International Journal of Current Advanced Research
ISSN: O: 2319-6475, ISSN: P: 2319-6505, Impact Factor: 6.614
Available Online at www.journalijcar.org
Volume 11; Issue 09 (A); September 2022; Page No.1488-1491
DOI: http://dx.doi.org/10.24327/ijcar.2022.1491.0330

Research Article

COMPARATIVE TRIAL OF SUBLINGUAL AND VAGINAL MISOPROSTOL IN INDUCTION OF LABOR

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A R T I C L E I N F O

Article History:

Received 06th May, 2022
Received in revised form 14th June, 2022
Accepted 23rd July, 2022
Published online 28th August, 2022

Keywords:

Artificial Initiation of Labour

A B S T R A C T

Induction of labour is the artificial initiation of labour before its spontaneous onset for the purpose of delivery of the fetoplacental unit. We did a study in 100 patients to compare the safety and efficacy of misoprostol by two different routes of administration i.e. sublingual and vaginal. Patients included in this study essentially had term pregnancies (37-42weeks) in cephalic presentation with parity less than five. Both the groups were equally matched with regards to age, gestational age, parity and cervical score. The primary outcome was number of vaginal deliveries in each group. Around 70% in the vaginal group and 80% in the sublingual group delivered vaginally and this difference was not statistically significant. The means (+/-SD) induction to delivery interval was 13.9(+/-3.5) hours in the vaginal group and 12.2(+/-2.7) in sublingual group. Induction to delivery interval was significantly less in the sublingual group (p-value=0.022).Hence, we concluded that sublingual misoprostol was more efficacious than vaginal misoprostol and was associated with a higher patient satisfaction rate compared with vaginal misoprostol. Sublingual group had a shorter induction to delivery interval and good neonatal safety profile.

INTRODUCTION

Induction of labour is the artificial initiation of labour before its spontaneous onset for the purpose of delivery of the fetoplacental unit[1,2].Common indications for the induction of labor include: Postdated pregnancy, premature rupture of the membranes, pregnancy-induced hypertension or preeclampsia, Chorioamnionitis, intrauterine fetal growth retardation[3,4]. It is performed when the perceived risks to the mother or fetus associated with continuation of pregnancy are greater than those associated with birth[5,6].The drugs commonly available for the purpose of induction are oxytocin, dinoprostone gel and off late misoprostol. The dinoprostone gel PGE2 requires an intracervical application, needs refrigeration and is expensive. Recently, the most fascinating synthetic prostaglandin E1 analogue misoprostol has been the focus of attention in the area of various labour inducing agents. Misoprostol was originally made for the healing of gastric ulcers induced by NSAIDs.[5, 6] Labour induction with misoprostol has become an intensely investigative topic. Various authors have reported its excellent efficacy, minimal side effects and cost saving benefits. However, some complications for the mothers and the fetuses have appeared during its use. The use of misoprostol has been associated with an increased incidence of tachysystole, hypertonus and hyperstimulation syndrome. Other uncommon complications resulting from misoprostol use include uterine rupture and foetal demise. Thus, this study was undertaken to evaluate and compare the safety and efficacy of 25 microgram of misoprostol by two different routes of administration i.e. sublingual and vaginal.

MATERIALS AND METHODS

The present comparative study was done among antenatal women admitted to Batra hospital and medical research centre, New Delhiand underwent labour induction were considered for this study after taking prior approval of hospital ethics committee. Patients were included or excluded on the basis of following criteria:

Inclusion criteria: Those pregnant women who had period of gestation between 37-42weeks with cephalic presentation and parity less than 5 were included in the study.

Exclusion criteria: Those pregnant women having cephalopelvic disproportion, previous LSCS or uterine scar, history of bronchial asthma, twin pregnancy, women in active labour, fetal distress, placenta previa, active herpes infection and having renal, cardiac or hepatic disorders were excluded.
We included 100 such antenatal women in our study after screening during period of one year. Detailed clinical history,

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obstetric examination and routine investigations were done from the study participants after their written informed consent. Patients were alternatively chosen for vaginal or sublingual misoprostol groups. Group A consisted of 50 patients who received 25 microgram of sublingual misoprostol 4 hourly and group B consisted of 50 patients who received 25 microgram of misoprostol by vaginal route every 4hourly. Bishops scores were assessed prior to each dose. Dosage was repeated every 4th hourly until an adequate contraction pattern set in or till the cervical dilatation reached 4cm up to maximum of 4 doses.

