

COMPARISON OF VAGINAL AND ORAL DOSES OF MISOPROSTOL FOR INDUCTION OF LABOUR IN POSTDATED PREGNANCIES

Shailaja Pinjala¹, Tejaswi P. B²

¹Associate Professor, Department of Obstetrics and Gynaecology, ACSR Government Medical College, Nellore, Andhra Pradesh.

²Resident Gynaecologist, Department of Obstetrics and Gynaecology, King George Hospital, Visakhapatnam, Andhra Pradesh.

ABSTRACT

BACKGROUND

Considering maternal complications, it is preferred to induce labour after 40 weeks. Induction of labour is the artificial initiation of labour before its spontaneous onset for the purpose of delivery of the foetoplacental unit using mechanical or pharmacologic methods.

Aim- The aim of this study was to compare 50 micrograms of oral misoprostol with 25 micrograms of vaginal misoprostol for induction of labour in postdated pregnancies.

MATERIALS AND METHODS

This is a randomised controlled trial conducted on 68 uncomplicated postdated pregnant women who were admitted to labour ward of King George Hospital, Visakhapatnam, Andhra Pradesh in the months of June, July and August in 2017. Sample size was taken conveniently. 68 pregnant women who were included in the study for induction were divided into either of the two groups and allocation of groups done by simple randomised lot method. In group A, 50 µg of oral misoprostol and in group B 25 µg of vaginal misoprostol was used for inducing labour. Gestational age, parity, Induction starting time with misoprostol, initiation of uterine contractions, induction delivery interval, caesarean section and vaginal delivery rate and other variables including tachysystole, improvement in Bishop score, foetal outcome were recorded on the checklist. The results were interpreted as mean and standard deviation and chi-square test was done to know the statistical significance using SPSS version 15.0.

RESULTS

In group A, 33 cases were included and in group B 35 cases were included. All women were between 20-25 years of age. The mean number of doses of 50 micrograms oral misoprostol that were required for induction of labour was 1.89 ± 0.769 which was significantly less compared to the mean number of doses required for induction in the vaginal group i.e. 2.94 ± 1.11 , with P- value 0.000. 42.4% of cases in Group A and 80.05% of cases in Group B required augmentation with oxytocin. The difference was statistically significant, with P-value 0.001.

CONCLUSION

In terms of labour induction and maternal outcomes in the postdated pregnant women, oral misoprostol 50 µg is more useful than vaginal misoprostol 25 µg. In mothers receiving oral misoprostol, induction delivery interval and the number of doses were less.

KEYWORDS

Labour, Induction, Misoprostol, Oral Vaginal.

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BACKGROUND

Normally, spontaneous onset of labour pains and vaginal delivery occurs between 37 and 42 weeks of pregnancy and the time of delivery is calculated from the first day of the last menstrual period. Post-term pregnancy extends to more than 42 weeks and its prevalence is 3-12%.⁽¹⁾ As the days go beyond the expected day of delivery, especially after 41 weeks, maternal and foetal morbidity and mortality increase significantly.⁽²⁾ Maternal complications include increased rates of caesarean sections, trauma due to foetal macrosomia, postpartum haemorrhage, and foetal complications include shoulder dystocia, oligohydramnios and meconium aspiration.⁽¹⁾

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Corresponding Author:

Shailaja Pinjala,

44-34-11/c, Nandagiri Nagar,

Visakhapatnam-530016.

E-mail: pinjalashailaja@gmail.com

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To avoid these complications it is preferred to induce labour after 41 weeks. Induction of labour is the artificial initiation of labour before its spontaneous onset for the purpose of delivery of the foetoplacental unit using mechanical or pharmacologic methods.⁽³⁾ The success of labour induction depends on the cervical status at the time of induction. It is generally predicted that the patients with a poor Bishop's score <3 have unacceptably higher rates of failure of induction.⁽⁴⁾ Misoprostol is conveniently administered through the oral, sublingual, buccal, vaginal and rectal routes. It is inexpensive, easily stored at room temperature and has few systemic side effects.⁽⁵⁾ Misoprostol may cause few side effects such as nausea, vomiting, diarrhoea, fever and abdominal pain. In addition, unlike other prostaglandins, misoprostol has a selective effect on the uterus and cervix and has no effect on the bronchi and blood vessels.^{(6),(7)} Maximum plasma concentration of orally administered misoprostol is produced faster than vaginal method, so that in oral method, peak plasma concentration, occurs within 30 minutes and in the vaginal method, it takes about an hour.^{(8),(9)} But the concentration of the drug in plasma stays longer when administered vaginally, so that oral misoprostol is cleared after 2-3 hours, but vaginal

misoprostol takes more than 4 hours for clearance.⁽⁶⁾ Oral misoprostol requires fewer vaginal examinations, reducing the risk of maternal and foetal infection and provides more freedom for the pregnant woman to move which may help in the progress of labour. Oral administration of Misoprostol is not only easier, but mother satisfaction is higher and it can be used outside the hospital.⁽²⁾ Considering all these factors, this study was conducted to compare the effect of oral misoprostol with vaginal misoprostol for induction of labour in postdated pregnancies.

