Original Research Paper

Volume - 14 | Issue - 06 | June - 2024 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Obstetrics & Gynaecology

COMPARATIVE STUDY TO EVALUATE THE EFFICACY AND SAFETY OF 25 MICROGRAM MISOPROSTOL FOR INDUCTION OF LABOUR WITH SUBLINGUAL VERSUS VAGINAL ROUTE

Dr Megha Omar PG Resident Dept of OBGY Fortis escorts hospital and research centre Faridabad

Dr Niti Kautish Senior Consultant Dept of OBGY Fortis escorts hospital and research centre Faridabad

ABSTRACT **Introduction** When the risk of continuation of pregnancy is more either to the mother or to the foetus, induction is indicated Timely induction can reduce maternal morbidity and mortality as well as assure the delivery of healthy baby .Sublingual misoprost is another route of administration that can be compared with vaginal administration as both require mucosal uptake of drug. Since pharmacokinetics is different for sublingual and vaginal misoprost, difference in efficacy and side effects needs to be compared. **Materials and Methods** This was a prospective parallel randomized controlled trial study conducted on 350 women who were admitted at dept of obstetrics and gynaecology, fortis escorts hospital and research centre Faridabad from june 2016 to june 2018 The subjects were categorized into two groups(sublingual and vaginal) of 175 patients in each group. The present study compares the efficacy of sublingual versus per vaginal route of Misoprostol administration in pregnant females at term in terms of successful vaginal delivery, induction delivery time interval, number of doses of Misoprostol required, need for oxytocin augmentation, side effects and foetal outcome measures such as APGAR score at birth, and admission to NICU. **Results and Discussion** Mean dose required for sublingual group was 72.43±21.79 mcg and for vaginal group was 78.43±23.73 p value was 0.002 which is statistically significant. Mean induction delivery interval was 12.11±3.87hrs in sublingual group while it was 20.1±1.5 hrs in vaginal group p value was 0.003 which is statistically significant. GI side effects were more in sublingual group Hyperpyrexia was almost similar in both groups Hypertonic uterine contractions were also similar in both groups. Foetal distress occured more in sublingual group. Cervical tear and vaginal lacerations were seen more in vaginal group. **Conclusion** Irrespective of various labour induction methods induction of labour with misoprostol is safe, efficacious and clinically acceptable. Sublingual misoprostol has better efficacy in terms of no of doses required and induction delivery interval. On the other hand side effects are less seen with vaginal route. Both groups are not associated with any significant Neonatal adverse outcome and both groups were equally efficacious in achieving successful vaginal delivery

KEYWORDS :

INTRODUCTION

Induction of labour means initiation of uterine contraction after the period of viability by any method (medical, surgical, combined). When the risk of continuation of pregnancy is more either to the mother or to the foetus, induction is indicated[1] Timely induction can reduce maternal morbidity and mortality as well as assure the delivery of healthy baby.

In developed countries induction of labour accounts for 25% of all deliveries.[2,3,4] In developing countries the rates vary, lower in some regions and high in some areas. African countries generally have lower induction rates compared with American and Asian countries. A study by WHO global survey on maternal and perinatal health in 24 countries reported that induction of labour accounted for 9.6 % of all deliveries[5]. Between 1990 and last reported data in 2011 by CDC, rates of labour induction have more than doubled rising from 9.5% to 23.2%.[6]

There is increasing evidence in the literature that PGE1 (misoprostol) plays an essential role in initiation and maintenance of parturition in humans. Misoprostol is a stable analogue at room temp and it does not require storage in refrigerator[7]. It is a uterotonic agent with a wide range of clinical applications in obstetrics like induction of labour at term. The most favorable route for the administration and the optimal dose of misoprostol has not yet been established. Several studies indicate that oral misoprost is less effective and results in more side effect than intravaginal route because of systemic diffusion and digestive passage[8,9].

The vaginal absorption of misoprostol is inconsistent. This may be due to variation between women in the amount and pH of vaginal discharge. The misoprostol tablet is very soluble and can be dissolved when it is put under the tongue.

