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Original Research Article

A Study of Oral versus Vaginal Misoprostol for Labour Induction

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Abstract

Background: Labor induction involves initiating uterine contractions before the onset of spontaneous labor. It is recommended in situations where the advantages to both the mother and fetus outweigh those of continuing the pregnancy. The present study aimed to compare the efficacy and safety of 50 µg of misoprostol vaginal with oral for labor induction.

Methods: Term pregnant women admitted to the labor room and antenatal wards of the Obstetrics and Gynecology department were included in the study. The oral drug consisted of 50 µg of misoprostol in the first dose and 100 µg in subsequent doses, while the vaginal drug contained 25 µg in all doses. Eligible participants were pregnant women between 37 and 42 weeks of gestation, carrying a single, live fetus in cephalic presentation, with reassuring fetal heart rates and intact membranes.

Results: The Bishop Score at the time of induction in both arms ranged between 0 and 6 with a mean of 3.30 in the vaginal group and 3.25 in the oral group. All patients were induced with misoprostol either the vaginal route or the oral route along with placebo. The median number of doses of misoprostol used in the vaginal and oral groups was 2 in each group. In the vaginal misoprostol group, 30 cases (60%) resulted in vaginal delivery, while in the oral misoprostol group, 28 cases (56%) ended in vaginal delivery, totaling 58 cases.

Instrumental: In the vaginal misoprostol group, 10 cases (20%) required instrumental delivery, and in the oral misoprostol group, 9 cases (18%) underwent instrumental delivery, totaling 19 cases. Both the vaginal and oral misoprostol groups had 10 cases (20%) and 13 cases (26%), respectively, that ended in cesarean section, totaling 23 cases.

Conclusion: Our study within its limitations determined that oral misoprostol exhibits comparable effectiveness to vaginal misoprostol in cervical ripening and achieving vaginal delivery within 24 hours. Rates of hyperstimulation and cesarean section were similar between both groups. Additionally, the oral misoprostol group demonstrated a reduced need for oxytocin augmentation.

Keywords: Vaginal misoprostol, Oral misoprostol, Induction of labor.

Introduction

Labor induction, the deliberate initiation of uterine contractions resulting in cervical effacement and fetal descent, is essential in obstetrics. However, inducing labor at term with an unfavorable cervix carries an elevated risk of failed induction and cesarean sections. While traditional methods like oxytocin and Foley's catheter have been employed for cervical ripening, they possess limitations. Hence, there is a quest for a more efficient inducing agent with fewer constraints [1]. To date, no ideal agent has been identified, but prostaglandins, particularly PGE_1 and PGE_2, have garnered interest for labor induction. Over 15% of gravid women require assistance in cervical ripening, with challenges during induction including ineffective contractions or overly strong uterine activity [2]. PGE_2, available in gel and tablet forms for intracervical or vaginal use, offers versatility but is costly and requires refrigeration. Misoprostol, a synthetic analog of PGE1 initially used for gastric protection, has emerged as a promising option for cervical ripening and labor induction [3]. Despite initial legal hurdles, it has gained popularity worldwide due to its affordability, stability at room temperature, and various administration routes (vaginal, oral, sublingual, or rectal). Oral misoprostol is absorbed rapidly, reaching peak serum concentrations within 30 minutes compared

to one hour with vaginal administration [4]. While oral misoprostol is eliminated more quickly (2–3 hours) than the vaginal route (4 hours), it may offer a more efficacious induction–delivery interval and reduce the need for oxytocin augmentation [5]. To compare the efficacy and safety of vaginal and oral routes of 50 µg misoprostol for cervical ripening and induction of labor, we initiated this study.

Material and Methods

This study is an observational cohort study approved by the institutional review board, conducted among patients who underwent pelvic reconstructive surgery. Informed written consent was obtained from all participants. The study aims to identify clinical predictors for early postoperative urinary retention following pelvic reconstructive surgery.

