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A Comparative Study of Efficacy of Oral Misoprostol versus Vaginal Misoprostol in the Induction of Labor from 34 to 40 Weeks Gestation

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Abstract: The aim of the present study was to compare the efficacy of oral versus vaginal misoprostol in the induction of labor after 34 weeks of gestation to 40 weeks gestation and to find out any variation in the maternal and fetal outcome. Methods: This study was conducted in the Department of Obstetrics and Gynaecology at Prathima Institute of Medical Sciences, Karimnagar, and Telangana state for the period of one year. In the present study 100, antenatal women who are more than 34 weeks of gestation and who need induction of labor were selected for the study. To calculate the EDD, calculated using Naegele's Formula. Women divided into Group A – 50 pregnant women, aged 18-32 years; with oral administration of 25 mcg Misoprost every 4th hourly, maximum of 6 doses (150mcg). Group B - 50 pregnant women, aged 18-32 years, with vaginal administration of 25mcg Misoprost every 4th hourly, maximum of doses of 6 doses(150mcg). In all the patients, the cervical status was assessed by using Bishop's score prior to induction. Repeat bishop's score was assessed at 4th hour and then before every repeat dose. Results: Parity a total of 57 women was primigravida while 43 were multigravida. For oral group 29 cases (58%) were primigravida, 21 cases (42%) were multigravida for the vaginal group, 28 cases (56%) were primigravida, 22 cases (44%) were multigravida. Augmentation with Oxytocin Of the total, 45% of the cases were on Oxytocin while remaining was not. For Oral Group 27 cases (54%) required augmentation with Oxytocin. Failed Induction In the study group, nearly 3% of the cases failed induction. In Oral group Failed induction incidence was in 3 cases (6%). In the Vaginal group, there was no failure of induction. 75% of the cases had a normal delivery, 12% showed vacuum delivery followed by C section (10%) and 3% cases had the forceps delivery.

Keywords: Oral Misoprostol, Vaginal Misoprostol, Induction of Labor.

INTRODUCTION

Induction of labor at term with unfavorable cervix is associated with increased risk of failed induction and cesarean section. Convention methods for cervical ripening (oxytocin, Foleys catheter) are being used, but have their own merits and demerits. Hence there is a need for a more efficient inducing agent with fewer limitations. There are various methods of induction of labor falling into two broad categories: non-pharmacological and pharmacological. The aim of the obstetrician should be to select the ideal method of induction which is safe, reliable, cheap, easily applicable, readily available, and which results in good maternal and fetal outcome. Prostaglandins as pharmacological agents have always fascinated the obstetrician for induction of labor as well as the cervical ripening agent. Recently, Prostaglandin E_1 (Misoprostol) tablets as an inducing agent of labor by various routes e.g. vaginal, oral, rectal etc have received huge attention. As it is cheap, easily available, has a long shelf life and easily administrable, it is fast gaining popularity. In Parkland Hospital, Misoprostol is the Prostaglandin of choice for induction of labor. The American College of Obstetricians and Gynecologists has reaffirmed the use of Misoprostol as a drug for induction of labor because of its proven safety and efficacy [1, 2]. Prostaglandins are the new drugs of interest in this field. Out of all prostaglandins, PGE_1 and PGE_2 have been tried for induction of labor. As PGE_2 is being used in gel and tablet form has the advantage of being used intra-cervical or vaginal. But it is expensive and needs refrigeration. PGE_1 synthetic analog, misoprostol originally used as a gastro protective drug and it is used as cervical ripened and labor inducer. It has the advantage of being cheap, stable at room temperature and easy to be administered by various routes i.e. vaginal, oral, sublingual, and rectal. Hence it is necessary to study the efficacy of oral misoprostol versus vaginal misoprostol in an induction of labor after 34 weeks gestation to 40 weeks gestation. We in the present study tried to compare the efficacy of oral

versus vaginal misoprostol in an induction of labor after 34 weeks of gestation to 40 weeks gestation.