In a pharmaco-kinetic study it has been observed that sublingual misoprostol has the shortest time to peak concentration, the highest peak concentration and the greatest bio availability when compared to other routes. This is due to rapid absorption through the sublingual mucosa as well as avoidance of first pass metabolism.[9,10] So sublingual misoprost is another route of administration that can be compared with vaginal administration as both require mucosal uptake of drug. Since pharmacokinetics is different for sublingual and vaginal misoprost, difference in efficacy and side effects needs to be compared.

The aim of this study is to compare safety and efficacy of sublingual versus vaginal administration of misoprostol for induction of labour in pregnancy at term.

Medical and Obstetrical Indications for Induction

1. Prolonged Gestation
2. Intrauterine Foetal Growth Restriction
3. Premature or Prolonged Rupture Of Membrane
4. Preecclampsia Or Ecclampsia (Hypertensive Disorder In Pregnancy)
5. Chorioamnionitis
6. Maternal Hypertension, Diabetes or Cholestasis Of Pregnancy
7. Intrauterine Death 8.Oligo or Polyhydramnios

Methodology

This was a prospective parallel randomized controlled trial study conducted on 350 women who were admitted at dept of obstetrics and gynecology, fortis escorts hospital and research centre Faridabad from june 2016 to june 2018. Inclusion criteria were Primiparous women with Singleton pregnancy with Cephalic presentation with complete 38-42 wks of pregnancy with obstetric or medical indication for induction with unfavorable cervix with bishops score ≤6 and a reassuring foetal heart tracing.

Women with Multiple pregnancies, Malpresentations, Antepartum hemorrhage, Previous uterine scar or any other uterine surgery, Severe oligohydroamnios AFI < 5 or polyhydroamnios AFI>25, Non reassuring foetal heart pattern, Cephalopelvic disproportion, Renal or hepatic disease, Hypersensitivity to prostaglandin Known contraindication to the use of prostaglandins (asthma or glaucoma), Significant foetal concern that made induction necessary under continuous monitoring (eg severe IUGR ,severe preeclampsia) were excluded from study.

350 women with term gestation who fulfilled the inclusion and exclusion criterion were randomized into group A and group B in the ratio of 1:1 GROUP A- was given 25 micrograms S/L misoprost every 4 hrs for maximum of 4 doses. GROUP B- was given 25 micrograms vaginal misoprost every 4 hrs for maximum of 4 doses. Foetal or maternal monitoring done by auscultation of foetal heart rate and uterine contraction by digital palpation. Progress of labour is assessed by abdominal examination which was done every 30 minutes. Vaginal examination done in every 4 hrs with repetition of doses if cervix found unripe.The dose was not repeated if foetal heart abnormality occurs. If labour not started within 12 hrs it was considered as failed induction and caesarean section was performed. Uterine hyper stimulation (contraction lasting > 90 seconds) and tachysystole (6 or more contraction in 10 min)l also recorded.

OBSERVATION AND RESULTS

The study consisted of total 350 women for induction of labour with 25 mcg of sublingual versus vaginal misoprostol, who gave consent for the study and fulfilled the inclusion and exclusion criteria. The subjects were categorized into two groups of 175 patients in each group.

Age Wise Distribution Of Patients

All the patients included in this study were between 18 to 35 years of age. Maximum patients (176 out of 350, 50.29%) were seen in the age group of 26 to 30 years. Mean age and standard deviation were 26.52±4.27 years in group A and 26.71±4.06 years in group B. The two groups were comparable and there was no statistically significant difference between two groups (p value=0.858)

Table1 Age wise distribution of patients

Age in years		Group	
		Sublingual	Vaginal
	1)18-20	18 (10.29%)	16 (9.14%)
	2)21-25	47 (26.86%)	44 (25.14%)
	3)26-30	84 (48.00%)	92 (52.57%)
	4)31-35	26 (14.86%)	23 (13.14%)
Total		175	175

Distribution Of Cases According To Indications For Induction

In both groups commonest indications were PROM AND PIH. In study group A out of 175 patients 53 patients(30.29%) were induced for PROM and 44(25.14%) for PIH. In study group B out of 175 patients 45(25.71%) patients were induced for PROM and 51(29.14%) for PIH. The two groups were comparable and there was no statistically significant difference between two groups (p value=0.644).

