

Comparison of the efficacy and safety of intracervical dinoprostone gel and intravaginal misoprostol tablet as a cervical ripening agent

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Abstract

Background: Cervical ripening is an important prerequisite for successful induction of labor, a procedure that is frequently necessary because of medical or obstetrical complications. Of several methods of ripening, intracervical dinoprostone gel and intravaginal misoprostol tablet are the most frequently used methods.

Aims and Objectives: To compare the efficacy and safety of intracervical dinoprostone gel and intravaginal misoprostol tablet as a cervical ripening agent.

Materials and Methods: A total of 138 pregnant women satisfying the inclusion criteria were studied. They were divided into two groups: 72 in group 1 (dinoprostone gel) and 66 in group 2 (misoprostol tablet). The safety and efficacy of both the drugs were analyzed. The primary outcome variables were change in Bishop's score, induction to delivery (I-D) time, Apgar score, and incidence of abnormal uterine action. The secondary outcome variables were need for oxytocin, indication for caesarean section, and mode of delivery. Statistical analysis was done using the unpaired *t*-test and χ^2 -test.

Results: No difference was observed between the two groups with respect to change in Bishop's score (3.015 vs 3.625, $p > 0.05$), but I-D time was more for group 1 (i.e., 15.04 vs 11.48 h, $p < 0.05$). Apgar scores were also similar in both the groups, that is, the number of babies with Apgar score of < 8 at 5 min was 3 for group 1 vs 6 for group 2, $p > 0.05$. Abnormal uterine action was not seen at all in group 1, whereas three patients had this problem in group 2. In secondary variables, requirement of oxytocin was more in group 1 (i.e., 48 vs 22, $p < 0.05$). In various indications of caesarean section, none got operated for abnormal uterine action in group 1, whereas three patients got operated for this reason in group 2. Mode of delivery was similar in both the groups.

Conclusions: Dinoprostone and misoprostol are similar in their action on cervical ripening. Misoprostol has an added benefit of being a uterotonic agent. Therefore, it has less I-D time. Low-dose of misoprostol has decreased the incidence of side effects.


KEY WORDS: Cervical ripening, dinoprostone gel, misoprostol, induction of labor

Introduction

Cervical ripening is an important prerequisite for successful induction of labor, a procedure that is frequently necessary

because of medical or obstetrical complications. Of several methods of ripening, intracervical dinoprostone gel and intravaginal misoprostol tablet are the most frequently used methods.

Dinoprostone or PGE₂ gel is a good cervical ripening agent, whereas misoprostol has action on both cervical ripening and uterine contractions. Misoprostol has various advantages such as lower cost and no need for refrigeration.^[1] It can cause problems such as fetal distress and uterine hyperstimulation.^[2] Vaginal application of low-dose (25 μ g) misoprostol has been reported in women worldwide and seems to have safety profile similar to that of dinoprostone, especially in high-risk pregnancies, but resulted in fewer adverse effects.^[3] Other trials involve use of isosorbide

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mononitrate and a combination of dinoprostone and oxytocin, but they are not very effective.^[4,5]

The aim of this study was to compare the safety and efficacy of intracervical dinoprostone gel with that of intravaginal misoprostol tablet as a cervical ripening agent.

Material and Methods

This study was conducted in 2010 on patients with various indications for termination of labor. The inclusion criteria were singleton pregnancy (at term), cephalic presentation, reassuring fetal heart rate (FHR) monitoring pattern, and cervical Bishop's score of <5. The exclusion criteria were premature rupture of membranes; active labor; vaginal bleeding; placenta previa; history of caesarean section; cephalopelvic disproportion; and history of asthma or glaucoma, multipara >3, and malpresentation.

A total of 138 pregnant women satisfying the inclusion criteria were studied. They were randomly divided into two groups (Table 1): 72 in group 1 (dinoprostone gel) and 66 in group 2 (misoprostol tablet). In group 1, dinoprostone gel was administered intracervically (0.5 mg) and repeated 6 hourly for 3 doses, if required. In group 2, misoprostol tablet was kept vaginally (25 µg) and repeated 4 hourly for a maximum of 6 doses, if required. Bishop's score assessed favorability of cervix. Patients were closely monitored for drug complications such as abnormal uterine action and fetal heart sound irregularity.

An oxytocin infusion was started when Bishop's score was 5 or more in the absence of spontaneous labor. Patient was given option of elective lower segment caesarean section if cervical score did not improve even after maximum allowed dose of ripening agent. All patients were monitored during labor using electronic FHR monitoring. Artificial rupture of the membranes was generally performed when cervix was more than 5 cm dilated and 80% effaced.

The primary outcome variables were change in Bishop's score, induction to delivery (I-D) time, Apgar score, and incidence of abnormal uterine action. The secondary outcome variables were need for oxytocin, mode of delivery, and indications for caesarean section in both the groups. Statistical analysis was done using unpaired *t*-test and χ^2 -test.

Result

Of 138 patients, 72 were administered dinoprostone and 66 were given misoprostol. The demographic characteristics of patients distributed according to age, parity, gestational age, and initial Bishop's score are given in Table 1. The table shows that the change in Bishop's score after the administration of drug was similar in both the groups (i.e., 3.015 vs 3.625, $p > 0.05$).