MATERIALS AND METHODS

This study was conducted in the Department of Obstetrics and Gynaecology at Prathima Institute of Medical Sciences, Karimnagar, and Telangana state for the period of one year. In the present study 100, antenatal women who are more than 34 weeks of gestation and who need induction of labor were selected for the study. To calculate the EDD, calculated using Naegele's Formula [6]. Inclusion criteria: Singleton pregnancy, vertex presentation, gravida, adequate pelvis Bishop score ≤ 4. Pre-Eclampsia, Eclampsia, Prolonged pregnancy, premature ruptures of membrane. Antepartum eclampsia, oligohydramnios and intrauterine death. Exclusion criteria: Placenta previa, abruption. Previous lower segment cesarean section, previous history of myomectomy Asymmetrical IUGR, grand multipara, Diabetic Mellitus, maturity onset DM, precious pregnancy, Cardiac and renal disease. The study includes 100 pregnant women divided as Group A – 50 pregnant women, aged 18-32 years; with oral administration of 25 mcg Misoprostol every 4th hourly, maximum of 6 doses (150mcg). Group B - 50 pregnant women, aged 18-32 years, with vaginal administration of 25mcg Misoprostol every 4th hourly, maximum of doses of 6 doses(150mcg). In all the patients, the cervical status was assessed by using Bishop's score prior to induction. Repeat bishop's score was assessed at 4th hour and then before every repeat dose. From the time of induction of labor to delivery, the patients were closely monitored for signs of labor, the progress of labor, uterine contractions, FHR monitored by intermittent auscultations. If the patient went into the active phase of labor, artificial rupture of the membrane was done if required. In case of failure of induction, the patient was taken for LSCS directly. Active Phase of Labor: It is defined in this study as cervical dilatation ≥ 4 cms and cervical effacement of ≥ 80% [3]. Bishop's Score: A quantifiable method used to predict the outcome of labor induction is the score described by Bishop where mainly the condition of cervix or favorability is described. It is given in the table below [4].

Table-1: Bishop Score in Table Form

Score	Dilatation (cms)	Effacement (%)	Station (-3 to +2)	Cervical Consistency	Cervical Position
0	Closed	0-30	-3	Firm	Posterior
1	1-2	40-50	-2	Medium	Mid position
2	3-4	60-80	-1	Soft	Anterior
3	>= 5	>=80	0, +1 , +2	-	-

Failed Induction: For this study, failed induction has been defined as failure to enter the active phase of labor after 24 hours of induction of labor. This definition is broadly based on various previous studies [5].

RESULTS

The indication for labor is 34 weeks to 40 weeks gestation without going into spontaneous labor, who need induction of labor In oral group Mean gestational week for induction of labor was 39 weeks, 2 days. Minimum gestational week for induction of labor was 34 weeks, 4 days. Maximum gestational week for induction of labor was 40 weeks. In vaginal group Mean gestational week for induction of labor was 39 weeks, 1 day. Minimum gestational week for induction of labor was 34 weeks, 4 days. Maximum gestational week for induction of labor was 40 weeks.

Table-2: Indication for Induction – Pregnancies between 34 weeks to 40 weeks gestation

Dose groups	N	Mean Gestational Age	SD	Minimum	Maximum	t-value	p-value
Oral	50	39.3 weeks	1.88	34 weeks 4 days	40 weeks		
Vaginal	50	39.14 weeks	1.33	34 weeks 4 days	40 weeks	0.307	0.759

Parity A total of 57 women was primigravida while 43 were multigravida. For oral group 29 cases (58%) were primigravida, 21 cases (42%) were multigravida for the vaginal group, 28 cases (56%) were primigravida, 22 cases (44%) were multigravida.

Table-3: Number of Doses of Drug Required for Delivery

Dose	Number of doses					Total N (%)
	1 N (%)	2 N (%)	3 N (%)	4 N (%)	5 N (%)	
Oral	2 (4.0%)	12 (24.0%)	23 (46.0%)	8 (16.0%)	5 (10.0%)	50 (100.0%)
Vaginal	15 (30.0%)	26 (52.0%)	8 (16.0%)	1 (2.0%)	0 (0.0%)	50 (100.0%)
Total	17 (17.0%)	38 (38.0%)	31 (31.0%)	9 (9.0%)	5 (5.0%)	100 (100.0%)

Number of Doses of Drug Required for Delivery Of the total women enrolled, the majority of the cases were on 2 doses (38%) followed by 3 doses (31%), 1 dose (17%), 4 doses (9%) and 5 (5%). For oral

group minimum number of the dose required was 1 (4% of cases) a maximum number of the dose required was 5 (10% of cases) majority of cases (46%) required 3 doses 24% of cases required 2 doses and the rest (16%) required 4 doses Table 3.