Table 2: Distribution of cases according to Indications For induction

Indication For induction	Group		Total	P value
	Sublingual	Vaginal		
GDM	7 (4.00%)	10 (5.71%)	17 (4.86%)	0.644
IHCP	10 (5.71%)	12 (6.86%)	22 (6.29%)	
IUD	2 (1.14%)	1 (0.57%)	3 (0.86%)	
IUGR	8 (4.57%)	3 (1.71%)	11 (3.14%)	
OLIGO	16 (9.14%)	13 (7.43%)	29 (8.29%)	
PIH	44 (25.14%)	51 (29.14%)	95 (27.14%)	
Postterm	35 (20.00%)	40 (22.86%)	75 (21.43%)	
PROM	53 (30.29%)	45 (25.71%)	98 (28.00%)	
Total	175	175	350	

Distribution Of Cases According To Bishop's Score

From the below table it is evident that maximum patients in both groups had pre induction Bishop's score 1 to 3. Mean pre induction Bishop's score were comparable in both groups and statistically insignificant (p value= 0.137)

Table 3: Distribution Of Cases According To Bishop's Score

Bishop's score `	Group		Total	P value
	Sublingual	Vaginal		
.00	16 (9.14%)	12 (6.86%)	28 (8.00%)	0.137
1.00	51 (29.14%)	36 (20.57%)	87 (24.86%)	
2.00	38 (21.71%)	31 (17.71%)	69 (19.71%)	
3.00	35 (20.00%)	43 (24.57%)	78 (22.29%)	
4.00	13 (7.43%)	20 (11.43%)	33 (9.43%)	
5.00	22 (12.57%)	33 (18.86%)	55 (15.71%)	
Total	175	175	350	

Mean pre induction Bishop's score.
In study group A= 2.25±1.5
In study group B=2.69±1.55

Distribution Of Cases According To Dosage Of Misoprostol Required

In group A maximum patients (67 patients 38.29%) delivered with 50 mcg of misoprostol in contrast to vaginal group in which 53(30.29%) patients delivered with 50 mcg. In group B maximum patients (87 patients 49.41%) were delivered with 100 mcg. It was observed that mean drug requirement in group A was72.43±21.79 and in group B was78.43±23.73. Mean drug requirement in group A was less than that in group B which is statistically significant (p value=0.002)

Table 4: Distribution Of Cases According To Dosage Of Misoprostol Required

Doses Of Misoprost Required	Group		Total	P Value
	Sublingual	Vaginal		
25.00	3 (1.71%)	5 (2.86%)	8 (2.29%)	0.002
50.00	67 (38.29%)	53 (30.29%)	120 (34.29%)	
75.00	50 (28.57%)	30 (17.14%)	80 (22.86%)	
100.00	55 (31.43%)	87 (49.71%)	142 (40.57%)	
Total	175	175	350	

Distribution Of Cases According To No Of Patients Who Require Augmentation With Oxytocin

In group A 17(9.71%) patients required augmentation with oxytocin while in group B 22(12.57%) patients required augmentation with oxytocin .Both groups were comparable and need for oxytocin augmentation is not statistically significant in both groups(p value=0.396).

Table 5: Distribution Of Cases According To No Of Patients Who Require Augmentation With Oxytocin

Failed Induction	GROUP		Total	P Value
	Sublingual	Vaginal		
NO	158 (90.29%)	149 (85.14%)	307 (87.71%)	0.143
YES	17 (9.71%)	26 (14.86%)	43 (12.29%)	
Total	175	175	350	

Distribution Of Cases According To Induction Delivery Interval

In sublingual group 70 patients (40%) delivered within 12 hrs while in vaginal group only 47 patients (26.85%) delivered within 12 hrs. Mean induction delivery interval was 12.11±3.87 hrs in study group A while in study group B mean induction delivery interval was 20.97±1.5 hrs which is statistically significant(p value =0.003).

