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Original Research Article

A randomised comparative study of induction of labour with sublingual misoprostol 50 µg and oral misoprostol 50 µg in term patients

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ABSTRACT

Background: Current study was conducted to compare the efficacy of tab Misoprostol 50 microgram by oral and sublingual routes for induction of labour.
Methods: A randomised comparative study of induction of labour in 200 cases of pregnant women at term and were divided into two groups of 100 each for 50 µg Misoprostol for oral and sublingual route repeated 4 hourly either by sublingual or oral route until an adequate contraction pattern set in (establishment of 3 uterine contractions in a period of 10 minutes) or once the cervical dilatation reaches 4 cm, maximum up to 6 doses. The patients were monitored for maternal vital signs, progress of labour and foetal heart rate.
Results: In this study, 86% women delivered vaginally with sublingual misoprostol while 76% were delivered vaginally with oral administration. In the present study, no significant maternal side effects were noted in either group. 4% cases of neonates in sublingual group and 6% cases of neonates in oral group required NICU admission. No still birth or neonatal deaths were seen.
Conclusions: Our study shows that sublingual Misoprostol has better efficacy, shorter induction to delivery interval, requirement of fewer doses of misoprostol when compared to oral route.

Keywords: Sublingual, Oral, Misoprostol, Labour induction

INTRODUCTION

Induction of labour is widely performed when continuation of pregnancy has more risks than benefits to the mother or fetus. Initiation of uterine contractions (after the period of viability) by any method (medical, surgical, or combined) for the purpose of vaginal delivery is called Induction of labor (IOL). It is important to take informed and written consent for induction of labor by explaining the advantages, risks, and potential of undergoing caesarean section to the patient as well as the relatives. Post-datism, Premature rupture of membranes, Oligohydramnios, polyhydramnios, pre-eclampsia, eclampsia, Intrauterine Growth Restriction (IUGR), Rh-isoimmunization, etc. are some common indications for Induction of labour.[1]

Misoprostol is a relatively new agent for pre-induction cervical ripening and labour and has very good cervical ripening and uterotonic properties.[2] and is on the WHO essential drug list for labour induction.[3] Food and Drug Administration in the year 2003 in the United States revised the contraindication for use of this drug in pregnancy and created a new labelling for use of Misoprostol in labour to explain its safety.[4] Misoprostol has undergone rigorous investigating in the past few years for use in ripening of cervix and induction of labour.[5-12] It has several advantages some of which are it is stable at

room temperature, can be administered in multiple dosage forms and can be used as it is convenient to the patient. It is given 50 µg every 3-6 hours by oral or sublingual route which shortens the induction to delivery time, multiple doses can be given, chances of failure of induction are less. Associated risks of induction with Misoprostol like uterine hyperstimulation, fetal distress, passage of meconium is seen. Uterine rupture though rare, has also been reported. Misoprostol has not been approved by FDA for use in induction in labour.[1] Keeping the aforementioned in mind, a randomized comparative study was undertaken to study and compare the safety and efficacy of induction of labour with Misoprostol 50 mcg by oral and sublingual route.

METHODS

Cases for the present study were taken from SBKS MI&RC, Vadodara, from the period September 2020 to September 2022. Cases admitted to labour ward at term were included in the study and the method of induction was chosen randomly. The total number of deliveries during the period September 2020 to September 2022 was 5320. 200 cases of pregnant women at term were approached for the study and were divided into two groups of 100 each for 50 µg Misoprostol for oral and sublingual route. Thorough history taking, examination, foetal evaluation by reactive CTG, assessment of cervical status by bishop score was done prior to induction. Informed consent was obtained. For inclusion in the study the following factors were considered including singleton gestation with gestational age of 37 weeks or more, with Vertex presentation, with a Bishop's score less than 6 and no contraindication to misoprostol. Cases with the following factors have been excluded from the study like Cephalopelvic disproportion. Placenta Previa, malpresentation, previous uterine scar, any sign of fetal compromise or other contraindications to induction of labour and any known contraindication to misoprostol as well as intra uterine fetal demise. Cases were divided into two groups 100 each to receive Misoprostol 50 µg (2of 25 µg tablet) and repeated 4 hourly either by sublingual or oral route. In all patients, the cervical status was assessed by using bishop score prior to induction.