Table-4: Response to Drug in terms of Bishop Score

	Groups	N	Mean	SD	Minimum	Maximum	t-value	p- value
Pre-induction Bishop Score	Oral	50	2.82	1.26	1	5	1.32	0.19
	Vaginal	50	3.12	1.17	1	5		
4 Hours Bishop Score	Oral	50	4.40	1.71	2	9	10.27	0.002*
	Vaginal	50	5.72	1.75	3	10		

Augmentation with Oxytocin Of the total, 45% of the cases were on Oxytocin while remaining was not. For Oral Group 27 cases (54%) required augmentation with Oxytocin. Rest 23 cases (46%) did not require any augmentation for Vaginal Group 18 cases (36%) required augmentation with Oxytocin. Rest 32 cases (64%) did not require any augmentation.

Table-5: Requirement of Augmentation with Oxytocin

Dose	Augmentation with oxytocin		Total N (%)
	Yes N (%)	No N (%)	
Oral	27 (54.0%)	23(46.0%)	50 (100.0%)
Vaginal	18 (36.0%)	32 (64.0%)	50 (100.0%)
Total	45 (45.0%)	55 (55.0%)	100 (100.0%)

Induction to Delivery Interval In oral group mean induction to oral delivery interval was 24.40 hours Minimum induction to oral delivery interval was 10 hours Maximum induction to oral delivery interval was 30 hours in vaginal group Mean induction to vaginal delivery interval was 16.26 hours. Minimum induction to vaginal delivery interval was 8 hours • Maximum induction to vaginal delivery interval was 26 hours

Table-6: Induction to delivery interval

Groups	N	Mean induction To delivery interval (Hrs)	SD	Minimum	Maximum	t - Value	P - Value
Oral	50	24.4	3.31	10	30	11.32	<0.0001
Vaginal	50	16.26	3.86	8	26		

In the study group, nearly 3% of the cases failed induction. In Oral group Failed induction incidence was in 3 cases (6%). In the Vaginal group, there was no failure of induction.

Table-7: Maternal Complication

Dose	Maternal Complication					Total N (%)
	Diarrhoea N(%)	Fever N(%)	Trachy Systole N(%)	Uterine hyperstimulation N(%)	No complication N(%)	
Oral	0(0%)	1(2.0%)	0(0%)	0(0%)	49(98.0%)	50(100.0%)
Vaginal	0(0%)	1(2.0%)	0(0%)	1(2.0%)	48(96.0%)	50(100.0%)
Total	0(0%)	2(2.0%)	0(0%)	1(1.0%)	97(97.0%)	100(100.0%)

Mode of delivery among the studied cases, 75% of the cases had a normal delivery, 12% showed vacuum delivery followed by C section (10%) and 3% cases had a forceps delivery. For oral group 70% (35 cases) proceeded for normal delivery 12% (6 cases) required LSCS intervention 4% (2 cases) required forceps application for delivery 14% (7 cases) required vacuum application for delivery For vaginal group 80% (40 cases) proceeded for normal delivery 8% (4 cases) required LSCS intervention 2% (1 case) required forceps application for delivery 10% (5 cases) required vacuum application for delivery.

DISCUSSION

100 women were checked for the eligibility criteria and enrolled for the study. The indication for induction 34 to 40-weeks' gestation without going into spontaneous labor and who need induction where included in this study. EDD was calculated by Naegele's formula [6]. Indication for Induction – 34 weeks to 40 weeks gestation Mean gestational age for the Oral group was 39 weeks 2 days and that for the vaginal group was 39 weeks 1 day. The mean gestational age did not differ between the groups and the p-value was statistically insignificant (p= 0.76).