Term pregnant women admitted to the labor room and antenatal wards of the Obstetrics and Gynecology department were included in the study. Randomization was achieved through computer-generated methods with variable block sizes, and allocation concealment was ensured by sealed opaque envelopes prepared by the Pharmacy department. Each envelope sequentially numbered based on randomization codes, contained two plastic packets labeled 1, 2, and 3, corresponding to the order of administration. One packet contained the oral drug while the other contained the vaginal placebo, or vice versa, with both appearing identical. The treating obstetrician and patients remained blinded throughout the study.

The oral drug consisted of 50 µg of misoprostol in the first dose and 100 µg in subsequent doses, while the vaginal drug contained 25 µg in all doses. Eligible participants were pregnant women between 37 and 42 weeks of gestation, carrying a single, live fetus in cephalic presentation, with reassuring fetal heart rates and intact membranes. Informed consent was obtained, followed by a vaginal examination to determine the Bishop's score. Women with a score less than 6 were randomized using the next sequentially numbered envelope. Exclusion criteria included non-reassuring fetal heart status, ruptured membranes, previous uterine scars, Bishop's score of 7 or more, and contraindications to vaginal delivery. Demographic data and baseline characteristics were recorded. Participants were randomized to receive either an oral drug with a vaginal placebo or a vaginal drug with an oral placebo. Uterine contractions and Bishop's scores were monitored every four hours, with drug administration occurring only if contractions were absent and the Bishop's score was less than 6. If contractions developed with a Bishop's score of less than 6, drug administration was delayed until contractions ceased. The administration continued every four hours until completion of the three doses, a Bishop's score of more than 6, or the onset of regular uterine contractions. Amniotomy was performed four hours after the last dose, followed by labor augmentation with oxytocin if necessary. Continuous fetal heart rate monitoring was conducted using cardiotocography, and further interventions were at the discretion of the treating obstetrician. Primary outcomes included the percentage of women delivering vaginally within 24 hours, uterine hyperstimulation with fetal heart rate changes, and the cesarean section rate. Secondary outcomes evaluated effectiveness and safety measures such as cervix status after 12 hours need for oxytocin augmentation, serious neonatal and maternal morbidity or death, meconium-stained liquor, Apgar score at 5 minutes, neonatal intensive care unit admissions, maternal adverse events, and postpartum hemorrhage exceeding 500 ml.

Statistical Analysis: The available data was refined and uploaded to an MS Excel spreadsheet and analyzed by SSS Version 21 in Windows format with descriptive statistics for continuous variables and frequencies/percentages for categorical variables. Fisher's exact test compared groups across categorical variables, while t-tests or Mann-Whitney U tests were used for continuous variables.

Results

In this study, a total of n=100 cases divided equally between two groups Oral group(n=50) and Vaginal group(n=50) were included in the study. Table 1 shows the distribution of various parameters between the groups receiving vaginal and oral misoprostol for labor induction. Age Distribution: Vaginal Group: The minimum age was 19 years, and the maximum age was 36 years, with a mean age of 25.5 years and a standard deviation (SD) of 3.25. Oral Group: The minimum age was 20 years, and the maximum age was 35 years, with a mean age of 26.4 years and a standard deviation (SD) of 3.02. Height Distribution: Vaginal Group: Heights ranged from 142 cm to 172 cm, with a mean height of 154.3 cm and a standard deviation (SD) of 4.27. Oral Group: Heights ranged from 139 cm to 170 cm, with a mean height of 153.7 cm and a standard deviation (SD) of 3.67. BMI Distribution (Kg/m^2): Vaginal Group: BMIs ranged from 16.25 to 35.7, with a mean BMI of 25.7 and a standard deviation (SD) of 3.4. Oral Group: BMIs ranged from 17.21 to 36.4, with a mean BMI of 26.1 and a standard deviation (SD) of 3.1. Gestational Age in Weeks: Vaginal Group: Gestational ages ranged from 37.2 weeks to 42 weeks, with a mean gestational age of 39.5 weeks and a standard deviation (SD) of 1.02. Oral Group: Gestational ages ranged from 37.1 weeks to 42 weeks, with a mean gestational age of 39.1 weeks and a standard deviation (SD) of 1.04.