Table 1 Bishops scoring system

Score	Dilatation of cervix	Effacement	Station	Cervical consistency	Cervical position
0	CLOSED	0-30%	-3	Firm	Posterior
1	1-2 cm	40-50%	-2	Medium	Mid position
2	3-4cm	60-70%	-1	Soft	Anterior
3	>=5cm	>80%	+1,+2	-	-

- Total score =13
- Favourable Score =6-13
- Unfavourable Score =0-5

Once in labour, women were cared for according to current obstetric practices. No augmentation was done if uterine contraction reached a frequency of 3 in 10 minutes lasting for 30 to 45 seconds. After induction the patients were monitored for signs of labour, when and labour ensued, they were closely monitored for maternal vital signs, progress of labour and fetal heart rate, which were monitored by continuous foetal heart monitoring. Maximum allowable doses were 4 i.e. 200 µg of the drug misoprostol either by sublingual or vaginal route. If labour did not ensure even after 4 hours following last dose it was considered as failed induction and caesarean section was done. We assessed various outcomes such as number of vaginal deliveries in each group, induction to delivery interval, uterine hyperstimulation, fetal heart rate, number of assisted deliveries in each group and associated adverse effects of misoprostol in each group.

Ethical issues: The study protocol was approved by Batra Hospital institute ethical committee. Written informed consent after explaining the study purpose was taken from pregnant women before participation in the study. Personal identifying information was kept confidential.

Statistical Analysis

Data were entered in MS Excel and analysed using Statistical Package for Social Sciences (SPSS) version 21.0 software. Categorical variables were presented as number and percentage and continuous variables as mean +/- SD. P-value of less than 0.05 was considered as statistically significant.

RESULT

In the present study, 100 pregnant women were studied, 50 women received misoprostol sublingually and 50 pregnant women received vaginally.

We found age of the patients ranging from 21 to 31 years in both the groups with the average age being 26.2 years. The mean age (±SD) of patients in the vaginal group was 26.04 years (±2.2) and 26.4 (±2.7) years in the sublingual group. The gestational age ranged from 37weeks to 41 weeks in both the group with the average age being 38.3weeks.

Table 1 Distribution of pregnant women as per basic characteristics.

Variable		Administration of misoprostol	
		Vaginal n=50	Sublingual n=50
Mean age in years (±SD)		26(±2.2)	26(±2.7)
Gestational Age (±SD)		38.6(±1.3)	38.7(±1.3)
Parity	Primi gravida No (%)	30(60)	29(58)
	Multi gravida No (%)	20(40)	21(42)

The mean (±SD) gestational age of patients in the vaginal group was 38.7 (±1.3) years and 38.6 (±1.3) years in the sublingual group. There were 30 primigravidas (60%) and 20 multigravidas (40%) in the vaginal group. The sublingual group had 29 primigravidas (58%) and 21 multigravidas (42%).(Table 1)

Table 2 Distribution of pregnant women according to obstetric Profile

Variable	Administration of misoprostol	
	Vaginal NO.(%)	Sublingual NO.(%)
Indication for induction		
a)Diabetes mellitus	5(10)	5(10)
b)Post term	11(22)	16(32)
c)Hypertension	18(36)	15(30)
d)Social reason	14(28)	13(26)
Mean Bishop score	3.5	3.7
Mean (±SD) induction to delivery interval in hour	13.9(±3.5)	12.2(±2.7)

The table 2 shows that indications for induction were similar in the both groups. Most common being hypertension in the vaginal group and post term in the vaginal group followed by diabetes mellitus. Post term was responsible for induction in 22% in the vaginal group and 32% in sublingual group. Hypertension was responsible for induction in 36% cases in the vaginal group and 30% cases in the sublingual group. Diabetes was responsible for induction in 10% cases in each group, vaginal and sublingual. The bishop's cervical score was statistically similar in both groups. The cervical score in the vaginal group was 3.56 and 3.7 in the sublingual group. The mean (±SD) induction to delivery interval was 13.9(±3.5) hours in the vaginal group and 12.3(±2.7) hours in the sublingual group. The difference was found to be statistically significant (P-value 0.22).