Repeat Bishop Scores were assessed prior to each dose. Dosage was repeated every 4 hourly until an adequate contraction pattern set in (establishment of 3 uterine contractions in a period of 10 minutes) or once the cervical dilatation reaches 4 cm, maximum up to 6 doses. Once the patient was in active phase of labour ≥4 cm then augmentation with oxytocin was done, if necessary, not before 6 hours of the last misoprostol dose. After induction, the patients were monitored for maternal vital signs, progress of labour and foetal heart rate which was monitored by intermittent auscultation in majority of cases. Maximum allowable doses were 6 i.e., 300 µg of the drug Misoprostol either by sublingual or oral route. If labour did not ensue even after 4 hours following the last dose, it was considered as failed induction and caesarean section was taken. Following parameters were recorded - number of doses, and the interval between induction to onset of uterine contraction, induction-delivery interval, mode of delivery, maternal and neonatal complications and adverse effects of the drug like fever, diarrhoea, nausea and others. Tachysystole was defined as more than 5 uterine contractions per 10 minutes without foetal heart rate changes for 2 consecutive 10-minute periods. Hyperstimulation was defined as exaggerated uterine response (tachysystole or prolonged uterine contraction of >90 seconds) accompanied by FHR deceleration or tachycardia and necessary intervention was done appropriately. Fetal status was evaluated by APGAR score at 1 min and 5 min and neonatal resuscitation and NICU admission.

RESULTS

Data was analyzed using SPSS software by using the appropriate statistical tests for calculating p value.

Table 1: Bishop scoring system (modified).

Score	Dilation(cm)	Position of cervix	Effacement (%)	Station (-3 to +3)	Cervical Consistency	Cervical length
0	Closed	Posterior	0-30	-3	Firm	>4
1	1-2	Mid-position	40-50	-2	Medium	2-4
2	3-4	Anterior	60-70	-1, 0	Soft	1-2
3	5-6	-	80	+1, +2	-	<1

Table 2: Time taken for initiation of active stage of labour after induction.

Time (hours)	Miso-50 µg SL N (%)	Miso-50 µg oral N (%)	P value
<6	84 (84)	24 (24)	0.00001
>6	16 (16)	76 (76)	Statistically significant

Total 80% of patients induced with sublingual misoprostol delivered with one dose without requiring multiple doses in which 84% reached active stage of labour within 6 hours, while only 30% of delivered after single dose of oral

misoprostol,70% required repeated doses with only 24% patients reaching active stage of labour within 6 hours of induction. As a result 84% given sublingual misoprostol delivered within 12 hours as compared to 76% with oral dosage form as seen (Table 2-6).

Table 3: Induction to delivery interval.

Time (hours)	Miso-50 µg SL N (%)	Miso-50 µg oral N (%)	P value
<12	84 (84)	24 (24)	1
12-24	16 (16)	76 (76)	Statistically insignificant
>24	-	2 (2)	

Table 4: Maternal and fetal complications.

Events	Miso-50 µg SL N (%)	Miso-50 µg oral N (%)	P value
Non- reassuring fetal status	8 (8)	10 (10)	
Maternal Tachycardia	8 (8)	8 (8)	
Nausea, Vomitting	4 (4)	6 (6)	0.99
Diarrhea	4 (4)	4 (4)	Statistically insignificant
Tachysystole	4 (4)	0	
Hyperstimulation	-	-	

Table 5: Mode of delivery.

Parameters	Miso-50 µg SL N (%)	Miso-50 µg oral N (%)	P value
Normal	86 (86)	76 (76)	-
With oxytocin augmentation	36 (36)	64 (64)	0.00013
Without oxytocin augmentation	64 (64)	36 (36)	Statistically significant
Instrumental	2 (2)	4 (4)	0.19
Cesearean section	12 (12)	20 (20)	Statistically insignificant

Table 6: Doses required for induction.

Doses given	Total dose (µg)	Miso-50 µg SL N (%)	Miso-50 µg oral N (%)	P value
Single	50	80 (80)	30 (30)	0.00001
2-4	100-200	18 (18)	66 (66)	Statistically significant
5-6	250-300	2 (2)	4 (4)	

Table 7: Patient compliance.

Parameters	Miso-50 µg SL N (%)	Miso-50 µg oral N (%)	P value
Unpleasant taste	8 (8)	-	
Undissolved tablets	2 (2)	-	1
Spits/vomits out	-	-	Statistically insignificant

