ORIGINAL ARTICLE

A Randomized Comparison Between Intravaginal Misoprostol and Intracervical Dinoprostone for Cervical Ripening and Labour Induction in Participants with Unfavourable Cervices

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Abstract

To compare efficacy, safety and tolerance of intravaginal misoprostol with intracervical dinoprostone for cervical ripening and labour induction in women with unfavorable cervices.Two hundred women requiring induction of labour at or beyond term were randomized to receive one of the two methods: intravaginal misoprostol 25 ug every 4 hours up to a maximum of eight doses and intracervical diniprostone gel 0.5 mg every 6 hours up to a maximum of three doses. Induction delivery interval was significantly shorter ($p< 0.01$) in the study group 10.86 hours (651.470 minutes) versus 13.31 hours (798.625 minutes). The proportion of women delivering vaginally within 24 hours was 84% in misoprostol group and 69% in dinoprostone group. The rates of women who needed oxytocin (28% versus 48%) were higher in dinoprostone group. Cesarean section rate in the study group was lower than in control group but not significantly so (15% versus 24%; $p=0.09$). Foetal distress was more common in the study group than in the control group but not significantly so (23% versus 18%; $p=0.38$). Neonatal outcome was comparable in the two groups. There were no significant maternal complications in both the groups. Intravaginal misoprostol 25 ug every four hours was more effective for cervical ripening and labour induction than intracervical dinoprostone 0.5 mg every six hours.

Key Words

Labour induction, Cervical Ripening, Intravaginal Misoprostol, Intracervical Dinoprostone

Introduction

The goal of obstetrics is a pregnancy that culminates in a healthy infant and a minimally traumatized mother. Ideally all pregnancies should go to term and labour should begin spontaneously. More often than not, the need for delivery is clear but the timing is not emergent and the route is not dictated by foetal demands. A method to initiate the normal process of labour at a time before labour begins naturally is needed. Cervical ripening is of fundamental importance for the successful induction of labour as measured by Bishop score (1).

Dinoprostone, a prostaglandin E2 analogue (either vaginally or intracervically) is widely used for cervical ripening and labour induction (2,3). However, dinoprostone gel preparations are expensive and need refrigeration for storage. Recently misoprostol, a methyl ester of prostaglandin E1, marketed for the prevention of peptic ulcer, has received increased attention as a highly effective cervical ripening agent. This medication has advantages of being inexpensive, easy to store and stable at room temperature. Many clinical trials have confirmed the safety and efficacy of misoprostol as an inducing agent (4,5). The purpose of our study was to determine whether the evidence from large number of clinical trials that support the use of misoprostol as a safe and effective ripening and inducing agent would be applicable to our population.

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Material & Methods

The present study was conducted on 200 pregnant women requiring induction of labour at or beyond term (between 37 to 42 weeks of gestation) admitted in obstetric wards of Government Lalla Ded Hospital, Srinagar after approval from the institute's ethical committee. Inclusion criteria for induction in the study were singleton term pregnancies (gestational age between 37 to 42 weeks), vertex presentation, unfavourable cervix, adequate pelvis, good foetal heart, age from 18 to 35 years in primigravidae and 23 to 40 years in multipara. Exclusion criteria included multiple pregnancies, parity of >4, polyhydramnios, non-vertex presentation, probable cephalopelvic disproportion, previous uterine scar or perforation, hypersensitivity to prostaglandins, previous history of difficult or traumatic vaginal delivery, vaginal bleeding of uncertain origin or vaginal bleeding in second half of pregnancy, pre-existing foetal distress, participants in whom prostaglandins are contraindicated like participants with history of bronchial asthma or history of glaucoma. After obtaining informed consent, the women requiring elective induction of labour or for various other indications were randomized to two groups using computer-generated random numbers. Group A (n=100) comprised of study participants who received misoprostol vaginal tablets (Cytolog; Zydus Alidac), 25 micro gm intravaginally in the posterior fornix. The dose was repeated every 4 hours until adequate uterine contractions were achieved (at least 3 contractions in 10 minutes). The maximum total dose of misoprostol required for successful induction was 200 micro gm. Participants in the active phase of labour (cervical dilatation of at least 5 centimeters) with arrest of dilatation (no change in cervical dilatation for 2 or more hours) received oxytocin for augmentation and a minimal interval of four hours was given after the last misoprostol dose. Group B participants (n=100) received dinoprostone gel (Cerviprime; AstraZeneca), 0.5 mg instilled in the cervical canal. Cervical scoring was repeated after 6 hours and reinstillation of dinoprostone gel was considered if required up to a maximum of 3 doses. If cervix was favorable, oxytocin infusion was started 6 hours after the last dose.

In both groups, labour was considered to be established if there were powerful uterine contractions at the interval of every 5 to 10 minutes. Once the active phase of labour (defined as complete cervical effacement and dilatation of at least 3 cm) was reached, the same intrapartum guidelines were followed in both groups.