Parity Primigravidas predominated in both the groups and is often considered as one of the known etiological factor [7]. 29 cases (58%) were primigravida. Number of Doses of Drug Required for Delivery Majority of cases in the oral group needed 3 doses for induction of labor. Only two cases delivered after 1 dose. In the vaginal group, majority required only two doses for induction of labor whereas 15 cases (30%) delivered after 1 dose of Misoprostol. Our findings are consistent with the observations made by Shetty Ashalatha *et al.* [5] 46% of cases in the oral group required 3 doses for induction and in the vaginal group, nearly 52% required 2 doses for induction. A study by Kwon *et al.* [8] showed similar results with the mean number of doses required was more in the oral group as compared to the vaginal group. This is of prime importance because pharmacokinetics varies with the mode of induction of Misoprostol whether administered oral or vaginal. For oral administration, the onset of action is 8 mins, T-max is 30 mins and duration of action is 2 hours. For vaginal administration, the onset of action is 20 mins, T-max is 70 mins and duration of action is 4 hours. It is clear by the pharmacokinetics, vaginal Misoprostol remains effective for the longest time and hence lesser dosage is required for induction of labor. Before administrating the next dose of Misoprostol, scoring was done by Bishop's score and for both, the groups, followed by next PV examination was done. If the patient had already gone into active labor, further Misoprostol administration was withheld. Mean pre-induction bishop score for an Oral group was 2.80 ± 1.26 and the vaginal group was 3.12 ± 1.17 which was statistically insignificant ($p = 0.19$). After 4 hours, the Bishop score for the oral group had a mean of 4.40 ± 1.71 and for a vaginal group, was 5.72 ± 1.75, which was also statistically significant ($p=0.02$). The induction to delivery interval is one of the primary outcomes of the present study. In the Oral group, the mean interval was 24.40 hours and the same in a vaginal group was 16.26 hours. The difference is statistically significant ($p < 0.001$), indicating that the vaginal route of administration leads to lesser induction to the delivery interval as compared to the oral route. Also, in the vaginal group, the maximum induction to delivery interval was 26 hours, i.e. all the cases delivered within 26 hours of induction of labor. The same measure was 30 hours in the oral group. Finding corroborates the pharmacokinetics of oral and vaginal route of administration of Misoprostol since the vaginal route has a longer duration of action than the oral route. It could be explained on the basis that there is the greater Oxytocic effect of Misoprostol on uterus via vaginal route due to direct access to myometrium via cervical canal [1, 2, 9-11]. According to Mishra *et al.* 2007 the systemic bio-availability of vaginally administered Misoprostol is 3 times greater than that of oral Misoprostol [9]. Majority of the assisted vaginal deliveries were meant to cut short the second stage of labor as these cases had meconium stained liquor. In a study by Sultana *et al.* [12] only nulliparous women in the oral group took a long time to deliver than vaginal group though it was not statistically significant and the mode of delivery also did not differ significantly similar to our findings. There was no difference in the mode of delivery, analgesic requirements or neonatal outcomes in the two groups. According to Abbassi *et al.* [13] and Mehrotra *et al.* [14], there was no statistical difference between the groups with respect to the mode of delivery and neonatal outcome. Maternal Complication Common side effects of Misoprostol for induction of labor are nausea, vomiting, watery diarrhea, uterine cramps, uterine hyperstimulation, fever, and tachycardia and chest pain [11]. In an Oral group, a total of 1 (2%) cases developed some kind of maternal complication and had pyrexia while in the vaginal group, a maternal complication developed in 2 (4%) cases Neonatal Outcome in terms of NICU admissions. In the present study, in oral 7 cases developed neonatal complications of these, 6 (86%) required NICU admission for preterm complication such as respiratory distress, low birth weight and 1 (14%) for Thick meconium aspiration syndrome. In vaginal, 20% (10 cases) neonates had to be admitted to NICU. Of these 4 (40%) cases were admitted due to respiratory distress and low birth weight, 5 (50%) had meconium aspiration syndrome and 1(10%) was kept for observation. In previous studies, NICU admissions were more because of associated comorbid conditions of the neonates. According to the findings of Nirmala *et al.* 12(20%) had meconium aspiration in the oral group and 11(22%) in the vaginal group. In terms of maternal outcome, induction to delivery interval was significantly shorter (mean 16. 26 hours) in vaginal group when compared to oral group (mean 24.4 hours) ($p < 0.001$). The need for Oxytocin augmentation was also significantly lesser in vaginal group (36% of cases) as compared to oral group.

CONCLUSION

The maximum number of doses required in the oral group was 3 whereas in a vaginal group it was 2. Favorability of the cervix was ascertained using Bishop Score. Bishop Score improvement after 1st dose of Misoprostol was better in the vaginal group and could be attributed to the direct action of Misoprostol on uterus and cervix in vaginal administration. Vaginal group required less Oxytocin augmentation for delivery. The number of doses required for induction of labor was more in the oral group. In a vaginal group, all the cases which delivered vaginally, delivered in less than 26 hours from the time of induction Neonatal complications were higher in the vaginal group than the oral group.

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