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Original Research Article

To compare the efficacy and safety of intravaginal misoprostol and intracervical cervigel for induction of labour

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ABSTRACT

Background: This randomized prospective study was conducted in the department of obstetrics and Gynaecology Batra Hospital and Medical Research centre from 1st March to 30th April 2008 to compare the safety and efficacy of intravaginal misoprostol and intracervical dinoprostone gel (cervigel) for cervical ripening and induction of labour.

Methods: 80 women were recruited in the study. 40 women were administered misoprostol tablet 25ug vaginally while the other 40 were given intracervical cervigel.

Results: A total of 85.1% (68 patients) delivered vaginally (33 in the misoprostol group and 35 in the cervigel group) i.e. spontaneous vaginal and assisted vaginal deliveries. The mean interval from start of induction to vaginal delivery was 707.63±146.511 minutes in the misoprostol group and 833.13 ±144.36 minutes in the cervigel group with $p=0.001$ which was significant statistically. Though both the groups showed a favourable change in Bishop's score after induction but this was not statistically significant. However, the number of doses required in both the groups to produce an effect on cervical ripening and dilation was statistically significant $p=0.001$, cervigel group requiring lesser dose (42.5% in cervigel versus 7.5% in the misoprostol group after administration of 1st dose).

Conclusions: Both 25ug misoprostol intravaginal and dinoprostone gel intracervical are equally effective and safe for cervical ripening and induction of labour.

Keywords: Dinoprostone, Induction of labour, Misoprostol

INTRODUCTION

Induction of labour is a common obstetric intervention, performed when the perceived risks to the mother or fetus associated with continuation of pregnancy are greater than those associated with birth (Rishin-Mashiah).¹

Labour may be induced for medical or obstetric indications such as hypertensive conditions, impaired glucose tolerance, prolonged pregnancy, intra uterine growth retardation or for the convenience of mother or obstetrician so called 'social indications. Induction is the initiation of cervical ripening and Uterine contractions

before spontaneous onset of labour (Calder).² It is estimated that prostaglandins are used in approximately 22.5% of all confinements to induce labour.^{3,4}

The overall incidence of induction of labour has increased globally. In a survey by the National center for health statistics the rate of labour induction was noted to have increased from 90 per 1000 live births in 1989 to 184 per 1000 live births in 1997.

Inductions of labour is a procedure not exempt of complications some potentially serious. Ideally, induction agents should mimic spontaneous labour and at the same

time not cause any untoward maternal/fetal complication. The major concerns associated with induction of labour are uterine hyperstimulation and fetal distress and finally failed induction leading to operative intervention.

Key factor for successful induction is the status of cervix. Labour induction in the presence of an unfavourable cervix may be prolonged and may lead to increased risk of Cesarean delivery with its associated maternal and fetal morbidity (Goepfert and Colleagues 2001).⁵ Therefore, the search for an ideal agent, timing and dosage interval to convert an unfavourable cervix to one receptive to delivery is an ongoing process.

The success of induction of labour is influenced by a combination of factors existing prior to initiation of labour such as ratio of progesterone to oestrogen, prostaglandin synthesis and the state of the cervical collagen matrix. Prostaglandins play and major role in initiation of labour. Hence, they deserve attention as effective pharmacological agents for induction of labour.⁶

There are various mechanical and pharmacological methods currently in use for induction of labour, however no single method or agent has been found suitable for all clinical conditions.

All available methods are associated with some medical risks. Our study aims to find a suitable agent, which is more effective for induction.

METHODS

Randomized prospective study carried out on Patients booked for antenatal care at Batra Hospital and research institute for induction of labour at or near term. It is expected that approximately 50 such patients (25 with Tab Misoprostol 25 ug and 25 with Cervigel 0.5 gms) were included during one-year period in this randomised comparative trial.

Inclusion criteria

Women with single pregnancy at 37 weeks or more in vx presentation with reassuring NST pattern and unfavourable CX E (Bishop <5) will be included after the decision had been made to induce labour. Indications for induction of labour will include-prolonged pregnancy; pre-eclampsia; oligohydramnios; antepartum haemorrhage after excluding placenta praevia, IUGR, gestational diabetes; and "other" indications, including social reasons.

- Pregnancy induced hypertension
- Post-dated pregnancy
- Gestational diabetes
- Ante partum hemorrhage after excluding placenta praevia
- Intra uterine growth retardation
- Oligohydramnios

- Decreased fetal movements

Exclusion criteria

Women with the following conditions will be excluded from trial participation

- Active labour (regular contractions and dilatation of 3 cms. or more and full effacement.
- Previous uterine surgery (Previous LSCS / Myomectomy)
- Maternal history of glaucoma, asthma, heart disease
- Suspected CPD
- Abnormal Fetal lie (Breech / Transverse)
- Multiple pregnancy
- Placenta praevia
- Fetal Distress
- Active herpes infection
- Maternal illness (renal or hepatic failure).

