International Journal of Clinical Obstetrics and Gynaecology

ISSN (P): 2522-6614
ISSN (E): 2522-6622

www.gynaecologyjournal.com
2019; 3(6): 27-31
Received: 16-09-2019
Accepted: 20-10-2019

Dr. Dharminder Sunda
Ex Resident, S.M.S. MC, Jaipur, Rajasthan, India

Dr. Shalini Agrawal
Assistant Professor, GMCH, Udaipur, Rajasthan, India

Dr. Subhash Jain
Assistant Professor, NIMS, Jaipur, Rajasthan, India

Dr. Madhu Bhatt
Senior Professor, S.M.S. MC, Jaipur, Rajasthan, India

Corresponding Author:
Dr. Shalini Agrawal
Assistant Professor, GMCH, Udaipur, Rajasthan, India

A comparative study on sublingual versus vaginal misoprostol for induction of labour in women with pre labour rupture of membranes at term with poor bishop's score

Dr. Dharminder Sunda, Dr. Shalini Agrawal, Dr. Subhash Jain and Dr. Madhu Bhatt

DOI: https://doi.org/10.33545/gynae.2019.v3.i6a.388

Abstract
Background: Maternal risk is increased with increased risk of chorioamnionitis and higher incidence of caesarean section with PROM due to cord prolapse, cord compression and foetal distress. This study is aimed to compare the safety and efficacy of sublingually equivalent dose regimen administered vaginally for induction of labour in patient with PROM with poor Bishop's Score.
Material & Methods: A prospective randomised controlled trial done on 180 Patients of PROM admitted in Mahila chikitsalaya, SMS Medical College, Jaipur as per inclusion and exclusion criteria, informed consent was taken and allocated according to computer generated randomization into two groups. Group 1- Received 25µg misoprostol, intravaginally 4 hourly up to maximum of 3 doses. Group 2- Received 25 µg misoprostol, sublingually 4 hourly up to maximum of 3 doses.
Results: Our study showed that mean age in intravaginal was 24.33±3.535 years and in sublingual was 23.73±3.151 years. Maximum patients were between 21-25 years 61.1% in intravaginal and 57.8% in sublingual group but the difference was not statistically significant. (p=0.172). Majority of women in both groups delivered vaginally; 76 patients (84.4%) in intravaginal and 79 patients (87.8%) in sublingual group.
Conclusion: We conclude that misoprostol is a safe, effective, well tolerated and economical method for induction of labour in patients of PROM with poor Bishop's score. Both sublingual and intravaginal route of administration of 25µg misoprostol are equally effective in achieving favourable Bishop's score, vaginal delivery rates, with comparable induction to delivery intervals without increasing the caesarean rates and the postpartum complications.

Keywords: Bishop's score, PROM, misoprostol, vaginal, sublingual

Introduction
Patients with Premature rupture of membranes (PROM) may present with chief complain of leaking fluid, increased vaginal discharge, vaginal bleeding or pelvic pressure. Pregnancies complicated with PROM have higher incidence of maternal and foetal complications. Maternal risk is increased with increased risk of chorioamnionitis and higher incidence of caesarean section with PROM due to cord prolapse, cord compression and foetal distress. Perinatal morbidity and mortality increased as pregnancy complicated with PROM is associated with neonatal complications like pneumonia, meningitis, respiratory syndrome, pulmonary hypoplasia, intra-ventricular haemorrhage and necrotizing enterocolitis.
Perinatal mortality increases three folds when mother's membranes have been ruptured for more than 24 hours. Women with term ruptured membranes whose labour were induced compared with those managed expectantly reported lower rates of chorioamnionitis, metritis and NICU admissions. This intervention was the accepted practice until challenged by Kappy and co-workers (1979) [1], who reported excessive caesarean delivery in term pregnancies with ruptured membranes managed with labour augmentation compared with those expectantly managed. In spite of the fact that 69% women deliver within 24 hours of PROM if managed expectantly, still induction of labour is advocated to decrease the risk of sepsis and perinatal morbidity associated with a delay between membrane rupture and delivery.
Prostaglandins have been shown to induce cervical ripening and stimulate uterine contractions

and have been found to be effective in numerous clinical trials at a variety of doses and routes of administration[2]. PGE_2 gel preparations have been commercially available in India in 3ml syringe containing 0.5mg of dinoprostone. Prostaglandin preparations increase the chances of successful induction, shorten induction delivery interval and reduce need for oxytocin infusion. However they are expensive and unstable at room temperature, requiring refrigerated storage. Uterine hyperstimulation has been identified as a particular problem during labour induction with prostaglandins, and has to be treated with tocolytics [3].

