12. For Group B, the distribution was 25 cases (45.5%) with scores between 1 and 3, 24 cases (43.6%) with scores between 4 and 6, 3 cases (5.5%) with scores between 7 and 9, and 3 cases (5.5%) with scores between 10 and 12.

The variation in Bishop's scores at 8 hours post IOL did not show a significant difference between the two groups (p=0.057). This suggests that the change in Bishop's score over 8 hours post IOL was similar for both groups (Table 2).

In the study, the mean number of Misoprostol doses required was higher in Group A (5.22±1.84) compared to Group B (3.49±1.30). The range of Misoprostol doses required varied from a minimum of 2 to a maximum of 8 in Group A, and from 1 to 7 in Group B. The distribution of the mean number of Misoprostol doses required in Group A was significantly higher as compared to Group B (p<.001). Out of 55 cases in Group A, 52 achieved a Bishop's score greater than 6, while the remaining 3 underwent emergency caesarean section for various reasons. In Group B, 47 out of 55 cases exceeded a Bishop's score of 6, with the remaining 8 not showing improvement and subsequently undergoing LSCS (Lower Segment Caesarean Section).

The median time to achieve a Bishop's score greater than 6 was 8 hours (range: 4-28 hours) for Group A and 12 hours (range: 4-49 hours) for Group B. This distribution of the median time to exceed a Bishop's score of 6 significantly differed between the two groups, with Group B taking a longer median time compared to Group A (p=0.014).

Out of 55 cases in Group A, 33 (60.0%) resulted in normal vaginal delivery, while 22 (40.0%) underwent LSCS. In Group B, also with 55 cases, 24 (43.6%) had normal vaginal delivery and 31 (56.4%) had LSCS. Regardless of the differences in delivery outcomes, the distribution of the mode of delivery between the two groups was not statistically significant (p=0.086), but the incidence of LSCS was relatively higher in group B compared to group A (Table 3).

Among the 22 cases in Group A that underwent LSCS delivery, the indications were as follows: 7 cases (31.8%) due to fetal distress, 7 cases (31.8%) due to non-reassuring CTG (Cardiotocography), 2 cases (9.1%) due to failure of induction of labor (IOL), 3 cases (13.6%) due to non-progress of labor, and 3 cases (13.6%) due to other reasons. In Group B, out of 31 LSCS cases, the indications were, 13 cases (41.9%) due to fetal distress, 4 cases (12.9%) due to non-reassuring CTG, 5 cases (16.1%) due to failure of IOL, 3 cases (9.7%) due to non-progress of labor, and 6 cases (19.4%) due to other reasons. The distribution of the indication for LSCS mode of delivery did not show a significant difference between the two groups (p=0.482) This indicates that the variety of indications leading to LSCS were evenly distributed across both Group A and Group B.

In the comparative analysis of induction to delivery intervals (in hours) between Group A and Group B, the overall mean (±SD) for Group A was 21.65 (±8.50) hours, ranging from 4.53 to 47.00 hours, while for Group B, it was 21.73 (±9.83) hours, ranging from 7.15 to 52.35 hours. For normal deliveries, Group A had a mean (±SD) of 22.20 (±9.87) hours (range 4.53–47.00 hours), and Group B had 23.73 (±11.67) hours (range 10.58–52.35 hours).

For cases that resulted in LSCS delivery, the mean (±SD) in Group A was 20.83 (±6.00) hours (range 6.00–31.88 hours), while in Group B, it was 20.18 (±7.98) hours (range 7.15–41.57 hours). In all these categories, the differences in the mean induction to delivery interval between the two groups were not statistically significant (p value>0.05) (Table 4).

Table 2: Between group distribution of Bishop's score at the time of IOL and at 8 hours.

	Group A (Oral) (n=55)		Group B (Vaginal) (n=55)		P value
	N	%	N	%	
Bishop's score at IOL					
<4	37	67.3	53	96.4	<0.05
>4	18	32.7	2	3.6	
Bishop's score at 8 hours					
1-3	16	29.1	25	45.5	0.057
4–6	23	41.8	24	43.6	
7–9	12	21.8	3	5.5	
10–12	4	7.3	3	5.5	

Table 3. Distribution of Mode of delivery and indications for LSCS in Group A and B.

	Group A (Oral) (n=55)		Group B (Vaginal) (n=55)		P value
	N	%	N	%	
Mode of delivery					
Normal	33	60	24	43.6	0.086
LSCS	22	40	31	56.4	
Indications of LSCS					
Fetal distress	7	31.8	13	41.9	0.482
Non reassuring CTG	7	31.8	4	12.9	
Failure of IOL	2	9.1	5	16.1	
Non progress of labour	3	13.6	3	9.7	
Other	3	13.6	6	19.4	

Table 4. Between group comparison of mean induction to delivery interval.

