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ORIGINAL ARTICLE

Comparative study between oral and vaginal administration of misoprostol in the induction of labour in cases with premature rupture of membranes (PROM)

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Abstract

Background: **Cervical ripening is mediated by membrane-bound G-coupled receptor prostaglandins. Boost leukocyte extravasation and collagenase. Biochemical mechanisms alter the distribution of proteoglycan and collagen, allowing cervical effacement and dilatation. The use of PG gel for induction began in the 1980s. Prior to the 1990s, oral PG was avoided for induction of labour due to its unpleasant gastrointestinal effects. Oral route may improve mother satisfaction more than vaginal route.**

Aim: **What is the difference between the effect of oral and vaginal misoprostol for induction of labor in pregnant females with PROM regarding efficacy, safety, maternal and fetal outcomes?**

Subject and methods: **100 Pregnant females presenting at Obstetrics and Gynaecology Emergency Department at El-Hussein University hospitals.**

Results: **There was no significant difference between the two groups regarding cesarean section indications Neonatal outcomes and Maternal outcomes.**

Conclusion: **Researchers investigated the vaginal and oral safety and efficacy of misoprostol. To obtain the desired results, a different schedule and greater doses were administered. This study demonstrates that oral misoprostol is as safe and effective as its vaginal counterpart. Misoprostol administered orally or vaginally was equally effective for initiating labour in preterm women. To identify the ideal oral and vaginal dosage, additional research is required. In a facility that does emergency C-sections, it can be used to induce labour.**

Keywords: Cesarean section, Membranes, Misoprostol, Rupture

1. Introduction

The last decades have seen an increase in the frequency of induction of labour. Particularly in prim parous women and those with an immature cervix, prolonged labour and caesarean sections (CS) are more likely following an induction of labour. For these women, cervical softening before to induction is crucial for a successful vaginal birth (VB). Worldwide CS rates are increasing, and reports of newborn and infant problems, as well as maternal complications like life-threatening obstetric hemorrhage and peripartum hysterectomy, are also rising.[1]

Women who have had a previous CS represent the majority of caesarean deliveries. Therefore, a woman has a higher chance of avoiding a subsequent CS if she manages a nonoperative first birth.[2]

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The main substances that cause cervical softening are prostaglandins (PGs), which act through membrane-bound G-coupled receptors. In addition to stimulating leukocyte extravasation and collagenase enzyme activity, PGs alter the expression of the progesterone receptor isoforms A and B, which results in a functional progesterone withdrawal. Cervical effacement and dilatation are made possible by these biochemical changes in the proteoglycan composition and the collagen fibrils' distribution.[3]

Since the 1980s, vaginal PG gel has been used to induce childbirth. Due to its alleged lower efficacies and gastrointestinal side effects, oral PG was avoided and was not utilised for labour induction until the 1990s.[4]

Despite the high efficacy of the vaginal method, oral medication for labour induction is becoming more common since it may lead to higher maternal satisfaction than the vaginal route. This is because it has advantages such as being less intrusive and simpler to administer, giving users more freedom to move and position themselves after use, preventing the need for recurrent vaginal exams, and being cost-effective due to the minimum material consumption during use. The cost effectiveness benefit is anticipated to be significantly more pronounced in low-resource areas.[5]

2. Patients and methods

100 Pregnant females presenting at Obstetrics and Gynaecology emergency department at El-Hussein University hospitals, diagnosed with PROM was divided into 2 equal groups and was subjected to trial of induction of labour using misoprostol via oral or vaginal routes. This study is a prospective study conducted through the time interval from December 2021 till end of the study.

2.1. Inclusion criteria

Primigravida, term pregnancy (37–42 weeks), definite PROM, singeleton living gestation, cephalic presentation, ROM $\leq$12 h, bishop score <6, reactive fetal Non stress test (NST) and free maternal medical history.

2.2. Exclusion criteria

Multiparity, multifetal gestation, patients with regular uterine contractions, prematurity or post term pregnancy, malpresentations, ROM >12 h, bishop score $\geq$6, non reassuring fetal NST, meconium stained liquor or signs of chorioamnionitis, indication for CS. e. g markedly contracted pelvis, fetal macrosomia and intra uterine fetal death (IUFD).