Thus there is a need for less costly and less temperature sensitive alternative which is safe and effective. A proposed alternative is misoprostol, a prostaglandin E_1 analogue. The pharmacokinetics of misoprostol suggests that it is more bioavailable when administered vaginally as compared to oral administration [4]. Modes of administration: Oral [6], vaginal [7, 8], intracervical [9], intrauterine [10], sublingual [12, 13], buccal [13]. Sublingual misoprostol has the advantage of a less invasive administration and lack of restriction of mobility. Since the pharmacokinetics of vaginal and sublingual misoprostol are almost similar we wish to study its efficacy, safety and tolerability compared to vaginal route considering its ease of administration. This study is aimed to compare the safety and efficacy of sublingually equivalent dose regimen administered vaginally for induction of labour in patient with PROM with poor Bishop's Score.

Material & Methods

A prospective randomised controlled trial done on 180 Patients of PROM admitted in labour room of Mahila chikitsalaya, SMS Medical College, Jaipur as per inclusion and exclusion criteria.

Inclusion criteria

1. All pregnant women with spontaneous rupture of membranes confirmed by demonstrating vaginal pooling of amniotic fluid at initial p/s examination and with positive litmus paper test.
2. Primigravida
3. Gestational age at or more than 37 weeks
4. Singleton pregnancy
5. Cephalic presentation
6. No regular uterine contraction (Less than 6 contractions/ hour)
7. No evidence of fetal distress
8. Maternal oral temperature less than 37.5 degree C.
9. Bishop's score (Less than 5)

Exclusion criteria

1. Less than 37 completed weeks of gestation (Preterm)
2. Foetal congenital malformations
3. Intra uterine growth restriction (IUGR)
4. Symptoms and signs suggestive of chorioamnionitis
5. Meconium stained liquor at the time of admission
6. Cord prolapse at the time of admission
7. Prior uterine surgery(myomectomy)
8. Bad obstetric history
9. Antepartum hemorrhage
10. Cephalopelvic disproportion
11. Dai handled patients
12. Medical disorder of pregnancy Hypertension/ Diabetes Mellitus/ Asthma/ Cardiac disease / ICP etc.

Methods: Detailed history was taken of all admitted patients and detailed general, systemic including per abdomen examination, Per speculum examination was done to confirm vaginal leakage either by frank passage of amniotic fluid through the cervical os or by demonstrating leak on coughing or by performing valsalva manoeuvre. Litmus paper test to test the change of vaginal pH due to leakage of amniotic fluid in PROM was done. Per vaginal examination for presence or absence of membranes, dilatation, effacement and position of cervix and station of presenting part, adequacy of pelvis and bishop score was noted. Informed consent was taken and allocated according to computer generated randomization into two groups.

Group 1- Received 25µg misoprostol, intravaginally 4 hourly up to maximum of 3 doses, placed in posterior fornix.

Group 2- Received 25 µg misoprostol, sublingually 4 hourly up to maximum of 3 doses.

Foetal heart and labour progress monitoring was done. Before every dose a pervaginum examination was performed to assess the Bishop score. Prophylactic antibiotics in form of inj. Cefotaxime 1gm i/v 12hourly and inj. Metronidazole 500mg i/v 8 hourly were given.

The next dose of misoprostol was withheld if: Bishop score >8, Adequate uterine contractions i.e. 3 per 10 minutes, Cervical dilatation> 3 cm with regular uterine contractions, Presence of hyperstimulation, as evident by tachysystole or hypertonus associated with foetal tachycardia, late decelerations and beat to beat variability.

Augmentation with oxytocin was done in patients with favourable bishop score (>5) with mild uterine contraction or patients with poor bishops score (<5) even after 3 doses of misoprostol. If leaking of more than 24 hours and unfavourable cervix (bishop <5) or any evidence of foetal distress then further management was at the discretion of attending obstetrician.