Table 6: Distribution Of Cases According To Induction Delivery Interval

INDUCTION DELIVERY INTERVAL	Group		Total	P value
	Sublingual	Vaginal		
0-4	4 (2.29%)	1 (0.57%)	5 (1.43%)	0.003
4.1-8	22 (12.57%)	25 (14.29%)	47 (13.43%)	
8.1-12	44 (25.14%)	21 (12.00%)	65 (18.57%)	
12.1-16	75 (42.86%)	76 (43.43%)	151 (43.14%)	
16.1-20	30 (17.14%)	52 (29.71%)	82 (23.43%)	
Total	175	175	350	

Distribution Of Cases According To Mode Of Delivery

130 patients (74.29%) delivered vaginally in sublingual group while in vaginal group 135 patients (77.14%) delivered vaginally.42 patients (24.00%) required caesarean section in sublingual group while 36 patients (22.29%) required caesarean section in vaginal group. In sublingual group only 3 patients required application of forceps while in vaginal group 4 patients delivered by application of forceps .Number of patients who delivered vaginally in both sublingual and vaginal group were almost similar and statistically insignificant.(p value=0.705)

Table 7: Distribution Of Cases According To Mode Of Delivery

Mode of delivery	Group		Total	P value
	Sublingual	Vaginal		
CS	42 (24.00%)	36 (20.57%)	78 (22.29%)	0.705
Forceps	3 (1.71%)	4 (2.29%)	7 (2.00%)	
NVD	130 (74.29%)	135 (77.14%)	265 (75.71%)	
Total	175	175	350	

Distribution Of Cases According To Failure Of Induction

17 patients had failure of induction in sublingual group while 26 patients had failure of induction in vaginal group. Although vaginal group had more number of cases who had failed induction but statistically it was not significant (p value=0.143).

Table 8: Distribution Of Cases According To Failure Of Induction

AugmentatIon With oxytocin	Group		Total	P Value
	Sublingual	Vaginal		
NO	158 (90.29%)	153 (87.43%)	311 (88.86%)	0.396
YES	17 (9.71%)	22 (12.57%)	39 (11.14%)	
Total	175	175	350	

Distribution Of Cases According To Incidence Of Side Effects Of Drug

Out of 175 patients 35 patients affected by gastrointestinal side effects in group 1 (sublingual group) in which 10 patients had only nausea, 7 patients had episodes of vomiting while 5 patients had nausea and vomiting both and 8 patients had diarrhoea, while in vaginal group out of 175 patients only 2 patient were affected by gastrointestinal side effects which is Statistically significant. Foetal distress occurred more in sublingual group, 25 patients had foetal distress in sublingual group while only 10 patients had foetal distress in vaginal group which is statistically significant. Cervical tear and vaginal laceration were seen more in vaginal group, 6 patients had cervical tear in vaginal group while in sublingual group only 1 patient had cervical tear. 16 patients had vaginal lacerations in vaginal group while only 5 patients had vaginal lacerations in sublingual group. Cases of hyperpyrexia were almost similar in both groups. 10 patients had hypertonic contractions in sublingual group while 7 patients had hypertonic contractions in vaginal group which is statistically insignificant.

Table 9: Distribution Of Cases According To Incidence Of Side Effects Of Drug

Side Effects	Sublingual	Vaginal	Total
CT	0(0.00%)	6(3.43%)	6(1.71%)
CT+GI	1(0.57%)	0(0.00%)	1(0.29%)
FD	24(13.71%)	10(5.71%)	34(9.71%)
FD+DI	1(0.57%)	0(0,00%)	1(0.29%)
GI	33(18.8%)	2(1.14%)	35(10%)
HP	4(2.29%)	2(1.14%)	6(1.71%)
HT	10(5.71%)	7(4.00%)	17(4.86%)
NIL	97(55.43%)	132(76.57%)	229(66.00%)
VL	5(2.86%)	16(9.14%)	21(6.00%)
	175	175	350

Overall sublingual group had more side effects than vaginal group. In sublingual group 78 (44.57%) patients had side effects while in vaginal group 41 (23.43%) patients had side effects which is statistically significant(p value-.0001).

