

**Research Article****A Comparative Study of Oral versus Vaginal 25µg Misoprostol for Induction of Labour in Post Dated Pregnancy****Nirmala Hanji, Sreelatha. S.<sup>2\*</sup>, Tejaswini.B.Hiremath<sup>3</sup>**<sup>1</sup>Junior Resident, Department of OBG, ESICMCPGIMSR, Bangalore, Karnaaka, India<sup>2</sup>Associate Professor, Department of OBG, ESICMCPGIMSR, Bangalore, Karnaaka, India<sup>3</sup>Senior Resident, Department of OBG, ESICMCPGIMSR, Bangalore, Karnaaka, India**\*Corresponding author**

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**Abstract:** Objective of this study was to achieve a safe vaginal delivery of patients with post datism by induction of labour. We sought to compare the efficacy and safety of oral misoprostol with vaginal misoprostol. 100 patients with post datism for induction of labour were divided into oral and vaginal group equally. Both the groups received 25mcg of misoprostol every 4<sup>th</sup>hrly, either orally with water or it was digitally administered in the posterior fornix in the vaginal group, maximum upto 6 doses in either group. Primary outcome of the study was shorter induction –delivery interval in both oral group (11.86±3.10) and vaginal group (12.92±3.36). Mean Apgar score at 1 min in oral group is 6.86±0.78 and at 5 min 9.24±0.87. In vaginal group 6.74±0.83 at 1 min and 9.04±0.99 at 5 min. NICU admissions are statistically not significant with minimal maternal side effects. Oral misoprostol (25mcg) is as effective as vaginal misoprostol (25mcg) for induction of labour in post dated pregnancy with shorter induction –delivery interval and good perinatal outcome with minimal maternal side effects. So, misoprostol is safe and inexpensive.**Keywords:** Cervical Ripening, Induction, Misoprostol, Post Datism.

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**INTRODUCTION**

Post-term pregnancy is defined as a pregnancy that continues to or beyond 42 weeks (294 days) from the first day of the last normal menstrual period or 14 days beyond the best obstetric estimate of the date of delivery [1, 2]. It represents approximately 7% of all pregnancies and the prevalence depends on the population characteristics like nulliparity, a prior post-term pregnancy and genetic predisposition.

The main complication associated with pregnancy beyond 40 and 41 weeks of gestation are still birth, perinatal mortality and morbidity and increased risk of cesarean delivery. In majority of women, labour starts spontaneously and results in vaginal delivery at or near term. Indeed the most appropriate prevention and management of post-term pregnancy includes accurate gestational age assessment in early pregnancy, antenatal fetal surveillance, and the timely initiation of delivery if spontaneous labor does not occur. In fact obstetricians favour a policy of routine induction for low risk pregnancies at 41 wks of gestation, and it appears to be an effective strategy to reduce the risk of late intrauterine death.

Induction of labor is stimulation of regular uterine contractions before the spontaneous onset of labor,

using mechanical or pharmacological methods in order to generate progressive cervical dilatation and subsequent delivery [3]. The incidence of induction of labor has increased over recent decades. Approximately 5-10% of women will continue their pregnancy beyond 294 days or 42 completed weeks of pregnancy and these women are considered post-term and are one of the main contributors to the high incidence of induction of labor. Although one of the commonest interventions in obstetrics, induction of labor should not be undertaken lightly as of all women who are induced, less than two thirds will give birth without further intervention, approximately 15% will have an instrumental delivery and over 20% will deliver by emergency cesarean section. In addition, studies have demonstrated that a vast majority of women prefer not to have induction of labor by any means. It is therefore imperative that women will be counselled appropriately antenatally regarding induction of labor, risks, benefits and alternatives. Induction of labor is an increasingly common practice that accounts for >20% of all births. Bishop's score is the main criteria for induction of labour to have successful vaginal delivery.