Aim

The aim of this study was to compare 50 micrograms of oral misoprostol with 25 micrograms of vaginal misoprostol for induction of labour in postdated pregnancies.

MATERIALS AND METHODS

This was a randomised controlled trial conducted in King George Hospital, Visakhapatnam during the period of three months of June, July and August 2017. 68 uncomplicated postdated pregnancies, admitted for induction of labour were included in the study. Sample size was taken conveniently. They were included to either of the two groups. Group allocation done by simple randomised lot method.

Inclusion Criteria

Gestational age more than or equal to 40 weeks (based on first trimester sonography and last menstrual period with regular menstrual cycles), single foetus, vertex presentation, Bishop score less than 4 and height more than 150 cm.

Exclusion Criteria

Contraindications to misoprostol (Allergies, asthma, Acute Cerebrovascular Disease, Coronary Artery Disease, seizures), placenta praevia, history of previous caesarean section or any uterine surgery, cephalopelvic disproportion, a Bishop score of 4 and above, abnormal vaginal bleeding and oligohydramnios, IUGR, pre eclampsia, or any other medical conditions.

Out of the total 146 postdated pregnancies, 68 were uncomplicated, included in the study for induction. In group A, 33 were included who were given 50 µg of oral misoprostol, and in group B, 35 were included and 25 µg vaginal misoprostol was used for inducing labour. Gestational age was determined based on first trimester sonography. Bishop score is determined thorough pelvic examination by Obstetrics and Gynaecology residents. Initial tests, including blood group, RH and CBC were requested. In order to ensure the foetal status non-stress test (NST) is carried out.

Labour induction was started in group 1 using 50 µg of oral misoprostol, in group 2 by 25 µg of vaginal misoprostol (posterior fornix). Medications were repeated every 4 hours for 4 doses based on the patients' condition. Vaginal examination to determine Bishop score was done before repeating each dose. Maternal vital signs and FHR was recorded every 4 hours. Labour augmentation was done with amniotomy once cervix is 3 cm and more dilated. Progress of labour was monitored with a partogram from 4 cm of cervical dilatation to delivery. Augmentation with oxytocin is done if uterine action is not adequate. If the woman did not enter active phase of labour i.e., cervical dilatation <4 cm and cervical effacement of <80% even after 24 hours of induction of labour,

it was considered as failed induction and pregnancy was terminated by caesarean section. Gestational age, parity, Induction starting time with misoprostol, initiation of uterine contractions, induction delivery interval, caesarean section and vaginal delivery rate and other variables including tachysystole, improvement in Bishop score, foetal outcome were recorded on the checklist. The results were interpreted as mean and standard deviation and Chi-square test was done to know the statistical significance using SPSS version 15.0.

RESULTS

G. A (in Weeks and Days)	Group - A (Oral)		Group - B (Vaginal)	
	n	(%)	n	(%)
40- 41 weeks	22	66.7%	15	42.9%
41-42 weeks	11	33.3%	20	57.1%
Total	33	100.0%	35	100.0%
Mean GA weeks	40.33 ± 0.479		40.57 ± 0.502	

Table 1. Distribution According to the Gestational Age

Gravida	Group - A (Oral)		Group - B (Vaginal)	
	n	(%)	n	(%)
Primi	24	72.7%	27	77.1%
Multi	9	27.3%	8	22.9%
Total	33	100.0%	35	100.0%

Table 2. Distribution of Cases According to Gravida

No. of Doses	Group - A (Oral)		Group - B (Vaginal)	
	n	(%)	n	(%)
1	13	39.4%	5	14.3%
2	13	39.4%	5	14.3%
3	7	21.2%	14	40.0%
4	0	0%	9	25.7%
5	0	0%	2	5.7%
Total	33	100.0%	35	100.0%
Mean	1.82 ± 0.769		2.94 ± 1.11	