In the present study, tachysystole was in 4% women with sublingual misoprostol while no cases were reported with 50 microgram sublingual administration at 6 hours interval as seen in table (Table 4). Augmentation with oxytocin was required in 64% of patients induced with oral misoprostol while augmentation with oxytocin was required in 36% cases in patients induced with sublingual misoprostol which was found to be statistically significant as seen in table (Table 5). About 8% patients experienced unpleasant taste while 2% complained of undissolved tablets with sublingual dosage form while no such complaints were seen with oral form. (Table 7). Only 2% of the indications of caesarean sections in these cases were for failure of induction in both cases. While non reassuring fetal status made up for 8% in sublingual and 10% in oral dosage forms and thick MSL was seen in 6% in sublingual and 8% in oral dosage forms (Table 8). Out of total 100 cases, 4% cases of neonates in sublingual group and 6% cases of neonates in oral group required NICU admission for birth asphyxia, respiratory distress. There were no still births and neonatal deaths in both the groups. Mean APGAR score at 1min 7.20±0.45 at 5 min 8.95±0.32 in the sublingual group and 7.08±0.34 at 1 min 9.04±0.28 at 5 min in the oral group. Out of total 100 cases, 1(2%) cases in sublingual group and 3(6%) cases in oral group and 2 (4%) cases in each group had birth asphyxia and respiratory distress respectively which was managed by neonatal resuscitation of Bag and mask ventilation and mechanical ventilation accordingly as shown in (Table 9).

Table 8: Indications of caesarean section.

Indications	Miso-50 µg SL N (%)	Miso-50 µg oral N (%)
Failure of induction	2 (2)	2 (2)
Cervical dystocia	4 (4)	4 (4)
Non reassuring fetal status	8 (8)	10 (10)
Meconium stained liquor (thick msl)	6 (6)	8 (8)

Table 9: Neonatal outcome.

Neonatal outcome	Miso-50 µg SL N (%)	Miso-50 µg oral N (%)	P value
APGAR score (mean±SD)			Chi square=0 p value=1 statistically insignificant
1 min	7.06±0.36	7.2±0.40	
5 min	9.05±0.45	8.95±0.32	
Neonatal resuscitation			
Bag and mask	2 (2)	2 (2)	
Mechanical ventilation	2 (2)	4 (4)	
Still birth	-	-	
Neonatal death	-	-	
NICU admission	4 (4)	6 (6)	
Neonatal complications			
Birth asphyxia	2 (2)	6 (6)	
Sepsis	-	-	
Respiratory distress	-	-	
Meconium aspiration syndrome	2 (2)	-	

Table 10: Age groups.

Age group (years)	Miso-50 µg SL N (%)	Miso-50 µg oral N (%)	P value
18-30	96 (96)	94 (94)	0.51 Statistically insignificant
31-36	4 (4)	6 (6)	

Table 11: Gestational age of cases.

Gestational age (weeks)	Miso-50 µg SL N (%)	Miso-50 µg oral N (%)	P value
37-39	16 (16)	22 (22)	0.405 Statistically insignificant
39-40	60 (60)	60 (60)	
40-41	24 (24)	18 (18)	

Table 12: Parity among cases.

Parity	Miso-50 µg SL N (%)	Miso-50 µg oral N (%)	P value
Primigravida	44 (44)	52 (52)	0.257 Statistically insignificant
Multigravida	56 (56)	48 (48)	

The majority of cases were in the age group of 18-30 years more than 90% in both groups (Table 10).

The gestational age of the cases taken in the study was most commonly in the 39-40 weeks group (Table 11). There are 44% primigravida compared to 56% multigravida given sublingual misoprostol; while 52% primigravida and 48% multigravida in oral group (Table 12).

DISCUSSION

The present study demonstrated comparable efficacy and safety of 50 µg of misoprostol sublingually to 50 µg oral dose for induction of labour in women at term. Safety and efficacy of 50 µg misoprostol sublingual was concluded while comparing it with oral and vaginal route in a study done by Elhassan.[9] Sublingual misoprostol at least as effective as when the same dose was administered orally for labour induction at term was quoted by Muzonzoni.[10] Shetty using 50 µg sublingual or orally, suggested that in comparable dose, the sublingual route had better efficacy with no increase in uterine contractility.[11] In another study, where 50 µg of sublingual misoprostol was compared with 100 µg orally every 4 hours had the same efficacy and safety profile.[12] 100 µg of sublingual misoprostol was more effective than 50 µg of sublingual misoprostol but the incidence of tachysystole and uterine hyperstimulation

syndrome was higher with that dose as reported by Shetty.[13]