There are variety of maternal and fetal conditions wherein the benefits of birth outweigh the risks of continued pregnancy for either mother or fetus that are

accepted indications for induction of labor [4]. Prostaglandins have been used for cervical ripening since the 1960s [5]. Misoprostol was first introduced into obstetrics in 1987. The use of misoprostol for cervical ripening and labor induction found significant decrease in the time from administration to delivery when compared to different comparison groups including other prostaglandins, oxytocin, Foley catheter, and extra amniotic saline or ricinus oil. There were no significant differences in cesarean birth rates or neonatal outcomes between women induced with misoprostol and all comparison groups [6]. The American College of Obstetricians and gynecologists recommends that women with post-term gestations who have unfavorable cervix can undergo labor induction or be managed expectantly, but they acknowledge that many physicians routinely induce labor by 42 weeks. There is no evidence regarding the effectiveness of antenatal testing in women who are post-term. However based on expert consensus, ACOG recommends a non-stress test and amniotic fluid index twice weekly, starting at 41 weeks [7]. In clinical practice the decision between induction and expectant management should include favorability of the cervix, maternal parity and patient preferences and often includes patient or physician convenience [8]. The study has been undertaken to compare the efficacy and safety of the drug with same low dosage (25µg) by different routes to know the effect and outcome.

Labour induction with misoprostol has become an intensely investigated topic. Various authors have reported its excellent efficacy, minimal side effects and cost saving benefits [9].

Investigations predominantly focus on the dosing and timing of administration with intra vaginal application. Few clinical studies report the use of orally administered misoprostol for induction of labour [10]. Thus, this comparative between the safety and efficacy of oral and vaginal routes of administration of misoprostol for induction of labour was undertaken.

**Aim of Study**

To compare the efficacy and safety of oral versus vaginal 25mcg misoprostol for induction of labor in postdated pregnancy.

**Objectives**

- To compare induction –delivery interval.
- To assess the perinatal outcome.

- To assess the maternal side effects of the drug.

**METHODOLOGY**

The present study was conducted in the department of obstetrics and gynecology, ESICMC-PGIMSR Rajajinagar Bangalore with the aim of comparing efficacy and safety of oral and vaginal misoprostol 25 mcg for induction of labor in postdated pregnancies who needed induction.

This is comparative prospective study for the duration of 6 months after an approval from the institutional ethical committee. Study included 100 consecutive women who attended out patient department with post dated pregnancy for safe confinement who fulfills following

**Inclusion Criteria**

- Singleton pregnancy
- Cephalic presentation
- Post dated pregnancy (>40wks and <42wks with informed consent)
- Bishop score 0-5

**Exclusion Criteria**

- Previous uterine scar
- Known allergy to prostaglandins
- Grand multipara
- Premature rupture of membranes
- Pregnancy induced Hypertention
- Intrauterine growth restriction
- Maternal illness
- Cervical dilatation>3cm
- Uterine contractions>3/10min
- Mal presentation
- Cephalo-pelvic disproportion.

After taking written informed consent about route of administration of drug, mechanism of action of drug, side effects of the drug, maternal and fetal complications, and detail history was taken. Baseline investigations were reviewed as per antenatal protocol. Dates were confirmed by history and serial (1, 2 and 3 trimester) ultrasonography. Clinical examination with Per abdominal examination was done to confirm lie, presentation, gestational age and amount of liquor. After confirming reactive cardiotocogram for 20 minutes, vaginal examination was done and Bishop Score 0-5 were included in the study.

**Table 1: Original Bishop Score (modified Calder’s method)**

Component	0	1	2	3
Cervical dilatation	0cm	1-2cm	3-4cm	>4cm
Effacement	0-40%	40-60%	60-80%	>80%
Station in cm	-3	-2	-1,0	+1,+2
Consistency	Firm	Average	Soft	
Position	Posterior	Mid	Anterior	

Depending upon the randomization, group 1 received vaginal misoprostol 25 mcg. The tablet was moistened with few drops of normal saline and inserted in the posterior fornix of the vagina. The woman was asked to lie down for at least 10 min after vaginal administration to allow the tablet to dissolve completely. The subsequent dosages were given four hourly and Bishop's score was noted before administration. Maternal and fetal parameters were assessed by partogram. Drug was repeated every 4<sup>th</sup>hrly till adequate uterine contractions were achieved (3 contractions/10 min or cervical dilatation>3cm) maximum 6 doses. Similarly group 2 received oral 25mcg misoprostol every 4<sup>th</sup>hrly maximum 6 doses with maternal and fetal parameters assessment.