On admission, each patient was thoroughly examined and after assessing the eligibility of the patient for recruitment in my study by clinical history and examination, the patient and attendants were informed about the need for induction.

The drugs used for the purpose, the route of administration, its benefits and possible side effects were clearly explained. A written informed consent for the procedure was taken.

Reassuring NST graph was taken. Thereafter patients were randomized into two groups, of 40 each to receive either tab misoprostol 25ug intravaginally or intracervical dinoprostone gel (cervigel) 0.5 mg. 80 closed identical envelopes with name of drug to be used written inside group M for misoprostol and group C for Cervigel were prepared. Randomization was done by asking the patients to choose one of the envelopes. The patients were allocated to either group depending on the name of the drug written inside the envelope.

Group M (misoprostol)

To start with, Tab misoprostol 25ug i.e. one quarter of 100 ug tablet of misoprost was inserted into the posterior vaginal fornix digitally every 4 hours for a maximum total of five doses.

Group C (cervigel)

Patients were put into lithotomy position under good light coverage and with the help of speculum cervix was visualized and the cannula with prefilled syringe containing PGE2 gel 0.5 mg was inserted into the cervical canal below the level of internal os, upto a maximum of three doses at 6hourly interval. Bishop's scoring was done prior to administration of drug in both the groups. Close fetal heart rate monitoring was done for

all patients following administration of drug. Uterine activity was also monitored with each dose to detect any contractile abnormalities i.e. Hyperstimulation >5 contractions in 10 minutes with abnormal fetal heart rate tracing (late deceleration/fetal tachycardia). Hypertonus (uterine contractions lasting for > 2 minutes).

Dose repetition was withheld when patients had any complications like hyperstimulation/abnormal fetal heart rate pattern.

The need for augmentation was assessed. If needed augmentation was done by artificial rupture of membranes followed by oxytocin.

The evaluation of response to misoprost and cervigel for cervical ripening and induction was done by assessing the change in Bishop's score, the number of doses of drug required and the need for augmentation in both the groups.

Failed induction was diagnosed when the women did not go into labor or cervix was not favorable enough for artificial rupture of membranes at the end of induction protocol. Comparison between the two groups was done in terms of

- Induction to vaginal delivery interval
- Need for Oxytocin augmentation
- Effect on uterine activity mild/moderate/tachycardia
- Mode of delivery
- Apgar score at one minute and 5 minutes

Statistical analysis was performed using student t-test, man Whitney u test. P values were taken out and results were categorized as follows

- <0.05 considered as significant.
- P<0.01 highly significant
- P<0.001 very highly significant.

RESULTS

This comparative study, conducted in the Department of obstetrics and gynecology at Batra Hospital and Medical Research Centre from 1st March 2007 to 30th April 2008 was aimed at finding the safety and efficacy of intravaginal misoprostol and intracervical dinoprostone gel for cervical ripening and induction of labour. The main outcome measure of the study was

- Induction delivery interval
- Need for oxytocin augmentation
- Associated fetal heart rate changes (bradycardia/tachycardia)
- Uterine hyperstimulation
- Incidence of meconium stained liquor
- Mode of delivery
 - >Normal vaginal
 - >Assisted vaginal delivery (forceps/ vacuum)
 - >Cesarean section
- Apgar score of baby (1min/5 min)

Overall 80 patients randomly divided into two groups of 40 each were recruited in the study.

Table 1: Demographic details of patients in study.

		Vaginal misoprostol		Intracervical dinoprostine	
Age	20-24 yrs	19	47.5%	14	35%
	25-29 yrs	17	42.5%	21	52.5%
	30-34 yrs	4	10%	5	12.5%
Parity	Primipara	29	72.5%	24	60%
	Multipara	11	27.5%	16	40%
Period of Gestation	< 37	4	10%	2	5%
	37-38	15	37.5%	7	17.5%
	39-4	8	20%	18	45%
	>40	13	32.5%	13	32.5%

The mean age at induction in misoprosol group was 25.58+ 2.87 which was comparable with cervigel group 26.23 + 3.42.

The mean period of gestation in both misoprosol and cervigel groups was 38.58 + 1.33 and 38.7 + 1.05 weeks respectively. This was also not statistically significant p=0.454.

There was no statistically significant difference in the number of primipara (29 in misoprostol group versus 24 in cervigel group) and multipara (11 in misoprostol group versus 16 in cervigel group) p=0.237.

