IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 17, Issue 3 Ver.17 March. (2018), PP 47-51
www.iosrjournals.org

Comparison of Vaginal Misoprostol versus Dinoprostone (PGE2) Gel for Induction of Labour in Preterm Premature Rupture of Membrane at ≥ 34 Weeks

Dr. Puneeta Mahajan[1], Dr. Poonam Kumari[2] , Dr. Neeraj Sharma[3]
[1]*Medical Director and Consultant OBG, Dr. Baba Saheb Ambedkar Medical College & Hospital, New Delhi. 110085, India*
[2]*DNB Resident 3rd year, Dr. Baba Saheb Ambedkar Medical College & Hospital, New Delhi. 110085, India*
[3]*Counsultant, Dr. Baba Saheb Ambedkar Medical College & Hospital, New Delhi 110085, India*
Corresponding author: Dr. Puneeta Mahajan

Abstract: *Preterm premature rupture of membranes (PPROM) is the spontaneous rupture of the fetal membranes during pregnancy before 37 weeks gestation in the absence of regular painful uterine contractions [1]. It increases the risk of prematurity and leads to other perinatal and neonatal complications with 1-2% risk of fetal death [2].PPROM is an important cause of perinatal morbidity and mortality because it is associated with brief latency from membrane rupture to delivery, perinatal infection and umbilical cord compression due to oligohydramnios[7]. Study was conducted on one hundred forty women who were admitted for management of preterm premature rupture of membrane at ≥34 to ≤37 weeks of gestation of pregnancy. They were randomized using block randomization with sealed envelope system. 70 women received vaginal misoprostol tablet 25µgm, 4 hourly for a maximum 3 dose and rest 70 received dinoprostone 0.5 mg gel in posterior fornix inserted 6 hourly for a maximum of 2 doses. Women in both groups were closely observed after induction up to 24 hours after delivery. This study concludes that the regime of low dose vaginal misoprostol tab - 25 µgm 4 hourly is better than current practice of use of dinoprostone gel in case of pre-term pre labour rupture of membrane because low dose vaginal misoprostol is safe and effective for cervical ripening and induction of labour.*

Keywords: *Vaginal Misoprostol, Dinoprostone (PGE2) Gel, Preterm Birth, Premature Rupture of Membrane*

Date of Submission: 16-03-2018 Date of acceptance: 31-03-2018

I. Introduction

Premature rupture of membrane (PROM) is the rupture of the fetal membranes before the onset of labour. Preterm premature rupture of membranes (PPROM) is the spontaneous rupture of the fetal membranes during pregnancy before 37 weeks gestation in the absence of regular painful uterine contractions [1]. It increases the risk of prematurity and leads to other perinatal and neonatal complications with 1-2% risk of fetal death [2].A number of risk factors for spontaneous preterm PROM have been identified. Intra-amniotic infection and decidual haemorrhage (placental abruption) occurring remote from term leading to rupture of membranes[3,4,6]. An inverse relationship exists between gestational age at the time of rupture of membrane and latency. In women with preterm PROM remote from term, 50% will go into labour within 24 to 48 hours and 70% to 90% within 7 days[3,4,5,6]. PPROM is an important cause of perinatal morbidity and mortality because it is associated with brief latency from membrane rupture to delivery, perinatal infection and umbilical cord compression due to oligohydramnios[7]. The traditional minimally invasive gold standard for the diagnosis of rupture of membrane relies on clinician's ability to document 3 clinical signs on sterile speculum examination: visual pooling of clear fluid in the posterior fornix of the vagina or leakage of fluid from the cervical os or microscopic ferning of the cervicovaginal discharge on drying. Evidence of pus leaking from the cervix on sterile speculum examination can also confirm the diagnosis. A prolonged interval from rupture of membrane to delivery is associated with an increase in incidence of chorioamnionitis and neonatal sepsis[8,9]. Labour induction is one of the most frequent procedures in pregnant women. Uterine contraction and an appropriate cervical ripening are two important factors in labour contributing to good pregnancy outcome. The aim of successful induction is to achieve vaginal delivery when continuation of pregnancy presents a threat to the life or well-being of the mother or her unborn child. Induction of labour in pregnancies complicated by preterm PROM is recommended once a favourable gestational age is reached (≥34 weeks) because of the high risk of ascending infection, the low risk of complications of prematurity, and the lack of proven efficacy of antenatal corticosteroids in improving perinatal outcome.