The adverse effects like tachysystole, hypertonus and uterine hyperstimulation were watched for. Tachysystole was defined as 6 or more contractions in 10 min for 2 consecutive 10 minutes period. Hypertonus was defined as a single contraction lasting for more than 2 minutes. Uterine hyperstimulation was defined as tachysystole and hypertonus associated with fetal tachycardia or bradycardia. The women were given left lateral position and continuous fetal heart rate monitoring was done for 15 minutes intervals. If any of the above condition persisted, further drug administration was withheld. Labor was managed

according to labor room protocols. Active phase of labor was defined as dilatation of at least 3cm along with uterine contractions 3/10 min. Once the delivery was achieved, duration of induction-delivery interval, mode of delivery and maternal side effects of the drug like nausea, vomiting, diarrhea and shivering were noted. The perinatal outcome was assessed by Apgar score at 1min and 5min, meconium stained liquor, still birth and perinatal mortality. The mother and fetus were followed up for a period of at least 72 hrs for signs of infection and hyperbilirubinaemia.

Operative cesarean delivery was done according to obstetric indications like fetal distress and induction failure. Induction failure was defined as failure to enter the active phase of labor within 24hr from the start of induction or unchanged Bishop's score and inadequate uterine contractions even after 6 doses.

**RESULTS**

This is a prospective comparative study undertaken to compare the safety and efficacy of oral versus vaginal 25mcg misoprostol for induction of labour in postdated pregnancy. Total number of patients assigned for the study were 100 which were divided into two groups of 50 each either oral or vaginal. Qualitative data are expressed in the form of percentage and quantitative data as mean ± standard deviation, p-value.

**Table 1: Age Wise Distribution**

Age in years	Oral Group		Vaginal Group	
	No	%	No	%
19-20	5	10.0	2	4.0
21-25	35	70.0	39	78.0
26-30	10	20.0	9	18.0
Total	50	100.0	50	100.0

Samples are age matched with p=0.460

Age	Oral group	Vaginal group
Mean &SD	23.28+ 2.39	23.82+ 1.98

The above table shows the age distribution of subjects. Maximum no of patients are at the age group of 21-25yrs. Statistical analysis: In oral group 70%

with mean & SD of 23.28±12.39 yrs. In vaginal group 78% with mean & SD of 23.82±1.98 yrs. P value was 0.460.

**Table 2: Route of Drug**

Route of drug	Oral Group		Vaginal Group	
	No	%	No	%
Oral	50	100.0	0	0.0
Vaginal	0	0.0	50	100.0
Total	50	100.0	50	100.0

Patients are equally divided into both oral and vaginal group (50 in each group). p value was <0.001.

**Table 3: Distribution According To Parity**

Parity	Oral Group		Vaginal Group	
	No	%	No	%
Primi	30	60.0	29	58.0
Multi	20	40.0	21	42.0
Total	50	100.0	50	100.0

Parity distribution is statistically similar with p=0.839

This table shows distribution of cases according to parity.

Statistical analysis: In oral group 60% are primigravidas and 40% are multigravida In vaginal group 58% are primi's and 42% are multigravida. p value was 0.83 .

**Table 4: According to Bishop Score on Admission**

Bishop score on admission	Oral Group		Vaginal Group	
	No	%	No	%
1(0-5)	5	10.0	6	12.0
2(0-5)	30	60.0	28	56.0
3(0-5)	15	30.0	16	32.0
Total	50	100.0	50	100.0

Bishop score on admission is statistically similar in two groups with p value 0.908.

This table shows Bishop Score on admission in patients for induction of labour. Statistical analysis: In oral group 10% of the patients had Bishop Score of 1(0-5) at the time of admission. Remaining 60% had 2(0-5) and 30% had 0(0-5).

In vaginal group 12% had 1(0-5), 56% had 2(0-5) and 32% had 3(0-5). In both the groups maximum patients are with Bishop Score of 2(0-5) on admission. p value was of 0.908.

**Table 5: Induction-Delivery Interval**

I-D interval	Oral Group		Vaginal Group	
	No	%	No	%
<6 hour	2	4.0	0	0.0
6-12 hour	26	52.0	26	52.0
>12 hour	22	44.0	24	48.0
Total	50	100.0	50	100.0

I -D interval	Oral group	Vaginal group
Mean ±SD	11.86±3.10	12.92±3.36

This above table shows induction-delivery interval in both groups.

Statistical analysis: In oral group 4% of the patients had <6hr induction to delivery interval. 6-12hrs in 52% and >12hr in 44%.