The various indications for induction are shown in Table 2. The maximum number of induction was found to be for postdated pregnancy. More patients required oxytocin for progress of labor in group 1 (66% vs 34%). This was statistically significant (χ^2 -test analysis). So that, I-D time (in hours) was more in group 1, as shown in Table 3 (i.e., 15.04 vs 11.48 h, $p < 0.05$).

The complications in both the groups were similar except that group 2 had three patients with abnormal uterine action and three with APH, whereas these were absent in group 1 [Table 4].

The modes of delivery were similar in both the groups, that is, no difference in caesarean section rate was observed in both the groups (i.e., 12 vs 15) [Table 5].

Table 6 shows that no difference in average birth weight was observed between the two groups. While more patients got operated for failed induction in group 1, more patients in group 2 got operated for abnormal uterine action and fetal distress. This was not statistically significant.

Discussion

The induction of labor is an important part of modern obstetrics. The most common indication being postdatism among others.^[6] The success of induction of labor depends on good cervical ripening. This study compared the efficacy and safety of low-dose misoprostol to that of dinoprostone gel as a cervical ripening agent.

At the dose of 25 µg, misoprostol had less I-D time and lesser requirement of oxytocin. This was similar to most other studies. Although Cochrane Database review^[7] stated that better results were obtained with dose higher than 25 µg misoprostol. Kulshreshtha *et al.*^[8] showed I-D time of 6.92 h in misoprostol (100 µg) group.

Table 1: Distribution of patients

| Parameters | Group 1 (mean ± SD) | Group 2 (mean ± SD) | t-Value | p-Value |
|--------------------------|---------------------|---------------------|---------|---------|
| Age | 23 ± 3.75 | 24 ± 3.31 | 1.6546 | 0.1003 |
| Parity | 2.1 ± 1.82 | 2.3 ± 1.54 | 0.6936 | 0.4891 |
| Gestational age (weeks) | 37.5 ± 1.58 | 38.15 ± 3.03 | 1.5989 | 0.1122 |
| Initial Bishop's score | 3.018 ± 2.49 | 3.190 ± 2.156 | 0.4320 | 0.6664 |
| Change in Bishop's score | 3.015 ± 2.16 | 3.625 ± 2.86 | 1.4211 | 0.1576 |

*Unpaired *t*-test is used for analysis.

Table 2: Indication for induction

| Cause | Dinoprostone | Misoprostol | p-Value |
|-----------|--------------|-------------|---------|
| Postdated | 38 | 32 | >0.05 |
| PIH | 11 | 12 | >0.05 |
| BOH | 9 | 9 | >0.05 |
| Diabetes | 3 | 3 | >0.05 |
| IUGR | 6 | 6 | >0.05 |
| High risk | 5 | 4 | >0.05 |

* χ^2 -Test is used for analysis.

PIH pregnancy induced hypertension

BOH bad obstetrics history

IUGR intrauterine growth retardation

Table 3: Induction to delivery time (in hours)

| Delivery time (in hours) | Dinoprostone | Misoprostol | t-Value | p-Value |
|--------------------------|--------------|-------------|---------|---------|
| Mean | 15.04 | 11.48 | 2.9732 | <0.05 |
| SD | 8.45 | 5.03 | | |

*Unpaired t-test is used for analysis.

Table 4: Complications

| Complication | Dinoprostone | Misoprostol | p-Value |
|-------------------------|--------------|-------------|---------|
| Abnormal uterine action | 0 | 3 | - |
| Dystocia | 3 | 3 | >0.05 |
| Fetal distress | 3 | 6 | >0.05 |
| APH | 0 | 3 | - |

* χ^2 -Test is used for analysis.

APH antepartum hemorrhage

Table 5: Mode of delivery

| Mode of delivery | Dinoprostone | Misoprostol | p-Value |
|------------------|--------------|-------------|---------|
| Forceps | 3 | 3 | >0.05 |
| Vacuum | 3 | 3 | >0.05 |
| Vaginal | 54 | 45 | >0.05 |
| LSCS | 12 | 15 | >0.05 |

* χ^2 -Test is used for analysis.

LSCS, lower segment caesarean section.

Table 6: Average birth weight in two groups

| Group | Average baby weight | t-Value | p-Value |
|-------|---------------------|---------|---------|
| 1 | 2.373 ± 0.390 | 1.404 | 0.1626 |
| 2 | 2.275 ± 0.430 | - | |

*Unpaired t-test is used for analysis.

In the context of side effects, Apgar scores at 5 min were similar in both the groups of our study, that is, the number of babies with Apgar score of <8 at 5 min was three in group 1 and six in group 2. This difference was not statistically significant.

Kulshreshtha *et al.*^[8] showed no difference in both the groups even at a higher misoprostol dose of 100 µg. This was reiterated in Cochrane Database review^[7]. Crane *et al.*^[9] showed increased incidence of meconium staining at dose more than 25 µg misoprostol.

The second problem was that of abnormal uterine action such as hyperstimulation. In our study, three patients had this problem in group 2 as compared to none in group 1. Cochrane Database review^[7] showed increased incidence with more than 25 µg dose, whereas Kulshreshtha *et al.*^[8] showed same incidence at 100 µg dose. But all other studies were in agreement that caesarean section rate does not change in both the groups as in our study.^[10,11]

Conclusion

Both dinoprostone and misoprostol are good ripening agents, but misoprostol has an edge because of its additional uterotonic action, thereby reducing the I-D time. Using low-dose misoprostol for induction of labor can reduce the incidence of its side effects.

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