Results

A total of 180 primigravida patients with PROM with gestational age at or more than 37 weeks were included in the study.

Table 1: Distribution of women according to age

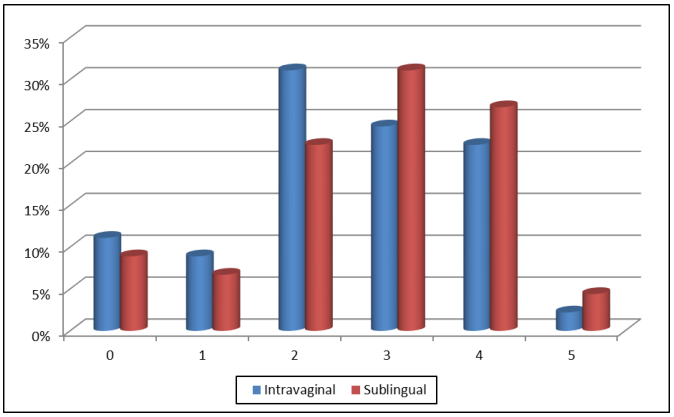
Age groups	Group		p-value
	Intravaginal	Sublingual	
<=20	10	14	0.172
	11.1%	15.6%	
21-25	55	52	
	61.1%	57.8%	
26-30	17	22	
	18.9%	24.4%	
>30	8	2	
	8.9%	2.2%	
Total	90	90	

Our study showed that mean age in intravaginal was 24.33±3.535 years and in sublingual was 23.73±3.151 years. Maximum patients were between 21-25 years, 61.1% in intravaginal and 57.8% in sublingual group but the difference was not statistically significant. (p=0.172).

Table 2: Distribution of women according to duration of leaking (hours)

Leaking duration	Group		p-value
	Intravaginal	Sublingual	
1-3 hrs	10	6	0.339
	11.1%	6.7%	
4-6 hrs	24	29	
	26.7%	32.2%	
7-9 hrs	35	37	
	38.9%	41.1%	
10-12 hrs	18	18	
	20.0%	20.0%	
>12 hrs	3	0	
	3.3%	.0%	
Total	90	90	

Majority of women in both Groups (38.9% in intravaginal and 41.1% in sublingual) were in leaking duration 7-9 hours with duration of leakage ranging from 1 hour to 14 hours. However there was no statistical difference between the two (p=.339)



Graph 1: Distribution of women according to bishop score at induction

Mean Bishop score at induction was 2.44±1.299 in intravaginal group and 2.73±1.296 in sublingual group. (p= 0.113) which is statistically comparable between two groups (Graph-1) and mean dose of misoprostol given was 49.1675±18.531µg in intravaginal group and 46.390±17.800µg in sublingual group.

Table 3: Distribution of women according to number of doses of misoprostol given for induction

Total dose of Miso	group		p-value
	Intravaginal	Sublingual	
1	26	30	0.540
	28.9%	33.3%	
2	41	43	
	45.6%	47.8%	
3	23	17	
	25.6%	18.9%	

Table 4: Distribution of women according to intrapartum complications

Intrapartum complications	Group		p-value
	Intravaginal	Sublingual	
1. Fetal distress	12	13	0.823
	13.32%	14.43%	
• Fetal Bradycardia (FB)	3	3	1
	3.33%	3.33%	
• FB+MSL	2	1	0.999
	2.22%	1.11%	
• Fetal Tachycardia (FT)	1	2	0.999
	1.11%	2.22%	
• Irregular FHR	1	0	0.999
	1.11%	0	
• Irregular FHR + MSL	1	1	1
	1.11%	1.11 %	
• Meconium stained liquor(MSL)	4	6	0.746
	4.44 %	6.66%	