Table 1: Distribution of parameters between vaginal and oral misoprostol groups

Group	Minimum	Maximum	Mean	SD
Age distribution				
Vaginal	19	36	25.5	3.25
Oral	20	35	26.4	3.02
Height distribution				
Vaginal	142	172	154.3	4.27
Oral	139	170	153.7	3.67
BMI distribution Kg/m^2				
Vaginal	16.25	35.7	25.7	3.4
Oral	17.21	36.4	26.1	3.1
Gestational age in weeks				
Vaginal	37.2 weeks	42 weeks	39.5	1.02
Oral	37.1 weeks	42 weeks	39.1	1.04

The distribution of age, height, BMI, and gestational age appears to be similar between the vaginal and oral misoprostol groups, as evidenced by comparable minimum, maximum, mean values, and standard deviations. The slight differences observed in mean values between the two groups are likely due to natural variations within the study population and are not indicative of significant disparities between the groups. Overall, the baseline characteristics of the participants in both groups seem to be adequately balanced, which is important for ensuring the comparability of the groups in the study.

Table 2 presents the distribution of parity within each group, comparing the vaginal and oral misoprostol groups. Nulliparous: In the vaginal group, 29 participants (58%) were nulliparous, and in the oral group, 28 participants (56%) were nulliparous, totaling 57 participants. Primiparous: In the vaginal group, 13 participants (26%) were primiparous, and in the oral group, 12 participants (24%) were primiparous, totaling 25 participants. Multipara: In the vaginal group, 8 participants (16%) were multipara, and in the oral group, 10 participants (20%) were multipara, totaling 18 participants. Total: The total number of participants in each group was 50, accounting for 100% in both the vaginal and oral groups, resulting in a total of 100 participants across both groups. Overall, the distribution of parity appears to be relatively similar between the vaginal and oral misoprostol groups, with no significant disparities observed.

Table 2: Distribution of parity within each group

Parity	Vaginal group	Oral group	Total
Nulliparous	29(58%)	28 (56%)	57
Primiparous	13(26%)	12 (24%)	25
Multipara	8 (8%)	10 (20%)	18
Total	50 (100%)	50 (100%)	100

Bishop score at induction: The Bishop Score at the time of induction in both arms ranged between 0 and 6 with a mean of 3.30 in the vaginal group and 3.25 in the oral group. *The number of doses of misoprostol used*: All patients were induced with misoprostol either the vaginal route or the oral route along with placebo. The median number of doses of misoprostol used in the vaginal and oral groups was 2 in each group.

Table 3: Indications for induction in either group were distributed as follows

Indication	Vaginal group N (%)	Oral group N (%)	Total
Past dates	26(52%)	24(48%)	50
PIH	3(6%)	3(6%)	6
IUGR	9(18%)	2(4%)	11
GDM	7(14%)	12(24%)	19
Others	5(10%)	9(18%)	14
Total	50(100%)	50(100%)	100

Table 3 displays the distribution of indications for induction in both the vaginal and oral misoprostol groups, along with the total number of cases for each indication.

Past dates: In the vaginal group, 26 cases (52%) were induced due to past dates, while in the oral group, 24 cases (48%) were induced for the same reason, totaling 50 cases.

PIH (Pregnancy-Induced Hypertension): Both the vaginal and oral groups had 3 cases each (6%) induced due to PIH, totaling 6 cases.