Need for the study:

- Labour induction in preterm PROM is frequently required because of high risk of ascending infection.
- Although various methods are available for induction in preterm PROM, there is a need for cheaper alternative which is also safe.
- Maintenance of cold chain & thus storage may be a problem at primary health centres & thus the need to study the safety aspect of misoprostol for use in low resource setting.
- ProstaglandinE2 (PGE2) gel can be used for induction, but it carries risk of ascending infection. There is still need of novel regime which would be safe & effective.
- Shorter induction to delivery time and quicker cervical ripening is the need of hour in view of increasing workload in hospital and to decrease period of anxiety for patient.

Although there is much data available with misoprostol induction in western population, there is scarcity of data forthe Indian population as misoprostol in low dose of 25 µgm was allowed for induction of labour in India only after the WHO recommendations of 2014. Thus, this study was done in the Indian populationto compare vaginal misoprostol with Dinoprostone (PGE2) Gel for induction of labour in preterm premature rupture of membrane at ≥ 34 weeks.

.

II. Material and Methods

This study was a prospective interventional randomized study conducted in the Department of Obstetrics & Gynaecology of Dr. Baba Saheb Ambedkar Hospital, Delhi, India from April 2016 – April 2017.

Study Population: Patient with ≥34 weeks of gestation with preterm PROM attending the gynaecology emergency at Dr Baba Saheb Ambedkar Hospital, Delhi

Study Design: Prospective and randomized study.

Sample Size: Study was conducted on one hundred forty women who were admitted for management of preterm premature rupture of membrane at ≥34 to ≤37 weeks of gestationweeks of pregnancy. The minimum required sample size with 90% power of study and 5% level of significance is 70 patients in each study group. So total sample size taken is 140 (70 patient per group)

Inclusion criteria

- Gestational age ≥34 to ≤37 weeks of gestation weeks with singleton pregnancy with preterm PROM
- Cephalic presentation
- Presenting with preterm PROM diagnosed by speculum examination with aseptic technique revealing pooling of amniotic fluid in the vagina.
- PROM ≥ 4 hours.
- Bishop score ≤ 5.
- No uterine contraction.
- Fetal heart rate normal and regular.

Exclusion criteria

- Noncephalic presentation
- Twins
- Cervix ≥3 centimetre dilatation
- Hypersensitivity to Prostaglandins.
- Previous LSCS
- History of any uterine surgery like myomectomy, hysterotomy
- Dates/Gestational age not confirmed, no USG available
- Placenta Previa
- Grand multiparity (≥ 4previous deliveries)
- History of medical disorder like asthma, glaucoma, or heart disease, gestational diabetes
- Any evidence of chorioamnionitis like temperature ≥ 37.5°c, uterine tenderness, ↑TLC
- Fetal distress
- Meconium stained liquor
- Refusal by patient.

The **primary outcome** measured was induction to delivery interval. The **secondary outcome** measured was the need for oxytocin augmentation, failed induction (failure of the cervix to dilate to ≥3cm), mode of delivery, rate of caesarean sections, meconium stained liquor, occurrence of tachysystole (≥6

contractions in 10 min), maternal infection (chorioamnionitis), post partum haemorrhage or any other complication. Follow up in postnatal ward for any infection.Neonatal Outcomeslike birth weight, APGAR score and need for transfer to a special care or neonatal intensive care unit, resuscitation, neonatal sepsis, respiratory distress and stay in NICU were noted.

Statistical analysis: The data was entered in MS EXCEL spreadsheet and analysis was done using Statistical Package for Social Sciences (SPSS) version 21.0.

III. Result

Total 140 patients were enrolled in the study. They were divided into 2 equal groups. Group A were induced with 25 µgm intravaginal Misoprostol tablets and Group B were induced with 0.5 mg intravaginal Dinoprostone gel.The age distribution in the two study groups has been shown in Table no. 1.