All participants were kept under continuous supervision and progress of labour was recorded. Vaginal examination was performed 4 hourly or as and when deemed necessary. Frequent observation of vital signs, uterine contractility and station of presenting part was made. Foetal heart sounds were auscultated at regular intervals as required. Membranes were ruptured (ARM) when the patient was considered to be in active labour (after 4 cm dilatation) or any change in foetal heart rate necessitated it and the head became engaged. Colour of liquor was noted as clear or meconium stained. Labour induction was considered successful if subjects delivered with in 24 hours of initiation of either of two methods. Participants were observed for first four hours postpartum and any maternal side effects were recorded in detail.

The primary outcome measured was the interval from start of induction of labour to vaginal delivery. Secondary outcome measured included mode of delivery (vaginal or cesarean), need for oxytocin augmentation, and side-effect like fever, gastrointestinal symptoms, hyperstimulation and neonatal outcome. Abnormalities of uterine contractility were defined as tachysystole (> 5 contractions/10 minutes for at least 20 minutes) and hypertonus (a contraction lasting at least 2 minutes). Hyperstimulation was defined as one of these abnormalities with foetal heart rate changes.

Statistical Analysis

It was performed with Microsoft Excel. Descriptive statistics was reported in the form of average/standard deviation. Paired and unpaired't' tests were used to establish statistical significance for continuous variables. p value < 0.05 was considered statistically significant. Statistically significant differences/associations in categorical variables were tested by use of qui ^{2} test.

Results

The baseline data of the study population i.e. maternal age, parity and gestational age were comparable in the two groups. The mean gestational age was identical i.e., 37-42 weeks. The indications for induction of labor were similar in both groups. Mean preinduction bishop score in both groups was comparable. (*Table 1*)

In both groups there was highly significant rise in Bishop score (p<0.0001) six hours after pharmacological intervention. The mean rise in Bishop score was 2.15 in

Table 1. Maternal Characteristics of Study Participants

Maternal characteristics	Group A: Misoprostol (n=100)	Group B: Dinoprostone (n=100)
Parity		
Primigravida	65 (65%)	74 (74%)
Multigravida	35 (35%)	26 (26%)
Mean age (years)	25.19	24.64
Gestational age (weeks)		
37-40	37 (18.5%)	46 (23%)
40.1-41.0	163(81.5%)	154 (77%)
Pre-induction Bishop's score		
< 5	90 (90%)	95 (95%)
> 5	10 (10%)	05 (05%)
Indication for induction of labour		
Elective	37 (37%)	42 (42%)
Indicated		
Prolonged pregnancy	15(15%)	24 (24%)
Preeclampsia	25 (25%)	23 (23%)
Others	23(23%)	11 (11%)

Table3. Showing Clinical Outcome of Induction of Labour

Group	Successful	Unsuccessful (LSCS + IDI > 24 hrs)
Group A: Misoprostol (n=100)	84 (84%)	16 (16%)
Group B: Dinoprostone (n=100)	69 (69%)	31 (31%)

group 'A' and 2.14 in group 'B'. In both the groups rise in Bishop score 6 hours after induction was comparable and very highly significant (p<0.0001). The mean induction delivery interval (IDI) was 651.47 minutes (11.26 hours) in Group 'A' and 798.62 minutes (13.31 hours) in Group 'B' and was highly significant (p<0.01). In Group 'A' in primigravidas mean IDI was 704.5 minutes (12.14 hours) and in multiparas it was 572.57 minutes (9.54 hours). In Group 'B' mean IDI in primigravidas

Table 2. Intrapartum Characteristics of Study Participants

Intrapartum characteristics	Group A: Misoprostol (n=100)	Group B: Dinoprostone (n=100)
Rise in Bishop's score after 6 hours of induction:		
1. Pre-induction mean		
2. Post-induction mean	3.09	3.18
3. Difference in mean	5.24	5.32
	2.15	2.14
Mean induction delivery interval (minutes):	651.470	798.625
Induction delivery interval (min.) according to parity:		
1. Primigravida	704.5	831.10
2. Multigravida	572.57	730.19
Mode of delivery:		
1. Vaginal	75 (75%)	70 (70%)
2. Instrumental	10 (10%)	06 (06%)
3. LSCS	15 (15%)	24 (24%)
Need for oxytocin augmentation:		
1. Oxytocin needed	28 (28%)	48 (48%)
2. No oxytocin needed	72 (72%)	52 (52%)
Indications for LSCS:		
1. AFD	10 (10%)	07 (07%)
2. Non progression of labour	02 (02%)	11 (11%)
3. Failed induction	02 (02%)	06 (06%)
4. CPD	01 (01%)	Nil