IUGR (Intrauterine Growth Restriction): In the vaginal group, 9 cases (18%) were induced due to IUGR, whereas in the oral group, 2 cases (4%) were induced for the same reason, totaling 11 cases. *GDM* **(Gestational Diabetes Mellitus):** In the vaginal group, 7 cases (14%) were induced due to GDM, while in the oral group, 12 cases (24%) were induced for the same reason, totaling 19 cases.
Others: Other indications for induction accounted for 5 cases (10%) in the vaginal group and 9 cases (18%) in the oral group, totaling 14 cases.
Total: The total number of cases in both groups was 50, representing 100% in each group and totaling 100 cases overall. There were variations in the distribution of some indications between the groups. For example, a higher proportion of cases in the oral group were induced due to GDM compared to the vaginal group.

Both the vaginal and oral groups have a median Bishop score of 5 at admission. This suggests that both groups have a similar level of cervical ripening and readiness for labor on average. The IQR is also the same for both groups, indicating a range of 5-7. This means that in both groups, half of the individuals had a Bishop score between 5 and 7, while the other half had scores either lower than 5 or higher than 7.

Table 4: Percentage distribution of oxytocin requirement

Oxytocin	Vaginal group	Oral group	Total	P value
Required	40(80%)	36(72%)	76	0.024*
Not required	10(20%)	14(28%)	24	

Table 4 shows the proportion of women who required oxytocin during childbirth in two groups. **Vaginal group:** 76 (51.3%) of the total women across both groups required oxytocin during childbirth. 24 (16.1%) of the total women did not require oxytocin. 80% (40 women) required oxytocin. 20% (10 women) did not require oxytocin. **Oral group:** 72% (36 women) required oxytocin. 28% (14 women) did not require oxytocin. A significantly higher proportion of women in the vaginal group required oxytocin compared to the oral group (80% vs. 72%, p-value = 0.024). This suggests that the vaginal group had more difficulty delivering their babies naturally without medical intervention.

Table 5: Mode of delivery in cases of the study

Mode of delivery	Misoprostol Vaginal group	Misoprostol Oral group	Total n
Vaginal	30(60%)	28(56%)	58
Instrumental	10(20%)	9(18%)	19
Cesarean section	10(20%)	13(26%)	23
Total	50(100%)	50(100%)	100

Table 5 illustrates the distribution of modes of delivery among the cases included in the study, categorized by the type of misoprostol administered (vaginal or oral).

Vaginal: In the vaginal misoprostol group, 30 cases (60%) resulted in vaginal delivery, while in the oral misoprostol group, 28 cases (56%) ended in vaginal delivery, totaling 58 cases.
Instrumental: In the vaginal misoprostol group, 10 cases (20%) required instrumental delivery, and in the oral misoprostol group, 9 cases (18%) underwent instrumental delivery, totaling 19 cases.

Cesarean Section: Both the vaginal and oral misoprostol groups had 10 cases (20%) and 13 cases (26%), respectively, that ended in cesarean section, totaling 23 cases. Overall, the distribution of modes of delivery suggests that both vaginal and oral misoprostol can be effective methods for labor induction, with vaginal delivery being the most common outcome in both groups. Understanding these outcomes can assist healthcare providers in selecting the most appropriate method of labor induction based on individual patient characteristics and preferences.

Table 6 presents the various indications for emergency cesarean section, categorized by the mode of delivery and the type of misoprostol administered (vaginal or oral). Trace abnormality:14 cases (12% in the vaginal group and 16% in the oral group) required emergency cesarean section due to trace abnormalities. Trace abnormality due to hyperstimulation: Only 1 case (2%) in the oral group required emergency cesarean section due to trace abnormality caused by hyperstimulation. Failure to progress: 4 cases (4%) (2 in each group) required emergency cesarean section due to failure to progress. CPD (Cephalopelvic Disproportion): 3 cases (2 in the vaginal group and 1 in the oral group) required emergency cesarean section due to CPD. Malpresentation: 4 cases (3 in the vaginal group and 1 in the oral group) required emergency cesarean section due to malpresentation. Failed induction: 10 cases (10% in each group) required emergency cesarean section due to failed induction. Not applicable* (Vaginal): The majority of cases (60%