The finding of our study was consistent with findings reported by Mundel and young and Bartha et al.^{7,8}

Table 2: Bishop's score at induction.

Variables	Vaginal misoprostol (n=40)		Intracervical dinoprostone gel (cervigel) (n=40)	
Unfavourable	37	92.5%	40	100%
Favourable	3	7.5%	0	0%

Bishop's score at induction statistically not significant in both the groups. 92.5% (37) patients of misoprostol group had unfavourable cervix as compared to 100% (40) pts in cervigel group.

Table 3: Indication of induction.

Variables	Misoprostol	Cervigel
PIH	12	18
GDM	9	11
Post dated	8	5
Oligohydramnios	4	5
IUGR	4	4
RH NEG	6	5
Decreased fetal movement	6	8

Indications for induction in both groups were comparable. Most common indication in both groups was PIH followed by GDM and post-dated.

Table 4: Change in Bishop's score.

	Unfavourable		Favourable		P Value
Misoprostol	8	20%	32	80%	0.210
Cervigel	4	10%	36	90%	

Both drugs were comparable in improving the bishops score. This was not statistically significant.

Table 5: Need for oxytocin augmentation.

	Yes		No	
Misoprostol	14	35%	26	65%
Cervigel	28	70%	12	30%

There was lesser need for Oxytocin augmentation in the Misoprostol group which was statistically significant.

Table 6: Uterine activity.

	Regular utrine activity		Hyperstimulation		P value
Misoprostol	38	95%	2	5%	0.152
Cervigel	40	100%	1	0%	

There was no incidence of hyperstimulation in the Cervigel group. The pattern of uterine activity in both the groups was not statistically significant though 2 patients in the misoprostol group had hyperstimulation.

Table 7: Fetal heart rate.

	Regular		Irregular		P value
Misoprostol	26	65%	14	35%	0.133
Cervigel	32	80%	8	20%	

Incidence of fetal distress was more in the Misoprostol group but it was not statistically significant.

Table 8: Meconium stained liquor.

Complications of MSL					
	No		Yes		P value
Misoprostol	30	75%	10	25%	0.152
Cervigel	35	87.5%	5	12.5%	

Incidence of Meconium staining was higher in the Misoprostol group, not statistically significant.

Table 9: Mode of delivery.

Mode of delivery					
	NVD	Forceps	Vaccum	LSCS	P Value
Misoprostol	29	3	1	7	0.878
Cervigel	32	2	1	5	

Instrumental delivery and Caesarean section were found to be higher in the Misoprostol group but this was not statistically significant.

Table 10: Induction-vaginal delivery interval.

Group	Minimum (minutes)	Maximum (minutes)	Mean	P Value
Misoprostol	375	960	707.63+146.511	0.001
Cervigel	540	1155	833.13+144.336	

The mean induction to vaginal Delivery was less in the Misoprostol group (Mean 707mins) than Cervigel group (833mins). This was statistically significant.

Table 11: APGAR score.

Group	Apgar 1	Apgar 5
Misoprostol	6.70±0.648	7.55 ± 0.543
Cervigel	7.50±0.599	8.555 ± 0.5.4

The Apgar score at 1min and 5min was found to be comparable in Cervigel and Misoprostol groups.

DISCUSSION

There was no statistically significant difference in the general and obstetric characteristics of patients in both the misoprostol and dinoprostone (cervigel) group. The mean age at induction in misoprostol group was 25.58+2.87 which was comparable with cervigel group 26.23 +

3.42. The mean period of gestation in both misoprostol and cervigel groups was 38.58 ± 1.33 AND 38.7 ± 1.05 weeks respectively. This was also not statistically significant $p=0.454$.

There was no statistically significant difference in the number of primipara (29 in misoprostol group versus 24 in cervigel group) and multipara (11 in misoprostol group versus 16 in cervigel group) $p=0.237$

The finding of our study was consistent with findings reported by Mundel and young and Bartha et al.^{7,8}

No. of doses

In our study 25 ug misoprostol 4 hourly for a maximum five doses intravaginally and 0.5mg dinoprostone gel (cervigel) 6 hourly for a maximum of three doses was chosen as many investigators reported high success rate and lower incidence of side effects with this dose when compared to other dosage regimens. This was also reported by van Gumund et al Gregsen et al.^{9,10} The number of doses required to achieve a favourable

chance in Bishop's score was less in the cervigel group where one dose resulted in 42.5% change for better as compared to 7.5% after first dose in the misoprostol group. The dose difference was statistically significant with $p=0.001$. Although more than one dose was required in the misoprostol group but ease of application and patient's compliance was better.

Change in Bishop's score

Both groups showed a favourable response to change in bishop's score post induction 80% in misoprostol group versus 90% in cervigel but this was not statistically significant $p=0.210$.