Table 4. Showing Distribution of Maternal Complications

Complication	Group A: Misoprostol (n=100)	Group B: Dinoprostone (n=100)
Gastrointestinal side effects	-	-
Tachysystole	1	-
Postpartum hemorrhage (PPH)	-	1
Vaginal tear	1	1
Extension of Episiotomy	3	2

Table 5. Showing Distribution of Neonatal Complications

Neonatal complications	Group A: Misoprostol (n=100)	Group B: Dinoprostone (n=100)
Meconium Present	23 (23%)	18 (18%)
Meconium Absent	77 (77%)	82 (82%)
Mean Apgar score @ 1 min.	8.16	8.17
Mean Apgar score @ 5 min.	9.15	9.04

was 831.1 minutes (14.25 hours) and in multiparas was 730.19 minutes (12.16 hours). In both the groups, difference in mean IDI between primigravida and multipara was significant ($p<0.08$ and $p<0.07$ respectively). Normal spontaneous vaginal delivery occurred in 75 (75%) participants in Group 'A' and 70 (70%) participants in Group 'B'. There were 10 (10%) ventouse deliveries in Group 'A' and 6 (6%) in Group 'B'. There were 15 (15%) caesarean deliveries in Group 'A' and 24 (24%) caesarean deliveries in Group 'B'. Oxytocin augmentation was needed in 28 (28%) participants in Group 'A' and 48 (48%) participants in Group 'B' and the difference was highly significant ($p <0.003$). LSCS was done for various indications in 15 (15%) participants among Group 'A' and 24 (24%) participants in Group 'B'. (*Table 2*) Labour induction was considered successful if participants delivered vaginally within 24 hrs. 84 (84%) participants in Group 'A' and 69 (69%) participants in Group 'B' delivered vaginally within 24 hours. (*Table 3*)

There were no significant intrapartum or postpartum complications in mother in each group. (*Table 4*) Gastrointestinal side effects like nausea and vomiting were not seen in any patient. Tachysystole signified by six or more contractions per minute for two consecutive 10 minute periods was seen in one patient in Group 'A' but none in Group 'B'. This patient delivered herself vaginally successfully and no foetal complication was seen. PPH was seen in one patient in Group 'B'. Vaginal tear was seen in one patient from each group. There was extension of episiotomy in 3 participants in Group 'A' and 2 participants in Group 'B'.

There were no significant neonatal complications as shown in table 5. Meconium staining of amniotic fluid was seen in 23 (23%) participants in Group 'A' and 18 (18%) participants in Group 'B' but all the babies were in fairly good condition and did not require any resuscitative measure other than suction and oxygen inhalation. The difference was not statistically significant. ($p=0.38$) Mean Apgar score at 1 minute was slightly lower in Group 'A' (8.16) than in Group 'B' (8.17) and mean Apgar score at 5 min was 9.15 in Group 'A' and 9.04 in Group 'B'. The difference was not statistically significant ($p=0.92$ at 1 minute; $p=0.20$ at 5 minutes) (*Table-5*)

Discussion

The present study was undertaken to compare the safety and efficacy of misoprostol tablets administered intravaginally and dinoprostone intracervical gel for induction of labour. The study was conducted in 200 participants with comparable age, gestational age, parity and Bishop score out of which 100 participants were induced with vaginal misoprostol tablets and 100 participants were induced with intracervical dinoprostone gel. We found better results with intravaginal misoprostol tablets than with intracervical dinoprostone gel for induction of labour. The induction delivery interval (IDI) is the gold standard for judging the efficacy of any inducing agent. In our study, mean IDI was shorter with misoprostol induction as compared to dinoprostone induction. This was comparable to results from other studies.(6,7) As the ultimate aim of successful induction of labour is vaginal delivery within stipulated time period of < 24 hours, successful outcome was seen in 84% participants with misoprostol induction and 69% in participants with dinoprostone induction which is comparable with other studies (8,9,10). Caesarean section rate in present study (15% with misoprostol induction and 24% with dinoprostone induction) is in accordance with caesarean delivery rates reported in similar studies (9,11,12). As with other studies, lesser number of participants with misoprostol induction required augmentation of labour with oxytocin as compared to dinoprostone induction (8,13,14). So, it is evident that vaginal misoprostol is more effective than dinoprostone cervical gel and serves the dual purpose of cervical priming as well as inducing labour with the need for augmentation required in comparatively smaller number of participants. No serious intrapartum or postpartum maternal or fetal effects attributable to misoprostol or dinoprostone gel were noted.

Conclusion

There is no doubt that induction of labour confers benefit in various maternal and foetal conditions. However, it can be a costly affair when cervix is unfavourable for delivery. Until recently, the agent of choice has been Prostaglandin E2. Misoprostol an analogue of Prostaglandin E1 appears to be perfect substitute. It is cheaper and does not require refrigeration.

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