Table 3. Distribution of Cases According to the Number of Doses Required for Induction

Bishop Score	Group - A (Oral)	Group - B (Vaginal)
Pre-induction BS	3.06 ± 1.345	2.69 ± 1.207
BS after 6 Hours	6.18 ± 1.648	4.77 ± 1.477

Table 4. Effect of Misoprostol on Bishop Score

Augmentation with Oxytocin	Group - A (Oral)		Group - B (Vaginal)	
	n	(%)	n	(%)
Yes	14	42.4%	28	80.05
No	19	57.6%	7	20.0%
Total	33	100.0%	35	100.0%

Table 5. Distribution of Cases based on Requirement of Oxytocin Augmentation

IDI (Hours)	Group – A (Oral)		Group – B (Vaginal)	
	n	(%)	n	(%)
< 12	7	21.2%	2	5.7%
12-24 hrs.	23	69.7%	17	48.65
> 24	3	9.1%	16	45.7%
Total	33	100.0%	35	100.0%
Mean	17.03 ± 4.964		22.49 ± 5.026	

Table 6. Distribution of Cases According to Induction Delivery Interval

Failed Induction	Group – A (Oral)		Group – B (Vaginal)	
	n	(%)	n	(%)
Yes	1	0.2%	3	0.6%
No	32	99.8%	32	99.4%
Total	33	100.0%	35	100.0%

Table 7. Distribution of Cases According to Failed Induction

Mode of Delivery	Group – A (Oral)		Group – B (Vaginal)	
	n	(%)	n	(%)
Normal	28	84.8%	29	82.9%
Forceps/Vacuum	0	0.0%	0	0.0%
LSCS	5	15.2%	6	17.1%
Total	33	100.0%	35	100.0%

Table 8. Distribution of Cases According to Mode of Delivery

Character of Liquor	Group – A (Oral)		Group – B (Vaginal)	
	n	(%)	n	(%)
Clear	26	78.8%	30	85.7%
MSAF	2	6.1%	4	11.4%
Thin MSAF	5	15.2%	1	2.9%
Total	33	100.0%	35	100.0%

Table 9. Distribution of Cases According to Character of Liquor

Maternal Complications	Group – A (Oral)		Group – B (Vaginal)	
	n	(%)	n	(%)
Uterine Tachysystole	0	0.0%	1	2.9%
Nil	33	100.0%	34	99.1%
Total	33	100.0%	35	100.0%

Table 10. Distribution of Cases According to Maternal Complications

APGAR Score	Group – A (Oral)		Group – B (Vaginal)	
	n	(%)	n	(%)
At 1 min.				
< 7	3	9.1%	5	14.3%
>=7	30	90.9%	30	85.7%
Total	33	100.0%	35	100.0%
At 5 min.				
< 7	1	3.0%	1	2.9%
>=7	32	97.0%	34	97.1%
Total	33	100.0%	35	100.0%

Table 11. Distribution of Cases According to Apgar Score at 1 and 5 Minutes

Mean APGAR Score	Group – A (Oral)	Group – B (Vaginal)
At 1 min.	7.58 ± 0.936	7.49 ± 1.040
At 5 min.	8.79 ± 0.696	8.74 ± 0.701

Table 12. Distribution of Cases According to Mean Apgar Score

NICU Admin	Group – A (Oral)		Group – B (Vaginal)	
	n	(%)	n	(%)
Yes	3	9.1%	5	14.3%
No	30	90.9%	30	85.7%
Total	33	100.0%	35	100.0%

Table 13. Distribution of Cases According to NICU Admissions

Group Variables	Group – A (Oral)	Group – B (Vaginal)	p- value	
No. of Doses	One	13 (39.4)	5 (14.3)	0.000**
	Two	13 (39.4)	5 (14.3)	
	Three	7 (21.2)	14 (40.0)	
	Four	0 (0.0)	9 (25.7)	
	Five	0 (0.0)	2 (5.7)	
Bishop Score After 6 hours	Three	1 (3.0)	8 (22.9)	0.056
	Four	5 (15.2)	9 (25.7)	
	Five	6 (18.2)	8 (22.9)	
	Six	7 (21.2)	5 (14.3)	
	Seven	5 (15.2)	3 (8.6)	
	Eight	8 (24.2)	2 (5.7)	
Augmentation with Oxytocin	Yes	14 (42.4)	28 (80.05)	0.001**
	No	19 (57.6)	7 (20.0)	
IDI (Hours)	< 12	7 (21.2)	2 (5.7)	0.002**
	12-24 hrs.	23 (69.7)	17 (48.65)	
	> 24	3 (9.1)	16 (45.7)	
Failed Induction	Yes	1 (0.2)	3 (0.6)	0.94
	No	32 (99.8)	32 (99.4)	
Character of Liquor	Clear	26 (78.8)	30 (85.7)	0.168
	MSAF	2 (6.1)	4 (11.4)	
	Thin MSAF	5 (15.2)	1 (2.9)	
Maternal Complications	Uterine Tachysystole	0 (0.0)	1 (2.9)	0.328
	Nil	33 (100.0)	34 (97.1)	
APGAR Score at 1 min	< 7	3 (9.1)	5 (14.3)	0.506
	>=7	30 (90.9)	30 (85.7)	
APGAR Score at 5 min.	< 7	1 (3.0)	1 (2.9)	0.966
	>=7	32 (97.0)	34 (97.1)	