The table 3 shows that 72% patients in the vaginal group delivered spontaneously and instrumental delivery was instituted in 6% of patients in the vaginal group whereas all the 78% patients in the sublingual group delivered spontaneously with no instrumental delivery. The spontaneous vaginal delivery rate in the vaginal group was slightly less but it was not statistically significant (p>0.05).Caesarean section rate was similar in both the groups (22% in each group).Variable indication of LSCS accounts for various factors amongst them. Non progress of labour accounted for three caesarean section in the sublingual group and five caesarean sections in the vaginal group that makes it 6% and 10%, respectively. Foetal distress occurred in 6 patients in the sublingual group i.e. 12% overall and 4 patients in the vaginal group i.e. 8%. Failed induction resulted in 1 caesarean section in each group making the incidence o failed induction as 2% in each group. Eclampsia was also responsible for 1 caesarean in each group. Tachysystole occurred in 10% (5/50) patients in the sublingual group and 8% in the vaginal group (4/50), p-value was found to be 0.727 which is statistically not significant. Uterine

hyperstimulation rate was 4% in both the groups i.e. (2/50) in each group.

Table No 3 Distribution of pregnant women as per obstetric outcome

Variable	Administration of misoprostol	
	Sublingual n=50 NO.(%)	Vaginal n=50 NO.(%)
Mode of delivery		
a)Caesarean section	11(22)	11(22)
b)Vaccum	3(6)	5(10)
c)Vaginal	39(78)	36(72)
Indication of LSCS		
a) Failed induction	1(2)	1(2)
b)Fetal distress	6(12)	4(8)
c)Non progress of labor	3(6)	5(10)
d)Pregnancyinduced hypertension	1(2)	1(2)
Need for oxytocin		
Yes	23(46)	15(30)
No	27(54)	35(70)
Tachysystole		
Present	5(10)	4(8)
Absent	45(90)	46(92)
Hyperstimulation		
Present	4(8)	4(8)
Absent	46(92)	46(92)

The incidence of nausea was 6% in both the groups which is comparable, three patients in each group. Vomiting occurred in 1 patient in the sublingual group and 2 patients in the vaginal group making an incidence of 2% and 4% which is comparable with a p-value of 0.558. Diarrhoea occurred only in 1 patient in the sublingual group, making an incidence of 2%.There was no shivering noted in any group. (Table 4)

Table 4 Distribution of pregnant women according side effects

Variable	Administration of misoprostol	
Side effects	Sublingual NO.(%)	Vaginal NO.(%)
Nausea	3(6)	3(6)
Vomiting	1(2)	2(4)
Shivering	0(0)	0(0)
Diarrhoea	1(2)	0(0)

The table 5 shows that intrapartum meconium was comparable in both the groups. It was 16% in the vaginal group and 14% in the sublingual group with a p-value of 0.8.FHR changes occurred in 8% in the vaginal group and 10% in the sublingual group with a p-value of 0.727. APGAR score <7 at 1 minute*:* 6% in each group. APGAR *score* <7 *at* 5minutes*:* 2% neonates in the vaginal group had and none in the sublingual group. This difference was found to be non-significant (p-value 0.315).NICUadmission:4%in both the groups. No statistically significant difference was found in any of the above outcomes.

Table 5 Distribution of pregnant women according to neonatal outcome

Variable	Administration of misoprostol		
Neonatal outcome	Sublingual No.(%)	Vaginal No.(%)	p-value
Intrapartum meconium			
Present	7(14)	8(16)	0.78
Absent	43(86)	42(88)	
Fetal heart rate change			
Yes	5(10)	4(8)	0.72
No	45(90)	46(92)	
APGAR score			
At one min.>**7**	47(94)	47(94)	1
<7	3(6)	3(6)	
APGAR score			
At five min >7	50(100)	49(98)	0.31
<7	0(0)	1(2)	
NICU admission			
Yes	2(4)	2(4)	
No	48(96)	48(96)	

DISCUSSION

There have been numerous studies comparing different routes of misoprostol and their effect on the induction of labour. The aim of our project was to study the efficacy and safety profile of sublingual misoprostol and compare it with the vaginal misoprostol. The efficacy and safety were compared in terms of number of vaginal deliveries, induction to delivery interval, uterine hyperstimulation rates, associated foetal heart changes, assisted vaginal deliveries and the adverse effects in terms of nausea, vomiting, shivering and diarrhoea. As labour inducing agent misoprostol by either route is an effective agent and has a good safety profile and also is an inexpensive alternative.