Table No. 1 : Age Distribution amongst the study groups

		Study Group			
		A	B	*Total*	*P value*
Age Distribution	1) <=25 years	42 (60.00%)	35 (50.00%)	77 (55.00%)	0.234
	2) >25 years	28 (40.00%)	35 (50.00%)	63 (45.00%)	
Total		70 (100.00%)	70 (100.00%)	140 (100.00%)	

Out of 70 women in Group A (misoprostol), only 18 required oxytocin augmentation and out of 70 women in Group B (dinoprostone), 29 women required oxytocin augmentation. In our study, we found that women given dinoprostone needed more oxytocin augmentation compared to women given misoprostol. P value = 0.049, which is statistically significant. (Table no. 2)

Table No. 2 : Comparison of the need for Oxytocin Augmentation in the study groups

		Study Group			
		A	B	Total	P value
Oxytocin Augmentation	NO	52 (74.29%)	41 (58.57%)	93 (66.43%)	0.049
	YES	18 (25.71%)	29 (41.43%)	47 (33.57%)	
Total		70 (100.00%)	70 (100.00%)	140 (100.00%)	

In group A (misoprostol), 46 women delivered within 12 hrs, and in group B (dinoprostone) only 28 women delivered within 12 hrs. In our study, we found that induction to delivery interval was significantly shorter in group A (misoprostol). (Table no. 3)

Table No. 3: Comparison of Induction to Delivery Interval (IDI) in the study groups

		Study Group				
		A	B	Total	P value	P value
IDI (in hrs)	1) 0-6	19 (27.14%)	14 (20.00%)	33 (23.57%)	0.010	0.426
	2) 6.1-12	27 (38.57%)	14 (20.00%)	41 (29.29%)		0.026
	3) 12.1-18	16 (22.86%)	18 (25.71%)	34 (24.29%)		0.844
	4) 18.1-24	3 (4.29%)	12 (17.14%)	15 (10.71%)		0.026
	5) >24	5 (7.14%)	12 (17.14%)	17 (12.14%)		0.12
Total		70 (100.00%)	70 (100.00%)	140 (100.00%)		

In group A(misoprostol), 91.43% (64) women delivered vaginally and 8.57%(6) women underwent caesarean delivery whereas in group B (dinoprostone) 80%(56) women delivered vaginally and 20%(14) women underwent caesarean delivery. The difference was not statistically significant (P=0.053) (Table no. 4)

Table 4: Comparison of mode of delivery in the study groups

		Study Group			P value
		A	B	Total	
Mode of delivery	Emergency LSCS	6 (8.57%)	14 (20.00%)	20 (14.29%)	0.053
	Vaginal delivery	64 (91.43%)	56 (80.00%)	120 (85.71%)	
Total		70 (100.00%)	70 (100.00%)	140 (100.00%)	

In the misoprostol group A, out of 6 caesarean deliveries (Table no. 4), 4 occurred due to fetal bradycardia and 1 occurred because of arrest of dilation and 1 due to meconium stained liquor. In the Dinoprostone group B, the total number of caesarean deliveries were 14 (Table no. 4), out of which 4 occurred due to arrest of dilatation, 5 occurred due to failed induction, 2 occurred due to meconium stained liquor and 2 occurred due to second stage arrest, 1 occurred due to foetal bradycardia. In our study, we found no significant difference in the indication for emergency LSCS between the 2 groups. In our study in group A (misoprostol) 58.57% babies were more than 2.5 kg.Also in group B (dinoprostone) maximum number of babies 57.14% were more than 2.5 kg.

IV. Discussion

In our study, synthetic PGE_1 analogue vaginal misoprostol has been compared to PGE_2 intravaginal dinoprostone gel with respect to outcome of induction in case of pre -term PROM at ≥ 34 week in term of change in bishops score, induction to delivery interval, mode of delivery, need for oxytocin augmentation and neonatal and maternal complication. Misoprostol used in a dose of 25 µgm 4 hourly for maximum 3 doses as per WHO recommendation 2014[13] and dinoprostone gel was used in dose of 0.5 mg in posterior fornix, 6 hourly for maximum 2 doses.