In vaginal group 52% of the patients had 6-12hr induction-delivery interval, >12hr in 48%. In oral group 11.86±3.10 (mean& SD) hrs. In vaginal group 12.92±3.36 (mean &SD) hrs. p value was 0.496.

**Table 6: Distribution According to Mode of Delivery**

Mode of delivery	Oral Group		Vaginal Group	
	No	%	No	%
FTND	46	92.0	44	88.0
Vacuum	2	4.0	0	0.0
LSCS	2	4.0	6	12.0
Total	50	100.0	50	100.0

This table shows distribution of cases according to mode of delivery. In oral group 92% had vaginal delivery, 4% had instrumental delivery and 4% had

lower segment cesarean delivery due to fetal distress. In vaginal group 88% had vaginal delivery and 12% had lower segment cesarean section. p value was 0.163

**Table 7: Distribution According to Apgar score of Neonates**

Apgar score	Oral Group(n=50)		Vaginal Group(n=50)		p value
	No	%	No	%	
Apgar 1 minutes					
• ≤7	40	80.0	42	84.0	0.795
• >7	10	20.0	8	16.0	
Apgar 5 minutes					
• ≤7	1	2.0	4	8.0	0.362
• >7	49	98.0	46	92.0	

Apgar score	Oral route	Vaginal route	p value
At 1min	6.86±0.78	6.74±0.83	0.458
At 5 min	9.24±0.87	9.04±0.99	0.286

Above table shows distribution of neonates according to their Apgar score at 1min and 5 minutes. In oral group 80% neonates had Apgar score of <7 at 1 min. In vaginal group 84% had Apgar score of <7 in 1 min. At 5 min 98% had >7 Apgar score in oral group and in vaginal group 92% had >7.

Statistical analysis: In oral group at 1 min mean Apgar score is 6.86±0.78. In vaginal group at 1 min mean Apgar score is 6.74±0.83. p value was 0.458.

At 5 min the mean Apgar score in oral group is 9.24±0.87. In vaginal group mean Apgar score is 9.04±0.99. p value was 0.286.

**Table 8: Oxytocin Augmentation**

Oxytocin Augmentation	Oral Group		Vaginal Group	
	No	%	No	%
No	26	52.0	33	66.0
Yes	24	48.0	17	34.0
Total	50	100.0	50	100.0

Oxytocin Augmentation is statistically similar with P=0.155. This above table shows requirement of oxytocin for augmentation during the process of labour.

Statistical analysis: In oral group 48% of patients required oxytocin augmentation and 34% in vaginal group with p value 0.155.

**Table 9: Neonatal Meconium Aspiration**

Meconium aspiration	Oral Group		Vaginal Group	
	No	%	No	%
No	38	75.0	35	70.0
Yes	12	25.0	15	30.0
Total	50	100.0	50	100.0

Distribution of Meconium aspiration in neonates is statistically similar with p value 0.82. This above table shows incidence of meconium aspiration in neonates in both oral and vaginal group.

Statistical analysis: In oral group 25% neonates had meconium aspiration. In vaginal group 30% had meconium aspiration with p value of 0.826.

**Table 10: NICU Admission**

NICU Admission	Oral Group		Vaginal Group	
	No	%	No	%
No	46	92	45	90.0
Yes	04	08	05	10.0
Total	50	100.0	50	100.0

Statistical analysis: In oral group 8% neonates had NICU admissions due to fetal distress with low Apgar

score. In vaginal group 10% required NICU admission. P value was 0.766.

**Table 11: No. of Doses Required for Induction**

No of doses	Oral group		Vaginal group	
	No	%	No	%
1	6	12	3	6
2	17	34	22	44
3	19	38	20	40
4	05	10	02	04
5	03	6	03	06
6	00	00	00	00
Total	50	100	50	100

In oral group: 12% patients required 1 dose, 34% required 2 doses and 38% required 3 doses. 10% required 4 doses and 6% required 5 doses.

In vaginal group: 6% patients required 1 dose, 44% required 2 doses, 40% required 3doses, 4% required 4 doses and 6% required 5 doses.

**Table 12: Maternal Side Effects**

Side effects	Oral group		Vaginal group	
	No	%	No	%
Fever	02	04	02	04
Shivering	01	02	02	04
Nausea & vomiting	03	06	05	10
Diarrhoea	03	06	04	08
Nil	41	82	37	74
Total	50	100	50	100

Above table shows incidence of maternal side effects in both oral and vaginal route of administration.