In the present study in agreement with the findings of the above-mentioned studies, 50 µg of sublingual misoprostol was comparable with a more optimal oral dose of 50 µg for induction of labour. In this study, 86% women delivered vaginally with sublingual misoprostol while 76% were delivered vaginally with oral administration. Shetty reported a vaginal delivery rate of 75.2% with sublingual and 75.1% with oral misoprostol.[14] While 24.8% had to undergo caesarean section as compared to 8% in the present study. The variation was probably to be due to the different selection criteria. In the later study, the indication of induction of labour was variable and mostly the distinction between women with intact and ruptured membranes was not made. In the present study, no significant maternal side effects were noted in either group, while nausea and vomiting were 4% in sublingual route and 6% in oral route, while diarrhoea was seen in about 4% in each group. The satisfaction rates were 82.5% and 85.7% in the oral and sublingual groups respectively, and 9.5% of patients thought that the sublingual tablets did not dissolve completely in the study by Shetty et al.[12] There was no case of hyperstimulation in our study while it was 1.6% in both groups as reported by Shetty and 9% by Wolf.[12,13] Difference could be due to inter observer variations and variable demographic profile of the women in these studies. In another study, amongst the 209 induced women, 90% delivered vaginally and 86% had a successful maternal and perinatal outcome without complications.[14] Results of randomized trials of women with ruptured membranes have similar findings to those when the membranes are intact: those induced with oral misoprostol rather than dinoprostone have fewer caesarean births and less hyperstimulation in another study.[15]

Limitations

There was no conflict of interest in this study. Risk of induction of labour and associated complications were explained to the patients and informed and written consent was taken.

CONCLUSION

Present study is in agreement with previous reports that sublingual Misoprostol is more efficacious than oral Misoprostol. Women who received sublingual Misoprostol experienced shorter induction to delivery interval, required fewer doses of Misoprostol as well as required oxytocin augmentation less frequently than those who received oral Misoprostol. No significant differences in maternal and neonatal complications were seen between the two groups.

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REFERENCES

1. Dutta DC. Textbook of gynecology. 7th ed. India: Jaypee; 2008:185-90.
2. Essential medicines: WHO model list (revised March 2005) explanatory notes. Available at: http://whqlibdoc.who.int/hq/2005/a87017_eng.pdf. Accessed on 6 December 2022.
3. Wears RL. New US food and drug administration labeling on cytotec (misoprostol) use and pregnancy. Obstet Gynecol. 2003;101(5):1049-50.
4. Sanchez-Ramos L, Kaunitz AM, Wears RL, Delke I, Gaudier FL. Misoprostol for cervical ripening and labour induction: a meta-analysis. Obstet Gynaecol. 1997;89:633-42.
5. Sanchez-Ramos L, Kaunitz AM, Del Valle GO, Delke I, Schroeder PA, Briones DK. Labour induction with the prostaglandin E1 methyl analogue misoprostol versus oxytocin: a randomized trial. Obstet Gynaecol. 1993;81:332-6.
6. Varaklis K, Gumina R, Stubblefield PG. Randomized controlled trial of vaginal misoprostol and intracervical prostaglandin E2 gel for induction of labour at term. Obstet Gynaecol. 1995;86:541-4.
7. Wing DA, Jones MM, Rahall A, Goodwin TM, Paul RH. A comparison of misoprostol and prostaglandin E2 gel for preinduction cervical ripening and labour induction. Am J Obstet Gynaecol. 1995;172:1804-10.
8. Wing DA, Rahall A, Jones MM, Goodwin TM, Paul RH. Misoprostol: an effective agent for cervical ripening and labour induction. Am J Obstet Gynaecol. 1995;172:1811-6.
9. Elhassan EM, Nasr AM, Adam I. Sublingual compared with oral and vaginal misoprostol for labour induction. Int J Gynecol Obstet. 2007;97:153-4.
10. Muzonzini G, Hofmeyr GJ. Buccal or sublingual misoprostol for cervical ripening and induction of labour. Cochrane Database Syst Rev. 2004;4: CD004221.
11. Shetty A, Danielian P, Templeton A. Sublingual misoprostol for the induction of labour at term. Am J Obstet Gynecol. 2002;186:72-6.
12. Shetty A, Mackie L, Danielian P, Rice P, Templeton A. Sublingual compared with oral misoprostol in term labour induction: a randomized controlled trial. BJOG. 2002;109:645-50.
13. Wolf SB, Sanchez-Ramos L, Kaunitz AM. Sublingual misoprostol for labour induction: a randomized clinical trial.Obstet Gynecol 2005;105:365.
14. Morris M, Bolnga JW, Verave O, Aipit J, Rero A, Laman M. Safety and effectiveness of oral misoprostol for induction of labour in a resource-limited setting: a dose escalation study. BMC Preg Childbirth. 2017; 17(1):298.
15. Kerr RS, Kumar N, Williams MJ, Cuthbert A, Aflaifel N, Haas DM, et al. Low-dose oral misoprostol for induction of labour. Cochrane Database Syst Rev. 2021;6:CD014484.

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