Pre-Induction Bishops Score and Progress in Bishops Score

In this study, pre-induction bishops score at 0 hrs was ≤ 5 for both the groups (Misoprostol & Dinoprostone group). Pre-induction mean modified bishops score in misoprostol group was 3.09 ± 1.34 and for dinoprostone group it was 2.94 ± 1.53, which was statistically not significant (P = 0.447). These result were consistent with observation of Nagpal et. al [12] (2009) with mean bishops score was 3.81 ± 1.27 in women with misoprostol group and 3.27 ± 1.12 in women with dinoprostone group (P=0.084). In some studies, progress of bishops score was compared at 6 hours and in some at 6 & 12 hours after induction. However, in our study bishops score was compared at 4, 6, 8, 10 and 12 hours after induction in both the groups. It was found that bishops score was significantly higher in misoprostol group (P < 0.05) which was consistent with the observation of Nagpal et. al[12] (2009).

Oxytocin Augmentation

In our study, only 25.71% women in group A (misoprostol) needed oxytocin augmentation as compared to 41.43% women in group B (dinoprostone).Also, the oxytocin dose required for augmentation was lesser in the former group. The result was comparable to the observation of Nagpal et. al[12] (2009).

Induction to Delivery Interval

In this study, induction to delivery interval was significantly shorter in group A (misoprostol) as compared to group B (dinoprostone). It was 11.11 hours and 15.58 hours in group A and group B respectively. The present study is comparable to the observation of Frohn et al[10](2002), Nagpal et at[12] (2009) with respect to induction to delivery interval.

Vaginal Delivery

In our study, the rate of vaginal delivery was 91.43% in the misoprostol group and 80% in dinoprostone group. The result was better than that obserseved by Shetty A et al[11] (2004) for the misoprostol group.

Caesarean Section Rate

In our study, rate of caesarean delivery was significantly lower in women with misoprostol group than dinoprostone. In the misoprostol group 8.57% women underwent emergency caesarean section whereas in dinoprostone group 20% women underwent emergency caesarean section. The results of our study were consistent with the observation of Patil P. et al[15] (2013) and Shetty A et al[11] (2004) with respect to rate of caesarean section.

Maternal Complication

In our study, maternal complication between two group were almost similar, the difference being not significant statistically (P > 0.05). The incidence of vomiting was 12.86% in misoprostol and 14.29 % in dinoprostone. The incidence of diarrhoea was equal in both group in our study. The incidence of fever was seen in 1.43% of women in dinoprostone group while there was no incidence of fever in misoprostol group. This result is comparable with study of Chaudhuri S et al[14] (2011). The incidence of hyperstimulation is 5.71 % in misoprostol group and 4.29 % in dinoprostone group. The result was consistent with the observation of Shetty A

et al[11] (2004).The incidence of tachysystole was 7.41 % in misoprostol group in compared to 5.71 % in dinoprostone group. This result is comparable to the study of Patil P. et al[15] (2013)

Neonatal Outcome

In our study, when mean birth weight was compared between two group, the difference was statically insignificant and result were consistent with the observation of Shetty A et al[11] (2004). The mean APGAR score was compared at 1, 5 and 10 mins in our study. The APGAR score of baby in misoprostol group was better than dinoprostone group at 1 minute. There was no statical difference in APGAR at 5 and 10 minutes in both group. The incidence of meconium stained liquor was comparable in both the groups and the results were comparable with Shetty A et al[11] (2004). Birth asphyxia was seen in 2.86% in misoprostol group as compared to 3.57 % in dinoprostone group. The difference was statistically not significant. The incidence of meconium aspiration syndrome in misoprostol was 1.43% as compared to 2.86% in dinoprostone group. Where as in Nagpal et at[12] (2009) study meconium aspiration syndrome was 0 v/s 1 in misoprostol and dinoprostone group (P = 0.492) which is comparable to our study. NICU admissions were seen in 1.43% in misoprostol group as compared to 4.29 % in dinoprostone group. In Nagpal et at[12] (2009) study it was 1 v/s 2 (P =0.534) which was comparable to our study.