Table 10: Distribution Of Cases According To Incidence Of Side Effects Of Drug

Side Effects	Group		Total	P Value
	Sublingual	Vaginal		
NO	97 (55.43%)	134 (76.57%)	231 (66.00%)	<.0001
YES	78 (44.57%)	41 (23.43%)	119 (34.00%)	
Total	175	175	350	

Distribution Of Cases According To Need For Analgesia

22 patients in sublingual group needed epidural analgesia while 14 patients in vaginal group needed epidural analgesia .Need for epidural analgesia were almost similar in both sublingual group and vaginal group and statistically Insignificant (p value=0.154).

Table 11: Distribution Of Cases According To Need For Analgesia

Apgar score1 min	Group		Total	P value
	Sublingual	Vaginal		
2)3-5	1 (0.57%)	1 (0.57%)	2 (0.57%)	0.320
3)6-7	15 (8.57%)	8 (4.57%)	23 (6.57%)	
4)8-10	159 (90.86%)	166 (94.86%)	325 (92.86%)	
Total	175	175	350	

Distribution Of Cases According To Neonatal Outcome By Apgar's Score

APGAR'S SCORE at 1 MIN and 5 MIN in both sublingual and vaginal group reveal that misoprostol given either by sublingual route or by vaginal route is not associated with significant adverse neonatal outcome.(p value at 1 min and 5 min is 0.320 and 0.592 respectively.)

Mean APGAR'S SCORE at 1 min

Sublingual group 8.27±0.83
Vaginal group 8.33±0.79

Table 12: Apgar's Score 1 Min

Apgar Score 5 min	Group		Total	P value
	Sublingual	Vaginal		
2)3-5	1 (0.57%)	1 (0.57%)	2 (0.57%)	0.592
3)6-7	10 (5.71%)	6 (3.43%)	16 (4.57%)	
4)8-10	164 (93.71%)	168 (96.00%)	332 (94.86%)	
Total	175	175	350	

Mean APGAR'S SCORE at 5 min

Sublingual group 9.07±0.89
Vaginal group 8.97±0.87

Table 13: Apgar's Score 5 Min

Need For Analgesia	Group		Total	P Value
	Sublingual	Vaginal		
No	152 (87.36%)	161 (92.00%)	313 (89.68%)	0.154
Yes	23(12.64%)	14 (8.00%)	37 (10.32%)	
Total	V	175	350	

Distribution Of Cases According To Admission To NICU

Although in sublingual group 12 babies were admitted to NICU while in vaginal group only 5 babies were admitted to NICU but this is statistically insignificant (p value =0.082)

Table 14: Distribution Of Cases According To Admission To NICU

Admission To NICU	Group		Total	P value
	Sublingual	Vaginal		
No	163 (93.14%)	170 (97.14%)	333 (95.14%)	0.082
Yes	12 (6.86%)	5 (2.86%)	17 (4.86%)	
Total	175	175	350	

DISCUSSION

The present study compares the efficacy of sublingual versus per vaginal route of Misoprostol administration in pregnant females at term in terms of successful vaginal delivery, induction delivery time interval, number of doses of Misoprostol required, need for oxytocin augmentation, side effects and foetal outcome measures such as APGAR score at birth, and admission to NICU. Induction of labour with 25 mcg of misoprostol either by sublingual or vaginal route was found to be safe, simple, effective, inexpensive, acceptable medical method for induction of labour.

Two groups (sublingual and vaginal) in the present study were comparable in terms of age, parity, indications for induction, bishop's score and foetal heart rate pattern.

The following results were drawn
Sublingual route of administration of misoprostolwas found to be more efficacious in terms of no of doses of misoprostol required. Mean dose required for sublingual group was 72.43±21.79 mcg and for vaginal group was 78.43±23.73 p value was 0.002 which is statistically significant.