Table 14. Table Showing p-value

DISCUSSION

The results observed while comparing the effect of 50 micrograms of oral misoprostol versus 25 micrograms of vaginal misoprostol for induction of labour in postdated pregnancy in 68 women are discussed below.

Distribution according to Gestational Age and Parity

There was no statistically significant difference in both groups with respect to gestational age and parity.

Number of Doses of Misoprostol Required for Induction

In the present study, the mean number of doses of 50 micrograms of oral misoprostol that were required for induction of labour was 1.89 ± 0.769 which was significantly less compared to the mean number of doses required for

induction in the vaginal group i.e. 2.94 ± 1.11 , with P- value 0.000.

In a similar study conducted by⁽¹⁰⁾ Hafizur Rahman et al, (2013) the mean number of doses of misoprostol required orally and vaginally for induction of labour was the same i.e. in the oral group was 2.33 ± 1.18 and in the vaginal group was 2.42 ± 1.28 with $P=0.59$.

Another study by⁽¹¹⁾ Kambhampati Komala et al (2013) also found that there was no significant difference in the mean number of doses of misoprostol required orally and vaginally with $P=0.11$.

This is attributed to pharmacokinetics of misoprostol which is different for each route. Although the bioavailability of vaginal misoprostol is greater, the peak plasma concentration attained by oral misoprostol is higher than the peak attained by vaginal route. Also, misoprostol is rapidly absorbed orally with the time for onset of action being shorter for oral route (8 min.) compared to vaginal route (20 min.). There is also a great variation in bioavailability between women with vaginal administration of misoprostol.

Effect of Misoprostol on Bishop Score

Before induction of labour, status cervix is noted by vaginal examination and Bishop score noted in both the groups, again after 6 hours. The Bishop score for oral group after 6 hours was 6.18 ± 1.648 and that for vaginal group was 4.77 ± 1.477 , which was statistically significant ($p=0.056$). It indicates that the effect of misoprostol on cervical score was significantly more when administered orally compared to the vaginal administration.

Requirement of Augmentation with Oxytocin

In the present study, it was found that 42.4% of cases in Group A and 80.05% of cases in Group B required augmentation with oxytocin. The difference was statistically significant, with P-value 0.001. This finding is consistent with the study by⁽¹²⁾ Shi-Yann Cheng which showed, only 10.9% (11 of 101) of patients in the titrated oral misoprostol group needed oxytocin augmentation, which was a far lower percentage than the 53.8% (57 of 106) in the vaginal misoprostol group (RR 0.11, 95% CI 0.05– 0.22). In the study conducted by⁽¹⁰⁾ Hafizur Rahman et al (2013), 30 out of 110 cases (27.27%) in the oral misoprostol group required augmentation with oxytocin and 26 out of 110 cases (23.64%) in the vaginal group required oxytocin augmentation for labour with $P=0.64$ which is not statistically significant.

Induction Delivery Interval

The mean induction to delivery interval in the present study was found to be 17.03 ± 4.964 hours in Group A (oral) which was significantly less compared to 22.49 ± 5.026 hours in Group B (vaginal) with $P=0.002$. In another study by Kambhampati Komala et al (2013), oral group had a shorter induction to delivery interval of 12.92 hours in oral group as compared to 14.04 hours in vaginal group. In the study by⁽¹³⁾ Khadija Bano et al, mean induction delivery interval was similar in both groups; vaginal (9.09 ± 3.4 hours) and oral (9.81 ± 4.43 hours $p=0.33$).