Need for augmentation

Need for oxytocin augmentation was seen in 35% (14 patients) in misoprostol group as compared to 70% (28 patients) of cervigel group. This was statistically significant $p= 0.002$. The findings of the study were consistent with those of Chuck and Huffaker and Surbek et al.^{11,12}

Table 12: Induction-vaginal delivery interval.

Authors	Dosage regimen	Vaginal Misoprostol	Dinoprostone gel	P
Wing et al	25 ug 3 hrly 0.5mg 6 hrly	1323±844 min.	1532±706 min	0.005
Murthy Bhaskar et al	25 ug 4 hrly 0.5mg 6 hrly	10.20±13.50hrs	14.27±5.51hrs	0.001
Sheela CN et al	25ug 6 hrly 0.5mg 6 hrly	912±641.52min	1322±733.74min	0.02
B Nasrin et al	50 ug 6 hrly 0.5mg 6 hrly	11.6±4.5 hrs	18.7±5.9 hrs	0.001
Current study	25 ug 4 hrly 0.5mg 6 hrly	707.63±146.511 mins	833.13±144.36 mins	0.001

Mode of delivery

Out of 40 patients in the misoprostol arm of the study 7 patients had to undergo lower segment cesarean section for various indications like fetal distress (3), uterine hyperstimulation with fetal distress (2) and two for meconium stained liquor. Out of 40 remaining 33 patients delivered vaginally (normal vaginal + assisted vaginal) 29 patients has normal vaginal delivery without any complications and 4 had assisted vaginal delivery (1 vacuum +3 forceps) for maternal exhaustion and associated fetal distress at full dilatation.

In the dinoprostone (Cervigel) group out of 40 patients 5 patients underwent lower segments cesarean sections 4 were done for fetal distress and 1 for failed induction (patient did not go in to labour, cervix not favourable for artificial rupture of membrane at the end of induction protocol.

35 patients had vaginal delivery (normal vaginal + assisted vaginal) 32 patients has normal vaginal delivery without any complications and 3 had assisted vaginal

delivery 92 forceps + 1 vacuum) for poor maternal efforts, exhaustion and associated fetal distress at full dilatation.

The difference of delivery outcome for both the groups was not found to be statistically significant $p= 0.878$. our study compared with Rowland S Moodley J et al.^{13,14}

Induction vaginal delivery interval

The main outcome measure of the study was induction-vaginal delivery interval. For the misoprostol group, the mean induction to delivery interval was 707.63 ± 146.511 minutes which was significantly less than the cervigel group 833.13 ± 144.36 minutes.

This difference was statistically significant $p=0.001$.

Clinical trials by Howards A, Blanchet et al, Nanda S et al, Murthy Bhaskar et al, Sheela N et al, with similar dosage regimens found similarly a statistically significant difference in the induction delivery interval between the two groups.¹⁵⁻¹⁸

Uterine activity

Both the groups had similar patterns of regular uterine activity except in the misoprostol arm where two patients had hyperstimulation but this was not statistically significant $p=0.152$.

None of the patients in the cervigel group had any uterine contraction abnormality. Our findings are similar to those of Danielian et al, Wing et al.^{19,20}

Meconium stained liquor

Incidence of meconium stained liquor was seen to be more in the misoprostol group 25 % (10 patients) versus 12.5% (5 patients) in the cervigel group. But this was not found to be statistically significant $p=0.152$. Similar finding was noted by Wing et al, Hofmeyr GJ et al.²¹

In the misoprostol group meconium could be due to associated factors for induction or reflect the direct effect of misoprostol on fetal intestinal motility.²⁰

Fetal distress (bradycardia/tachycardia)

Fetal distress was seen to be more in the misoprostol group 35% (14 patients) versus 20% (8 patients) in the cervigel group but the difference was not found to be statistically significant. The increased incidence of fetal distress could be attributed to various factors like IUGR, PIH, Oligo hydramnios contributing to decreased tolerance for induction.

Apgar score

The difference in the APGAR score at 1 and 5 minutes in both the groups was not found to be statistically significant $p=0.800$.

Out of 40 patients in the misoprostol group only two neonates had APGAR score of 5 at five minutes. One of the neonates was shifted to neonatal intensive care unit for observation in view of groaning. The diagnosis was term average for gestational age with respiratory distress. This was a delivery by lower segment cesarean section done for fetal distress. The baby remained in nursery for 24 hours and was sent home with the mother on fourth post-operative day.

In the cervigel group a low APGAR of six at one minute was seen in two babies but this improved to 8 in five minutes. Our findings corroborated with Rowland S et al and Howard A, Blanchette et al.^{13,15}

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