Sublingual misoprostol was more efficacious than vaginal misoprostol and associated with a higher patient satisfaction rate compared with vaginal misoprostol. It had a shorter induction to delivery interval as compared to vaginal misoprostol and was statistically significant. The mean (±SD) induction to delivery interval in the sublingual group 12.2(+/- 2.69)hrs. Was significantly lessthan in the vaginal group 13.9 (+/- 3.54) hrs.(p value = 0.022) in our study. This was in concordance to various studies that show decreased induction delivery interval in the sublingual group. Bartusevicius *et al*[7]showed decreased induction delivery interval in the sublingual group vs. Vaginal group (15.0, +/- 3.7 hrs vs 16.7, +/- 4.1 hrs :p<0.05). However a systemic review done by Souza AS *et al*[8] found no significant difference in induction to delivery interval in the sublingual and vaginal groups. The caesarean section rate was statistically similar in the vaginal group and the sublingual group, 22% in each group. Studies by Bartusevicius A *et al*[7], Feitosa *et al*[13], Souza AS *et al*[7], Nassar *et al*[10] and Caliskan E[11] also showed that there were no significant differences in the mode of delivery, caesarean section rate, and indications of caesarean section between the vaginal and sublingual group. It also had a good safety profile and similar neonatal outcomes as those of vaginal misoprostol. Fetal distress accounted for caesarean section in 8% patients in the vaginal group and 12% in the sublingual group, it did not reach statistical significance. Even in the study by Caliskan[11] seven cases (8.8%) in the vaginal group and 12 cases in the sublingual group (15%) required emergent caesarean delivery for fetal heart rate abnormalities. Other studies by Bartusevicius A *et al*[7], Feitosa *et al*[9]] did not show any difference in regard to fetal distress as indication of caesarean section.

The incidence of tachysystole was 10% in the sublingual group vs 8% in the vaginal group (p-value= 0.727). Caliskan E *et al* [11] found significantly increased incidence of tachysystole in the sublingual group (17.5% vs 3.8%, p=0.005). Bartusevicius A *et al* [7]also found increased incidence of tachysystole in the sublingual group(14% vs 4.3%, p=0.005).In the study by Feitosa *et al* [9]the incidence of tachysystole in the sublingual group was 10% vs 7% in the sublingual group, but not significant. Souza AS *et al*[8] found an increased risk of uterine tachysystole in the sublingual misoprostol group. In contrast to this Nassar *et al*[10] from AMU Beirut found no difference in the tachysystole rates between two groups. The increased

incidence of tachysystole is attributed to the rapid peak onset and greater bioavailability of the sublingual misoprostol.

We found that intra-partum complications and neonatal outcomes are similar irrespective of the method of induction used and misoprostol by any route does not have any deleterious neonatal outcome. Studies by Bartusevicius A *et al* [7], Feitosa *et al*[9], Souza AS *et al*[8], Nassar *et al*[10] and Caliskan E [11] have clearly shown that there is no difference in neonatal outcomes between vaginal and sublingual group. In fact Zahran KM *et al*[12] in their study have shown significantly less incidence of intra partum meconium, Apgar score less than 7 at 1 minute and NICU admission in the sublingual group as compared to vaginal and oral group. Although foetal heart changes in the sublingual group were more than that in vaginal group in our study as well as the study by Caliskan E [11]and Feitosa *et al*[9] but it did not attain statistical significance. However the neonatal outcome was similar in both the groups thus negating any effect of FHR changes in the groups. One parameter which we did not consider while starting the study was patient satisfaction and acceptability. This parameter was also not analysed statistically. However we can consider that sublingual misoprostol was associated with a significantly higher patient satisfaction rate compared with vaginal misoprostol probably because of less frequent vaginal examinations. In fact a study by Nassar *et al*[10] form AMU Beirut comparing patient satisfaction with vaginal and sublingual misoprostol for induction of labour at term, found significantly higher patient satisfaction rate in the sublingual group.

CONCLUSION

It was found that induction to delivery interval was shorter in the sublingual misoprostol group than vaginal misoprostol group and it was also statistically significant. However, the chances of adverse maternal effects and neonatal outcomes were similar in both the groups with no statistically significant difference. Hence, we favor the use of sublingual misoprostol in Induction of labour.

Funding source: None

Conflict of Interest: None to declare.

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How to cite this article:

Manpreet Sodhi *et al* (2022) 'Comparative Trial of Sublingual and Vaginal Misoprostol in Induction of Labor', *International Journal of Current Advanced Research,* 11(08), pp. 1488-1491.
DOI: http://dx.doi.org/10.24327/ijcar.2022.1491.0330

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