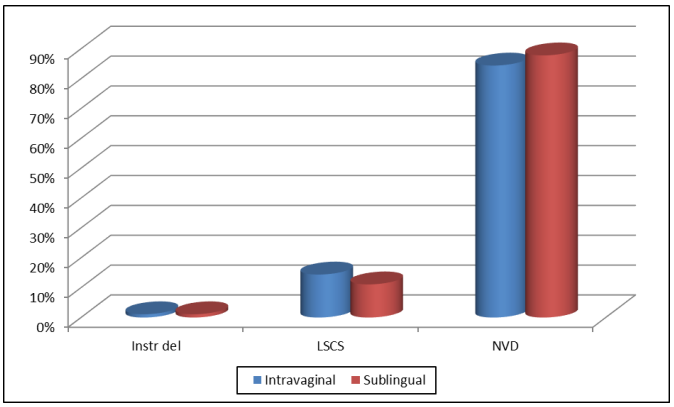
2. Hyper tonus	1	3	0.621
	1.11%	3.33%	
3. Tachysystole	4	1	0.368
	4.44%	1.11%	
4. Nil	73	73	
	81.03%	81.03%	
Total	90	90	

Foetal distress (Foetal heart rate (FHR) abnormalities; FB<120bpm, FT >160bpm) was most common intrapartum complication in both groups, 14.43% in sublingual and 13.32% in intravaginal (p=0.823) which was comparable in both groups. 3 patients in sublingual and 1 patient in intravaginal group had hypertonus.1 patient in sublingual and 4 patients in intravaginal group had tachysystole. However, none of the women had to be given subcutaneous Terbutaline as uterine relaxant. Intravenous drip, O2 inhalation, left lateral position and more frequent monitoring of foetal heart rate was done in them.

Table-5: Distribution of women according to prom –delivery interval

Prom Del Interval time (hrs)	Group		p-value
	Intravaginal	Sublingual	
≤12 hrs	6	9	0.681
	6.7%	10.0%	
12-24 hrs	80	78	
	88.9%	86.7%	
>24 hrs	4	3	
	4.4%	3.3%	

Mean PROM delivery interval in intravaginal group was 15.43±3.90 hours and in sublingual group was 14.94±3.77 hours. As shown in table 5, maximum patient delivered within 12 to 24 hours , 80 patients (88.9%) in intravaginal group and 78 patients (86.7%) in sublingual group which is statistically comparable (p=0.681).



Graph-2: Distribution of women according to outcome of labour

Majority of women in both groups delivered vaginally; 76 patients (84.4%) in intravaginal and 79 patients (87.8%) in sublingual group.

Table 6: Admission in NICU group

Admission in NICU	Group		p-value
	Intravaginal	sublingual	
Nil	87	88	0.650
	96.7%	97.8%	
Yes	3	2	
	3.3%	2.2%	
Total	90	90	

3 newborn in intravaginal and 2 newborn in sublingual group required admission in NICU (p=0.650) which is not statistically significant. In intravaginal group one newborn was admitted with foetal bradycardia after vaginal delivery, there were 2 tight loops of cord around neck and two babies had bradycardia. In sublingual group one baby was admitted with tachypnoea, who had spontaneous respiration at birth but cried after 3 minutes. Another baby was admitted with meconium aspiration syndrome. All newborns were admitted for observation and treatment if needed and all were discharged in satisfactory condition. There was no neonatal mortality.

Discussion

PROM complicates about 10% of all pregnancies (Gunn *et al* 1970) and result in loss of natural protection of foetus and intrauterine contents from bacterial invasion [14]. As such, PROM turn pregnancy into high risk situation which warrants induction of labour with or without pre induction cervical ripening to reduce maternal and foetal morbidity and mortality. To tide over such situation common regimens employed universally for induction are oxytocin and prostaglandin analogue like misoprostol.

Accordingly this analysis provides strong support for the conclusion that misoprostol safely decreases the caesarean delivery rate among women undergoing labour induction compared with that of women receiving alternate induction regimens. Induction of labour in patients performed with unfavourable cervix is associated with a higher incidence of prolonged labour and caesarean delivery. It can also lead to uterine contraction abnormalities and also affect the foetus. In the study by Bartusevicious *et al*. [15], occurrence of tachysystole was significantly different between the groups (15% in sublingual vs 4.3% in vaginal group) probably because they used a 50µg sublingual dose. No difference in incidence of hypertonus was noted between the two treatment groups and 5 women in each group had hyperstimulation syndrome.

In our study, four patients in vaginal group and two patients in sublingual group had atonic PPH which was controlled with oxytocin infusion and $PGF_{2\alpha}$ administration and blood transfusion was not required.