Failed Induction

In this study, number of cases who did not progress to active labour after 24 hours of induction was considered as failed

induction. There was no statistical difference with respect to this outcome with $P=0.94$. This finding was consistent with the study by Hafizur Rahman et al. (2013) where 19 out of 110 cases (17.2%) in oral group and 22 out 110 cases (20%) in vaginal group were declared as failed induction with $P=0.73$. In the study by Kambhampati Komala et al (2013), failed induction rate was more in vaginal group, which had a 6% rate as compared to oral group, which had a rate of 2%.

Mode of Delivery after Induction

Patients who had normal delivery were 84.8% in Group A (oral) and 82.9% in Group B (vaginal). 15.2% in Group A and 17.1% Group B underwent emergency caesarean section in the present study.

This finding is consistent with a similar study by Hafizur Rahman et al (2013) who found no significant difference in the number of vaginal, instrumental and caesarean delivery rates between oral and vaginal misoprostol groups. In the study by Kambhampati Komala et al (2013), caesarean rate in oral group was 6% and in vaginal group it was 14%. Major indication for operative delivery rates in both the groups was non-reassuring CTG. The incidence of instrumental delivery was same in both the groups.

Characteristics of Liquor

In the present study, 78.8% cases in Group A and 85.7% cases in Group B had clear liquor; and 6.1% cases in Group A and 11% cases in Group B had meconium-coloured liquor indicating no significant difference with p value 0.168. Three cases out of the four cases of meconium-stained liquor from vaginal group showed a non-reassuring CTG and underwent LSCS for foetal distress. All the three babies were admitted in NICU for respiratory distress. Both 2 cases of meconium-stained liquor from oral group showed non-reassuring CTG and underwent LSCS for foetal distress. All the two cases had NICU admission.

Similar findings were observed by Hafizur Rahman et al (2013) where 18.18% in oral group and 23.64% in the vaginal group developed meconium-stained liquor.

In the study by Kambhampati Komala et al (2013), incidence of meconium-stained liquor was more in vaginal group (20 out of 78) as compared to that in oral group (14 out of 86), but there was no significant difference.

Maternal Complications

In the present study, only one case from Group B (vaginal) developed Tachysystole (2.9%), this difference was not statistically significant. Other common adverse effects of misoprostol like nausea, vomiting, watery diarrhoea, fever were not encountered in the present study.

In the study by Hafizur Rahman et al (2013), adverse effects like nausea, vomiting, diarrhoea and fever were encountered but the incidence was similar in both oral and vaginal groups. Tachysystole developed in two women (1.8%) in the oral misoprostol group and six women (5.5%) in the vaginal misoprostol group.

In the study by Kambhampati Komala et al (2013), the rate of hyperstimulation in vaginal group was only 1%, where caesarean section was done immediately and it was nil in oral group. Gastrointestinal side effects were reported more in oral group and incidence of hyperpyrexia was also more in oral group in this study.

APGAR Score at 1 and 5 Minutes

In the present study, mean APGAR score at 1 minute was 7.58 ± 0.936 and that after 5 minutes was 8.79 ± 0.696 in group A and in group B it was 7.49 ± 1.040 and 8.74 ± 0.701 respectively. NICU admissions 5 and 3 in group B and A respectively with P-value 0.5 at 1 min. and P-value 0.9 at 5 min.

In the study by Hafizur Rahman et al, (2013) 8 out of 110 in oral group and 15 out of 110 in vaginal group had APGAR score less than 7 at 5 minutes indicating no significant difference between the two groups with respect to this outcome with P-value 0.19. In the study by Kambhampati Komala et al (2013), 24 cases out of 74 in vaginal group and 14 cases out of 86 in oral group had low 5-minute APGAR scores of 6-8 with overall good neonatal outcome in both the groups.

CONCLUSION

This study concludes that oral misoprostol in a dose of 50 µg has the potential to induce labour as safely and effectively as 25 µg vaginally administered misoprostol because of similar labour outcome with significantly shorter induction delivery interval, lesser number of doses required for delivery, more improvement in Bishop score after 6 hours of induction, lesser requirement of oxytocin augmentation with similar maternal and foetal outcome. A limitation of our study is the lack of blinding after randomisation. The clinicians involved in the study were aware of the allocated treatment. Further, the present study had a relatively small sample size. There is a need for a greater number of appropriately designed randomised controlled trials (preferably double blinded) with a larger sample size to validate the efficacy and safety of 50 µg oral misoprostol in comparison with 25 µg vaginal misoprostol. Oral use of the drug is easier and more convenient for both patients and caregivers.

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