When the efficacy in terms of induction delivery interval was compared it was concluded that Sublingual route of administration of misoprostol was more efficacious than vaginal route. Mean induction delivery interval was 12.11±3.87hrs in sublingual group while it was 20.1±1.5 hrs in vaginal group p value was 0.003 which is statistically significant.

Need for additional oxytocin requirement was almost similar in both group. 9.71% in sublingual group and 12.57% patients in vaginal group required additional oxytocin which is statistically insignificant (p value=0.396).

Vaginal delivery rates were almost similar in both groups. 74.29% patients delivered vaginally in sublingual group while in vaginal group 77.14% patients delivered vaginally. 24.00% required caesarean section in sublingual group while 36 patients (22.29%) required caesarean section in vaginal group which is statistically insignificant p value=0.705.

Although vaginal group had more number of cases who had failed induction (9.71% in sublingual group, 14.86% in vaginal group) but statistically it was not significant (p value=0.143).
Most common side effects were GI side effects, hyperpyrexia , hypertonic uterine contractions, foetal distress ,cervical tear and vaginal lacerations.

GI side effects were more in sublingual group Hyperpyrexia was almost similar in both groups Hypertonic uterine contractions were also similar in both groups. Foetal distress occurred more in sublingual group. Cervical tear and vaginal lacerations were seen more in vaginal group.

Need for epidural analgesia was almost similar in both sublingual group and vaginal group and statistically insignificant(p value=0.154).

Neonatal outcome in terms of apgar's score at 1min and 5min in both sublingual and vaginal group reveal that misoprostol given either by sublingual route or by vaginal route is not associated with significant adverse neonatal outcome.(p value at 1 min and 5 min is 0.320 and 0.592 respectively.)

Although in our study sublingual group 12 babies were admitted to NICU while in vaginal group on 5 babies were admitted to NICU but this is statistically insignificant (p value =0.082)

CONCLUSION

Irrespective of various labour induction methods induction of labour with misoprostol is safe, efficacious and clinically acceptable.

Sublingual misoprostol has better efficacy in terms of no of doses required and induction delivery interval. On the other hand side effects are less seen with vaginal route. Both groups are not associated with any significant Neonatal adverse outcome and both groups were equally efficacious in achieving successful vaginal delivery. Careful patient selection, evaluation and counseling are highly needed to attain this success rate safely. Careful maternal and foetal monitoring during labour are the pillars of successful induction of labour.

REFERENCES

1. Riskin-Mashiah S 1 , Wilkins I. Cervical ripening obstet gynaecol clin. North America june 1999; 26(2):243-57(Pubmed)
2. Caughey AB, Sundaram V, Kaimal AJ, et al. Maternal and neonatal outcomes of elective induction of labor. Evidence Report/technology Assessment. 2009 Mar (176):1-257. PMID: 19408970.
3. Declercq ER, Sakala C, Corry MP, Applebaum S. Listening to Mothers II: Report of the Second National U.S. Survey of Women's Childbearing Experiences: Conducted January-February 2006 for Childbirth
4. Martin JA, Hamilton BE, Sutton PD, Ventura SJ, Menacker F, Kirmeyer S, Munson ML; Centers for Disease Control and Prevention National Center for Health Statistics National Vital Statistics System. Births: final data for 2005. Natl Vital Stat Rep. 2007 Dec 5;56(6):1-103.
5. WHO Global survey on maternal and perinatal health. Induction of labour data: Geneva; World health organization 2010.
6. http/cdc.gov/nchs/fastats/obstetrical-procedures.htm 7.Kamal M Zahran,Ahmed Y Shahin,Mohamad S Abdellah and Khalid I Elsayh sublingual versus vaginal misoprostol for induction of labour at term: A randomized prospective placebo controlled study. Jobstet, gynecology. Res December 2009 vol 35 no 6:1054-1060.
8. Muzozine G,Hofmeyr GJ. Buccal or sublingual misoprostol for cervical ripening and induction of labour.Cochraine database system Rev 2004; 4:CD004221.
9. Tang os, Schweer H,Seyberth HW, Lee SW HO PC.Pharmacokinetics of different routes of admistraton of misoprostol. Hum reprod. feb 2002;17(2)