2.3. Methodology in detail: all patients subjected to the following

Informed consent following disclosure of the study's purpose, its methodology, and any potential risks. Comprehensive obstetric history, medical and surgical history, and comprehensive physical examination, including Bishop scoring and evaluation of the pelvic cavity, Routine *trans*-abdominal obstetric ultrasound including confirmation of the gestational age, fetal presentation, estimated fetal weight and amount of liquor, assessment of fetal wellbeing using NST, candidates was divided into two equal groups: group A who was offered induction of labour by administration of 50 μg of oral misoprostol and group B who was offered induction of labour by administration of 25 μg of vaginal misoprostol,[6] Candidates are randomized (using closed envelopes) to either group A or group B, Regular fetal heart tracing was done, Pelvic examination was done with the onset of uterine contractions in the group taking oral misoprostol and with time of each dose in the group taking vaginal misoprostol, Doses was repeated every 6 h with a maximum of 4 doses, Doses stopped with the onset of regular uterine contractions or when the maximum dose is reached and Documentation of all data.

2.3.1. The following was studied

The likelihood of overstimulation, the length of time from induction to the start of labour, the length of time from induction to delivery, the need for oxytocin to speed up labour, and recording any uterine rupture caused by maternal illness, chorioamnionitis, obstructed labour or accidental hemorrhage and any fetal morbidity in the form of fetal distress, or meconium stained amniotic fluid.

2.3.2. Outcome: primary outcome

Comparing the durations of the induction to the beginning of labour and the induction to delivery of misoprostol administered orally and vaginally to pregnant women with PROM. **Secondary outcome:** identifying any maternal or foetal issues with misoprostol treatment for labour induction in pregnant women with PROM.

2.3.3. Ethical consideration

The AL-Azhar University's faculty of medicine's ethical committee in Cairo submitted the study protocol for approval. Following an explanation of

the study's objectives and methods, each participant gave their verbal informed consent to participate in the investigation.

3. Results

Regarding both groups' basic traits, there was no discernible difference between the two groups. In the oral group, the total number of dosages was noticeably higher (Table 1).

In the oral group, labour time increased significantly (Table 2).

Between the two groups, there was no discernible difference in the method of delivery (Vaginal, Caesarean).

Table 3 shows that there was no discernible difference in the two groups' indications for caesarean sections. Table 4 Although the vaginal delivery group had improved neonatal outcomes, there was no discernible difference between the two groups.

Table 5 Despite better maternal outcomes in the vaginal birth group, there was no obvious distinction between the two groups (Table 6).

4. Discussion

Premature membrane rupture is the term for spontaneous membrane rupturing before the start of labour (PROM). 5–10% of pregnancies are complicated by premature membrane rupture. Several variables, including gestational age, foetal weight, lung development, and the accessibility to high-quality neonatal care, must be considered while balancing the risk of chorioamnionitis, cord compression, and neonatal infection. It is still debatable whether to treat PROM actively or expectantly.[7]

The main objective of this study was to compare the efficacy, safety, maternal, and foetal outcomes of oral versus vaginal misoprostol for labour induction in pregnant women with PROM. This intervention study included 100 Pregnant females presenting at Obstetrics and Gynaecology emergency department at El-Hussein University hospitals, diagnosed with PROM were divided into 2 equal groups and were subjected to trial of induction of labour using misoprostol via oral or vaginal routes. From

Table 1. Patients basal characteristics in both groups.

	Oral ($N = 50$)	Vaginal ($N = 50$)	P Value
Age	22.38 ± 1.66	22.1 ± 0.71	0.276
BMI	26.72 ± 1.64	26.32 ± 1.26	0.18
Gestational Age (Weeks)	39.86 ± 1.13	39.64 ± 1.29	0.366
Initial Bishop's Score	3.14 ± 0.61	3.18 ± 0.69	0.759
Cervical length by ultrasound (mm)	26.32 ± 4.82	24.84 ± 5.23	0.144
Cephalic presentation	50	50	1~
ROM(Hours)	7.56 ± 1.45	7.96 ± 1.95	0.246

DM, Diabetes mellitus; HTN, Hypertension.
$P > 0.05$ No Significant difference $|P < 0.05$ Significant difference T. Test |~chi Square Test.

Table 2. Number of doses in both groups.

	Oral ($N = 50$)	Vaginal ($N = 50$)	P Value
1	8 (16%)	15 (30%)	0.096
2	17 (34%)	20 (40%)	0.534
3	15 (30%)	11 (22%)	0.362
4	10 (20%)	4 (8%)	0.084
Total number of doses	2.54 ± 0.99	2.08 ± 0.92	0.018~

$P > 0.05$ No Significant difference $|P < 0.05$ Significant difference Chi Square Test | ~T. Test.