Conclusion

We conclude that misoprostol is a safe, effective, well tolerated and economical method for induction of labour in patients of PROM with poor Bishop's score. Both sublingual and

intravaginal route of administration of 25µg misoprostol are equally effective in achieving favourable Bishop's score, vaginal delivery rates, with comparable induction to delivery intervals without increasing the caesarean rates and the postpartum complications. Misoprostol maximum of 75µg is an effective method of improving the inducibility score and induction of labour in properly selected cases. Misoprostol in above doses is without any untoward effect on maternal and foetal outcome and hence, safe.

References

1. Kappy KA, Cetrulo CL, Knuppel RA, Ingardia CJ, Sbarra AJ, Scerbo JC *et al* Premature rupture of membranes: a conservative approach. Am J Obstet Gynecol. 1979; 134(6):655-61.
2. Keirse MJNC. Prostaglandins in pre induction cervical ripening: meta-analysis of worldwide clinical experience. J Report Med. 1993; 38:89-100.
3. Egarter CH, Husslein PW, Rayburne WF. Uterine hyper stimulation after low dose prostaglandin therapy: tocolytic treatment in 181 cases. Am J Obstet Gynecol. 1990; 163:794-796.
4. Zeiman M, Fong SK, Benowitz NL, Banskter D, Darney PD. Absorption kinetics of misoprostol with oral or vaginal administration . Obstet Gynecol. 1997; 90:88-92.
5. Danielsson GK, Marious L, Rodriguez A, Spur BW, Wong PYK, Bygdeman M. comparison between oral and vaginal administration of misoprostol on uterine contractility. Obstet Gynecol. 1999; 93(2):275-280.
6. Shetty A, Martin R, Danielian P, Templeton A. A comparison of two dose regimens of oral misoprostol for labour induction at term. Acta Obstet Gynecol Scand. 2002; 81:337-42.
7. Wing DA, Tran S, Paul RH. Factors affecting the likelihood of successful induction after intravaginal misoprostol application for cervical ripening and labour induction. Am J Obstet Gynecol. 2002; 186(6):1237-40.
8. Sanchez – Ramos L, Danner CJ, Delke I, Kaunitz AM.The effect of tablet moistening on labour induction with intravaginal misoprostol: a randomized trial. Obstet Gynecol. 2002; 99(6):1080-4.
9. Chang Y, Chen W, Yu M, Liu H. Intracervical misoprostol and prostaglandin E_2 for labour induction. Int J Gynecol Obstet. 2003; 80(1):23-28.
10. Oboro VO, Tabowei TO, Bosah JO. Intrauterine misoprostol for refractory postpartum hemorrhage. Int J Gynecol Obstet. 2003; 80:67-68.
11. Shetty A, Mackie L, Danielian P, Rice P, Templeton A. Sublingual compared with oral misoprostol in term labourinduction: a randomized control trial. Br J Obstet Gynecol. 2002; 109:645-50.
12. Tang OS, Lau WN, Ng EH, Lee SW, Ho PC. A prospective randomized study to compare theuse of repeated doses of vaginal with sublingual misoprostol in the management of first trimester silent miscarriages. Hum Reprod. 2003; 18:176-181.
13. Todd CS, Soler M, Castleman L, Rogers MK, Blumenthal PD. Buccal misoprostol as cervical preparation for second trimester pregnancy termination. Contraception. 2002; 65:415-8.
14. Gunn GC, Mishell, Morton DG. Premature rupture of fetal membranes. Am J Obstet Gynecol. 1970; 106:469.
15. Bartusevicius A , Barcaite E, Krikstolaitis R, Gintautas V, Nadisauskiene R. Sublingual compared with vaginal misoprostol for labour induction at term: a randomized controlled trial. Br J Obstet Gynecol. 2006; 113:1431-1437.
16. Malik HZ, Khawaja NP, Zahid B, Rehman R. Sublingual versus oral misoprostol for induction of labour in prelabour rupture of membranes at term. J Coll Physicians Surg Pak. 2010; 20(4):242-5.
17. Feitosa FEL, Sampaio ZS, AlencarJr CA, Amorim MMR, PassiniR Jr. Sublingual versus vaginal misoprostol for induction of labour. Int J Gynecol Obstet. 2006; 94:91-95.