V. Conclusion

Regimes of low dose vaginal misoprostol tab 25 µgm 4 hourly is better than current practice of use of dinoprostone gel in case of pre-term pre labour rupture of membrane because low dose vaginal misoprostol is safe and effective for cervical ripening and induction of labour. Misoprostol shortens the induction to delivery interval significantly compared to dinoprostone with mean reduction of induction to delivery interval by 4 hours in misoprostol group. In conclusion, we believe that low dose vaginal misoprostol is more safe, efficient and cost effective and it has a potential to become the drug of choice for induction of labour in case of pre-term PROM at ≥ 34 weeks.

References

[1] Fowlie A. Preterm pre-labour rupture of membranes, In: Arukumaran S, Symonds IM, Fowlie A (eds): Oxford Handbook of Obstetrics and Gynaecology. 2nd edition New Delhi, Oxford University Press 2004; 247-249.

[2] Shucker JL, Mercer BM. Midtrimester PROM. Semin Perinatol 1996; 20:389-400.

[3] American College of Obstetricians and Gynecologists, authors. Premature Rupture of Membranes. Washington, DC: American College of Obstetricians and Gynecologists; 1998. (ACOG Practice Bulletin No. 1).

[4] ACOG Committee on Practice Bulletins-Obstetrics, authors. Clinical management guidelines for obstetrician-gynecologists. (ACOG Practice Bulletin No. 80: premature rupture of membranes). Obstet Gynecol 2007; 109:1007-1019 [PubMed].

[5] Dale PO, Tanbo T, Bendvold E, Moe N. Duration of the latency period in preterm premature rupture of the membranes. Maternal and neonatal consequences of expectant management. Eur J Obstet Gynecol Reprod Biol. 1989; 30:257-262[PubMed].

[6] Bengtson JM, Van Marter, Barss VA, et al. Pregnancy outcome after premature rupture of membranes at or before 26 weeks' gestation. Obstet Gynecol. 1989; 73:921-927 [PubMed].

[7] Borna S, Borna H, Khazardoost S, Hantoushzadeh S. Perinatal outcome in preterm premature rupture of membranes with amniotic fluid index <5(AF1>5). BMC pregnancy and childbirth 2004; 4:15.

[8] Fayez, J.A., Hasan, A.A., Jonas, H.S., Miller, G.L. Management of premature rupture of the membranes. Obstet Gynecol. 1978; 52:17-21.

[9] Guise, J.M., Duff, P., Christian, J.S. Management of term patients with prelabor rupture of membranes and an unfavorable cervix. Am J Perinatol. 1992; 9:56-60.

[10] Frohn WE, Simmons S, Carlan SJ. Prostaglandin E2 gel versus misoprostol for cervical ripening in patients with premature rupture of membranes after 34 weeks. Obstet Gynecol. 2002 Feb;99(2):206-10.

[11] Shetty A, Livingstone I, Acharya S, Rice P et al. A randomized comparison of oral misoprotol and vaginal prostaglanding E2 tablets in labour induction at term. BJOG. 2004 May;111(5):436-40

[12] Nagpal MB, Raghunandan C, Saili A. Oral misoprostol versus intracervical prostaglandin E2 gel for active management of premature rupture of membranes at term. Int J Gynaecol Obstet. 2009 Jul;106(1):23-6. doi: 10.1016/j.ijgo.2009.03.014. Epub 2009 Apr 17.

[13] Kundodyiwa TW, Alfirevic Z, Weeks AD. Low dose oral misoprostol for induction of labor: a systematic review. Obstet Gynecol 2009 Feb; 113(2 pt 1): 374-83.

[14] Chaudhuri S, Mitra SN, Banerjee PK, Biswas PK, Bhattacharyya S. Comparison of vaginal misoprostol tablets and prostaglandin E2 gel for the induction of labor in premature rupture of membranes at term: A randomized comparative trial. J Obstet Gynaecol Res. 2011; 37:1564-71.

[15] Patil P1, Patil A2. Misoprostol v/s Cerviprime Gel for Induction of Labour. Int J Med Res Rev 2013; 1(2):63-70.

Dr. Puneeta Mahajan "Comparison of Vaginal Misoprostol versus Dinoprostone (PGE2) Gel for Induction of Labour in Preterm Premature Rupture of Membrane at ≥ 34 Weeks."IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), vol. 17, no. 3, 2018, pp 47-51.