Statistical analysis: In oral group: 4% had fever, 2% had shivering, 6% had nausea and vomiting and 6% had diarrhoea. In vaginal group: 4% had fever, 4% had shivering, 10% had nausea and vomiting and 8% had diarrhoea.

#### Statistical Methods

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean  $\pm$  SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance. The following assumptions on data is made,

- Dependent variables should be normally distributed,
- Samples drawn from the population should be random, Cases of the samples should be independent

Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups.

#### Significant figures

- + Suggestive significance (P value:  $0.05 < P < 0.10$ )
- \* Moderately significant (P value:  $0.01 < P \leq 0.05$ )
- \*\* Strongly significant (P value:  $P \leq 0.01$ )

#### Statistical software

The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

#### DISCUSSION

The study was conducted in the department of Obstetrics and Gynaecology in ESIC-PGIMS, Bangalore. In the present study, 100 women with

postdatism were divided into oral and vaginal group equally. Both groups received 25mcg of misoprostol every 4<sup>th</sup> hourly either orally with water or with vaginally administered in the posterior fornix, maximum upto 6 doses in either group.

#### Oxytocin Augmentation

##### Oral Group

In the present study Oxytocin required in 24 (48%) of women which is in correlation with Deborah A *et al.* [11] and Ashalatha Shetty *et al.* [12].

##### Vaginal Group

In the present study Oxytocin required in 17(34%) of women which is in correlation with C. David *et al.* [13], and Ashalatha Shetty *et al.* [12].

#### Induction Delivery Interval

##### Oral Group

In a study conducted by C. David Adair *et al.* [13] the induction – delivery interval was  $749 \pm 464$  mins. In the present study induction – delivery interval was  $720.2 \pm 62$  mins in correlation with C. David Adair *et al.* [13].

##### Vaginal Group

In a study conducted by C. David Adair *et al.* [13] induction- delivery interval was  $843 \pm 479$  mins. In the present study induction – delivery was  $1080 \pm 132$  mins in correlation with C. David Adair *et al.* [13].

#### APGAR Score

##### Oral group

In a study conducted by Akter *et al.* [14], Apgar score at 1 min was 8.58 and 10 at 5 min. In the present study Apgar score at 1 min was  $6.86 \pm 0.78$  and  $9.24 \pm 0.87$  at 5 min in correlation with Akter *et al.* [14].

##### Vaginal group

In a study conducted by Akter *et al.* [14] Apgar score at 1 min is  $8.70 \pm 1.12$  and 9.92 at 5 min. In the present study Apgar score at 1min is  $6.74 \pm 0.83$  and  $9.04 \pm 0.99$  at 5 min in correlation with Akter *et al.* [14].

### Meconium Aspiration

In a study conducted by Hafizur Rahman *et al.* [15] 20 (18%) had meconium aspiration in oral group and 26(23%) in vaginal group.

In present study 12(25%) had meconium aspiration in oral group and 15(30%) in vaginal group in correlation with Hafizur Rahman *et al.* [15].

### NICU Admission

In a study conducted by Hafizur Rahman *et al.* [15] 5(6%) required NICU admission in oral group and 9(8%) in vaginal group. In the present study 4(8%) required NICU admission in oral group and 5(10%) in vaginal group in correlation with Hafizur Rahman *et al.* [15].

### Maternal Side Effects

#### Oral group

In a study conducted by Hafizur Rahman *et al.* [15] had hyper stimulation in 2(1.8%), diarrhoea in 2(1.8%), fever in 2(1.8%), nausea and vomiting in 7(3.36%).

In the present study 3(6%) had diarrhoea, 2(4%) fever, 3(6%) nausea & vomiting, 1(2%) shivering in correlation with Hafizur Rahman *et al.* [15].

#### Vaginal group

In a study conducted by Hafizur Rahman *et al.* [15], had hyper stimulation in 6(5.4%), diarrhoea in 9(8%), fever in 4(3.6%), nausea & vomiting in 3(2.7%). In the present study 4(8%) had diarrhoea, 2(4%) fever, 3(5%) nausea & vomiting, 2(4%) shivering.

### CONCLUSION

In our study Oral misoprostol 25 mcg is as effective as vaginal misoprostol 25mcg for induction of labour in post dated pregnancy with less induction-delivery interval and good perinatal outcome with minimal maternal side effects.

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