in the vaginal group and 56% in the oral group) delivered vaginally and did not require emergency cesarean section. MSAF (Meconium-Stained Amniotic Fluid):** 2 cases (4%) in the oral group required emergency cesarean section due to MSAF. Prolonged second stage: 1 case (2%) in the vaginal group required emergency cesarean section due to a prolonged second stage of labor. IUGR (Intrauterine Growth Restriction) with low AFI (Amniotic Fluid Index): 1 case (2%) in the oral group required emergency cesarean section due to IUGR with low AFI. Arrest of dilatation: 2 cases (1 in each group) required emergency cesarean section due to arrest of dilatation.

Table 6: The various indications for emergency cesarean section

Mode of delivery	Misoprostol Vaginal group	Misoprostol Oral group	Total n
Trace abnormality	6(12%)	8(16%)	14
Trace abnormality due to hyperstimulation	0(00%)	1(2%)	1
Failure to progress	2(4%)	2(4%)	4
CPD	2(4%)	1(2%)	3
Malpresentation	3(6%)	1(2%)	4
Failed induction	5(10%)	5(10%)	10
Not applicable* (Vaginal)	30(60%)	28(56%)	58
MSAF	0(00%)	2(4%)	2
Prolonged second stage	1(2%)	0(00%)	1
IUGR with low AFI	0(00%)	1(2%)	1
Arrest of dilatation	1(2%)	1(2%)	2
Total	50(100%)	50(100%)	100

Among the 100 patients who were analyzed, 39 patients delivered vaginally within 24 hours from the start of induction, 19 patients delivered vaginally after 24 hours, and 23 patients underwent cesarean section. The median duration from the start of induction to delivery was 16.5 hours in the vaginal misoprostol group and 15.5 hours in the oral misoprostol group.14 % of the patients had uterine hyperstimulation with or without trace abnormality of which 8 patients were in the vaginal group and 6 patients in the oral misoprostol group. Serious maternal side effects like postpartum hemorrhage and retained placenta had occurred in 2 patients from the vaginal misoprostol group and 3 patients from the oral misoprostol group. The average birth weight in both groups was 3.15 Kg and 3.21 Kg in the vaginal and oral misoprostol groups respectively. N=7 neonates were admitted to the neonatal intensive care unit of which 4 were in the vaginal misoprostol group and 3 were in the other group.

Discussion

Numerous studies have been conducted globally to identify the most effective, safe, and practical agent for cervical ripening to induce labor, prioritizing the benefits of delivery over the risks of prolonging pregnancy. [6-10] While dinoprostone is FDA-approved as the gold standard, its cost and storage requirements pose challenges to accessibility in developing nations. Consequently, extensive trials, including randomized controlled trials, have explored misoprostol, a prostaglandin analog, due to its affordability, ease of administration, and widespread availability. Hofmeyer et al. [8] conducted a systematic review on misoprostol, demonstrating its superior efficacy in achieving vaginal delivery compared to conventional methods of cervical ripening, albeit with instances of uterine hyperstimulation and fetal heart rate changes. The World Health Organization (WHO) has recommended a 25 µg dose of misoprostol as the safest and optimal for vaginal use in term pregnancies, with minimal complications [11]. Although oral misoprostol has shown comparable effectiveness to vaginal administration in various trials, its optimal dosage remains undetermined. This study aimed to assess the safety and efficacy of oral misoprostol using a novel titrated dosing regimen and compare it with the standard vaginal regimen of 25 µg every 4 hours. Concerns regarding uterine hyperstimulation and intense contractions with oral misoprostol, particularly at higher doses, persist despite achieving shorter intervals for vaginal delivery compared to vaginal administration.