Induction to delivery interval	Group A (Oral) (n=55)	Group B (Vaginal) (n=55)	P value
	Mean±SD	Mean±SD	
Overall	21.65±8.5	21.73±9.83	0.964
LSCS	20.83±6	20.18±7.98	0.748
Normal	22.2±9.87	23.73±11.67	0.594

DISCUSSION

In recent years, there has been a notable rise in the rate of labor induction, with approximately 15-20% of deliveries now initiated through this process. Labor induction is typically considered when the risks associated with continuing a pregnancy outweigh the benefits of allowing it to proceed naturally. Common indications for induction include postdatism, severe preeclampsia, GDM, oligohydramnios, and IUGR, which refers to poor growth of a baby while in the mother's womb during pregnancy. The study aimed to compare the effects of two methods of cervical ripening on various parameters in a group of 110 eligible patients. These patients were divided into two groups. Group A-This group consisted of 55 term pregnant women who were over 37 weeks into their pregnancy. They received oral Misoprostol at a dose of 25 mcg every 2 hours. Group B-Similarly comprising 55 term pregnant women over 37 weeks gestation, this group received intravaginal Misoprostol at a dose of 25 mcg every 4 hours. There was no significant difference in baseline characteristics such as age, height, and weight between the two groups. The induction of labor in these patients was carried out for various medical and obstetrical reasons. In the current study, the mean gestational age in group A (oral) was 39.81±0.79 and in group B (vaginal) it was 39.81±0.54. These results were consistent with the earlier studies. Shelly et al. reported that both oral and vaginal groups had a mean gestational age of 40 weeks with a SD range (1-2 weeks), indicating a slightly later gestational age at induction compared to the present study, but with greater variability.[9] Wing DA et al showed a lower mean gestational age for vaginal induction (38 weeks) compared to oral (39 weeks), with a higher variability (SD of 1.7 and 2 respectively).[10] Iris Colon MD et al, the mean gestational age was slightly lower for the oral group (38.81 weeks) and slightly higher for the vaginal group (39.1 weeks) compared to the present study, with a higher SD in both groups.[11] Reported similar mean gestational ages to the present study but with greater variability, especially in the vaginal group (SD of 3.1 weeks).[12]

The results of various studies on the mean Bishop Score before induction of labor, comparing oral and vaginal

methods, show distinct variations. In the present study, the oral group had a mean Bishop Score of 3.1, slightly higher than the vaginal group's 2.4, indicating marginally better cervical readiness in the oral group. In Contrary results of Wing DA's study, both methods yielded an identical mean score of 2, suggesting uniform cervical conditions across both groups.[10] However, Shelly's research showed a higher readiness in the vaginal group (mean score 4.1) compared to the oral group (3.5).[9] In Helen's study, the trend was reversed, with the oral group having a slightly higher mean score of 3.8 compared to 3.5 in the vaginal group.[12] These varying outcomes across different studies highlight that the cervical status before labor induction, as measured by the Bishop Score, can differ depending on the method of Misoprostol administration, although the direction and extent of these differences are not consistent across all studies.

In the present study, the oral group had a Bishop Score of 3.1, while the vaginal group had a slightly higher score of 4.3. This difference, however, was not statistically significant (p value>0.05). Similarly, in Wing DA's study, the scores were close, with the oral group at 4 and the vaginal group slightly higher at 4.2.[10] These findings align with previous studies like those conducted by Shelly et al.[9]

In the present study, the group receiving oral Misoprostol reached a Bishop score greater than 6 on average 4 hours earlier than the vaginal group. Specifically, the oral group achieved this score in an average of 8 hours, compared to 12 hours for the vaginal group. This suggests that, in this study, oral Misoprostol was more efficient in promoting cervical ripening within a shorter time frame compared to the vaginal route. However, Shelly et al study presents an opposite trend. In their research, the vaginal group attained a Bishop score greater than 6 earlier than the oral group. The interval from the first dose to delivery is a key parameter in studies comparing oral and vaginal Misoprostol for labor induction. In our study, the mean induction to delivery interval did not show a significant difference between the oral and vaginal groups (p value > 0.05), a finding consistent with Iris Colon's study. However, other studies, including those by Shelly et al, Wing DA et al, Helen Y, and I. Adam, observed that vaginal Misoprostol shortened the induction to delivery interval by approximately 5-7 hours compared to oral Misoprostol.[9-13] The mode of delivery across different studies comparing oral and vaginal Misoprostol shows varied outcomes. In the present study, vaginal deliveries were more frequent in the oral Misoprostol group (60%) compared to the vaginal group (43%), while Caesarean sections were more common in the vaginal group (56%) than in the oral group (40%). Contrastingly, Wing DA's study reported higher rates of vaginal delivery in both groups, with 84.4% in the oral group and 77.3% in the vaginal group, and correspondingly lower Caesarean rates.[10] Iris Colon's study also found a higher rate of vaginal delivery in the oral group (80.6%) compared to the vaginal group (67.6%).[11] However, Helen Y's study showed an opposite trend with a higher rate of vaginal delivery in the vaginal group (83%) compared to the oral group (68%).[12]

CONCLUSION

The study comparing oral and vaginal Misoprostol for preinduction cervical ripening found that both methods are equally effective. Although the oral group required more frequent dosing, both approaches showed similar times to delivery and comparable modes of delivery. Therefore, oral Misoprostol is as effective as vaginal Misoprostol for inducing labor.

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