Table 3. Labor characteristics in both groups.

	Oral ($N = 50$)	Vaginal ($N = 50$)	P Value
Duration of Labor (hours)	21.52 ± 3.75	13.9 ± 6.2	<0.0001~
Vaginal delivery			
SVD	35 (70%)	39 (78%)	0.362
FVD	5 (10%)	3 (6%)	0.461
Vacuum	1 (2%)	1 (2%)	1
Lower Segment Caesarean Section	9 (18%)	7 (14%)	0.585

FVD, Forceps vaginal delivery; SVD, Spontaneous vertex delivery.
$P > 0.05$ No Significant difference $|P < 0.05$ Significant difference Chi Square Test | ~T. Test.

Table 4. Indication of cesarean section in both groups.

	Oral ($N = 50$)	Vaginal ($N = 50$)	P Value
Fetal Distress	2 (4%)	2 (4%)	1
Failed Induction	2 (4%)	2 (4%)	1
Failed Progress	1 (2%)	0	0.98~
Impending eclampsia	1 (2%)	1 (2%)	1
Hyperstimulation	3 (6%)	2 (4%)	0.646

IOL, Induction of labor.
$P > 0.05$ No Significant difference $|P < 0.05$ Significant difference Chi Square Test | ~Fisher Exact test.

Table 5. Neonatal outcomes in both groups.

	Oral ($N = 50$)	Vaginal ($N = 50$)	P Value
Apgar score			
In 5 min	5.52 ± 1.16	5.62 ± 1.26	0.681~
In 10 min	7.64 ± 1.31	8.04 ± 1.18	0.111~
Low Apgar (<6)	7 (14%)	5 (10%)	0.538
Birth weight (kg)	3.05 ± 0.35	3.14 ± 0.32	0.187~
Meconium aspiration	10 (20%)	7 (14%)	0.424
Fetal CTG changes	9 (18%)	7 (14%)	0.585
NICU Admission	10 (20%)	7 (14%)	0.424
Neonatal mortality	1 (2%)	1 (2%)	1

CTG, Cardiotocography; NICU, Neonatal Intensive Care Unit.
$P > 0.05$ No Significant difference $|P < 0.05$ Significant difference Chi Square Test | ~T. Test.

Table 6. Maternal outcomes in both groups.

	Oral ($N = 50$)	Vaginal ($N = 50$)	P Value
Hyperstimulation	3 (6%)	2 (4%)	0.558
Hyperpyrexia	3 (6%)	1 (2%)	0.307
Nausea, Vomiting	6 (12%)	2 (4%)	0.14
Diarrhea	1 (2%)	1 (2%)	1

CTG, Cardiotocography.
$P > 0.05$ No Significant difference $|P < 0.05$ Significant difference Chi Square Test.

December 2021 until the end of the study, this research was carried out. Regarding both groups' basic traits, there was no discernible difference between the two groups. According to the study by Komala et al.,[8] the patients were randomly assigned to one of the two groups of administration routes, provided support for our findings. (Vaginal misoprostol) 100 women in Group-I: pill Misoprostol comes in 200 g, 100 g, and 25 g doses. Every 4 h, one 25 g misoprostol pill was administered intravaginally with a four dose maximum. 100 women in Group II received two oral 25 g misoprostol tablets each. For a total of four doses, the dose was given again every 4 h. Regarding both groups' basic traits, there was no discernible difference between the two groups.

Galidevara et al.[9]'s Our results are consistent with the discovery that the three groups into which the study's participants were divided were determined by computer-generated random numbers. A 50 mg dose of misoprostol was given orally to group 1 every 4 h, a 25 mg dose was given intravaginally to group 2, and a 50 mg dose was given sublingually to group 3. A total of 4 doses were allotted to each of the three groups. At the most fundamental level, all three groups shared the same demographic traits. The average age for the oral group was 24.4 years, for the vaginal group it was 24.7 years, and for the sublingual group it was 24.1 years. As a result, the age distribution across the three groups was similar. The current investigation demonstrated that the oral group received a significantly higher number of doses overall. In contrast, the study by Galidevara et al.[9] found that the average number of doses needed to induce labour in the oral, vaginal, and sublingual groups was 2.58, 2.67, and 2.51, respectively, with a P value of 0.5 that did not indicate statistical significance. The majority of the three groups needed two to three doses of the medication. The results of the current investigation demonstrated a notable increase in labour length in the oral group. Between the two groups, there was no discernible difference in the method of delivery (Vaginal, Caesarean).