At a dosage of 50 µg, labor duration was prolonged, and there was a greater requirement for oxytocin augmentation, as evidenced by previous studies [12-14]. Therefore, our study opted to initiate the induction process with a lower dose of 50 µg orally. Oral misoprostol's pharmacokinetics reveal a rapid onset of action, typically within 8 minutes, with peak plasma levels reached in 30 minutes. It induces uterine tonus without immediate contractions unless administered repeatedly. The duration of action lasts around 2 hours, with effects persisting thereafter [13]. Cheng et al. [15] found titrated doses of misoprostol to be effective; however, due to the inconvenience of hourly administration, we opted for repeated doses at 4-hour intervals, gradually

increasing to 100 µg until regular uterine contractions ensued or cervical favorability improved [16]. In the present study out of 100 patients were included n=50 in each group. Within the vaginal misoprostol group, 30 cases (60%) resulted in vaginal delivery, while in the oral misoprostol group, 28 cases (56%) concluded with vaginal delivery, totaling 58 cases. In the vaginal misoprostol group, 10 cases (20%) necessitated instrumental delivery, and in the oral misoprostol group, 9 cases (18%) underwent instrumental delivery, summing up to 19 cases. Both the vaginal and oral misoprostol groups experienced 10 cases (20%) and 13 cases (26%) respectively, resulting in cesarean section, totaling 23 cases.

In the vaginal misoprostol group, the mean age was 25.5 years, while in the oral group, it was 26.4 years. The mean BMI in the vaginal group was 27.7 kg/m², whereas in the oral group, it was 26.1 kg/m². Regarding gestational age, the mean was 39.5 weeks in the vaginal group and 39.1 weeks in the oral misoprostol group. The indications for induction were evenly distributed, with the most common being for past dates, accounting for 56% of the total. Other reasons included gestational hypertension, gestational diabetes, intrauterine growth restriction, and various obstetric or medical indications for induction at term. The Bishop Score at the time of induction ranged between 0 and 6 in both groups, with a mean of 3.30 in the vaginal group and 3.25 in the oral group. The median number of misoprostol doses used was 2 in both groups. At the time of the artificial rupture of membranes, the median Bishop score was 5 in both groups. Oxytocin was required in 76% of cases overall, with 40 cases in the vaginal group and 36 cases in the oral group. The obtained p-values were significant, as indicated in Table 4. This contrasts with a similar study conducted by Colon et al., [7] where the same dose and dosing schedule of misoprostol were employed, but no statistical significance was found between the two groups in terms of oxytocin requirement. There was no difference observed in the number of patients achieving vaginal delivery within 24 hours or 12 hours from the start of induction, suggesting that oral misoprostol at this dosing regimen was equally effective compared to vaginal misoprostol. A total of 7 neonates were admitted to the neonatal intensive care unit, with 4 in the vaginal misoprostol group and 3 in the other group. The reasons for nursery admission of the other babies included non-serious conditions such as transient tachypnea of the newborn, hypoglycemia, ambiguous genitalia, being large for gestational age, and low birth weight. One major concern associated with the use of misoprostol is the potential risk of uterine rupture and fetal asphyxia. To mitigate these risks, patients in this study were meticulously monitored using continuous cardiotocography. Additionally, the majority of patients received only 2 doses of misoprostol, with subsequent doses withheld for those with a favorable cervix or ongoing uterine contractions. Determining the optimal safe dose of misoprostol remains elusive. However, we selected this regimen as it represents the safest and most effective dose feasible for implementation in a busy labor room setting.

Conclusion

Our study within its limitations determined that oral misoprostol exhibits comparable effectiveness to vaginal misoprostol in cervical ripening and achieving vaginal delivery within 24 hours. Rates of hyperstimulation and cesarean section were similar between both groups. Additionally, the oral misoprostol group demonstrated a reduced need for oxytocin augmentation. Importantly, oral misoprostol did not result in increased incidence of adverse maternal or neonatal outcomes when compared to vaginal misoprostol.

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