Our findings were consistent with a research by Komala et al.,[8] which revealed the proportion of patients who delivered by oral and vaginal methods as well as the quantity of dosages needed for induction. The number of patients who gave birth vaginally and the necessary number of dosages did not change statistically significantly, with a P-value of 0.111. Additionally, Sultana et al.[10] reported that there were no appreciable differences in the delivery methods between the two groups (oral and vaginal misoprostol). In both groups, a nearly similar number of patients spontaneously gave birth vaginally. There was no correlation between the manner of delivery and the route of administration. In the study at hand, there was no discernible difference in the indications for caesarean sections between the two groups. CS occurred at an incidence of 7% and 9%, respectively.

According to Galidevara et al. study 's,[9] Our results agree with those of another study, which reported a caesarean section rate of 8.8% in the oral group, 6% in the vaginal group, and 8.4% in the sublingual group. In all three groups, caesarean procedures were performed most frequently due to an unsettling foetal heart rate. Induction failure, labour not progressing, and cephalopelvic disproportion were additional reasons of caesarean delivery, although none of these differences were statistically significant. Additionally, there were 16.7% caesarean sections in the oral group and 16.2% in the vaginal group in the study by Mehrotra et al.[11]

There was no discernible difference in the two groups' rates of caesarean sections, which were 15% in the oral group and 17% in the vaginal group, according to Hall et al.'s study.[12] The diverse study population and higher pre-induction rates may explain why our study's overall caesarean section rate was lower than those of other studies. Bishop victories, or the practise of deploying a delivery device in a few carefully curated circumstances. While there was no obvious difference between the two groups, the current investigation showed, newborn outcomes were better in the vaginal group. Our findings were validated by a research by Komala et al.,[8] which found that 14 out of 86 oral deliveries and 24 out of 74 vaginal deliveries, respectively, had low Apgar values of 6–8 at 5 min In both groups, no one reported any newborn deaths. The main factor contributing to low Apgar scores at 5 min was both groups' (39%) longer pregnancies. This was brought on by placental insufficiency brought on by placental ageing and secondary to oligohydramnios, umbilical cord compression. Two babies were admitted to the NICU, where they were kept

under observation for two days before being released. Ratnakhatri et al.[13] found that 96% of the vaginal group and 100% of the oral group had Apgar levels greater than 6 at 5 min The groups receiving sublingual and vaginal misoprostol showed no discernible differences in the study by Feitosa et al.[14] and Zahran et al.[15]

In a study by Shetty et al.[16] comparing the oral and sublingual routes of misoprostol, the rate of hospitalisation was reported as 10% in the sublingual group and 12% in the oral group. In every study, respiratory distress, a low APGAR score, and birth asphyxia were the primary causes of neonatal unit hospitalisation. According to what we've found, vaginal delivery resulted in better mother outcomes, although there was no discernible difference between the two groups. While the rate of hyperstimulation in the trial by Komala et al.[8] was only 1% in the vaginal group, where a caesarean section was performed right after, and it was zero in the oral group. A higher bioavailability in the vaginal group led to hyperstimulation. The oral group also experienced a higher incidence of hyperpyrexia and reported greater gastrointestinal side effects. Prior to the commencement of natural labour, uterine contractions are encouraged during labour induction, giving delivery vaginally. Misoprostol, a methyl ester of prostaglandin E1, causes myometrial contractions. It was initially used to induce early labour, but it has now been found to work well in smaller doses to end pregnancies early.[17]

4.1. Conclusion

The findings of this study suggest that oral misoprostol is equally reliable and secure as vaginal misoprostol. According to the study, misoprostol can cause prematurely ruptured membranes in women to go into labour when given orally or vaginally. The appropriate oral and vaginal dose, however, still has to be determined by additional research. It can be used to induce labour while being closely watched in a situation when an emergency caesarean section is possible.

Authorship

All authors have a substantial contribution to the article.

Disclosure

The authors have no financial interest to declare in relation to the content of this article.

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Conflict of interest

There is no conflict of interest, according to the authors.

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