A prospective randomized controlled trial that compared misoprostol, Foley catheter, and combination misoprostol-Foley catheter for labor induction

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OBJECTIVE: The purpose of this study was to determine the efficacy of combination intravaginal misoprostol and intracervical Foley catheter for prelabor cervical ripening.

STUDY DESIGN: A prospective, randomized controlled trial was conducted. Women who were undergoing labor induction, with a singleton gestation ≥28 weeks and an unfavorable cervix (Bishop score ≥6), were assigned to one of three groups: (1) intravaginal misoprostol 25 μg every 3 hours, (2) intracervical 16F Foley catheter, or (3) combination misoprostol-Foley catheter.

RESULTS: Among 146 patients, 49 patients were assigned to misoprostol, 54 patients were assigned to Foley catheter, and 43 patients were assigned to combination therapy. There was no difference in vaginal delivery rates (misoprostol, 63.3%; Foley, 57.4%; combination, 58.1%; P = .81). There were also no statistically significant differences in the interval between induction to active phase, active phase to delivery, or induction to delivery among the three groups.

CONCLUSION: Intravaginal misoprostol and intracervical Foley catheter are comparable for preinduction cervical ripening. The combination of the two methods did not provide additional efficacy. (Am J Obstet Gynecol 2003;189:1031-5.)

Key words: Labor induction, cervical ripening, misoprostol, Foley catheter

The induction of labor is an important part of modern obstetric practice that occurs in 15% of all pregnancies.1 One factor that greatly influences the success of labor induction is the state of the cervix. Studies have established that prelabor cervical status highly correlates with the inducibility of labor and that cervical ripening improves the success of labor induction.2 Cervical ripening refers to the process of preparing the cervix for labor induction by promoting dilatation and effacement. A variety of methods have been used to effect cervical change.

Prostaglandins have become popular as labor induction agents. When applied directly to the cervix, prostaglandins induce modification of collagen and alteration of the relative concentration of glycosaminoglycans in the cervix and promote the maturational changes of cervical ripening.3 Both prostaglandin E1 (misoprostol) and prostaglandin E2 have been used with success.4,5

Mechanical dilatation of the cervix has also been used for prelabor cervical ripening. A variety of methods have been used that include osmotic dilators (laminaria tents) and Foley catheters.6,7 Several studies have documented the effectiveness of the intracervical placement of a Foley balloon catheter in cervical ripening.8 Although the effects of cervical ripening agents differ, these methods have resulted in an improved rate of successful labor induction.9 As mechanical devices result in cervical dilatation and prostaglandin agents both soften and efface the cervix, the combination of the two methods may result in a greater degree of cervical ripening and successful labor induction. The objective of this study was to evaluate the efficacy of combination misoprostol and Foley catheter compared with misoprostol or Foley catheter alone for prelabor cervical ripening.

Material and methods

A prospective, randomized controlled trial was conducted between July 1, 2000, and September 21, 2002, at Long Beach Memorial Medical Center and the University of California, Irvine. Institutional review board approval was obtained at both centers, and candidates
who met criteria were provided informed consent before randomization.

Eligible subjects were pregnant women with a singleton gestation who were admitted for labor induction. Inclusion criteria were ≥28 weeks of gestation with an unfavorable cervix (Bishop score ≤6), vertex presentation, intact membranes, absence of labor (<4 contractions per hour), and reassuring fetal heart rate tracing (reactive non-stress test results without decelerations). Patients with a history of antepartum bleeding, intrauterine fetal death, placenta previa, previous uterine scar, evidence of chorioamnionitis, previous use of induction agent during the index pregnancy, and contraindication to receive or known allergy to latex or prostaglandin were excluded from the study.

The randomization of patients was accomplished with the use of Epistat (Epistat Service, Richardson, Tex) with a block size of 10. The methods of cervical ripening were written on index cards and placed in consecutively numbered, opaque, sealed envelopes. The randomization sequence was masked until the interventions were assigned to eligible and consenting patients in consecutive order. Once randomization had taken place, the patient and treating physician were not blinded to the method of induction.

All patients underwent routine admission laboratory studies, intravenous saline solution infusion, and continuous fetal heart rate and contraction monitoring. Patients were assigned to one of 3 groups: (1) the misoprostol group, (2) the Foley catheter group, or (3) the combination group. Patients who were allocated to the misoprostol group received 25 µg of misoprostol (Cytotec), which was placed in the posterior fornix of the vagina every 3 hours until the onset of labor (>3 contractions in 10 minutes). Because the 25-µg tablets were not available commercially, a 100-µg tablet was cut into fourths by the hospital pharmacist. The maximum dose of misoprostol was 150 µg or 6 total doses. Intravenous oxytocin was begun 3 hours after the last dose of misoprostol for women who did not have spontaneous labor.

Patients who were assigned randomly to the Foley group received a 16F Foley catheter, which was inserted with visualization of the cervix by sterile speculum examination. Effort was made to avoid contact of the catheter with the vagina or ectocervix and to perform the procedure with sterile technique. After proper placement was ensured, the catheter balloon was inflated with 30 mL of sterile normal saline solution. Traction was applied to the catheter until the balloon was taut against the internal cervical os. The catheter was then taped with traction to the inner thigh of the patient until spontaneous expulsion. If this did not occur, the catheter was deflated and removed after 12 hours. Oxytocin was initiated in those patients who were not in labor after the expulsion or removal of the catheter.

Patients who were assigned randomly to the combination group had the Foley catheter placed intracervically, with the concurrent intravaginal administration of 25 µg of misoprostol every 3 hours, for a maximum of 6 doses. Oxytocin was administered to those women who were not in labor after the expulsion of the Foley catheter or six doses of misoprostol, whichever was the preceding event.

No uniform guidelines for oxytocin were enforced, although most physicians used the hospital protocol; intravenous oxytocin infusion was initiated at a rate of 1 mIU/min and increased in an increment of 1 mIU/min every 15 minutes until an adequate contraction pattern was achieved. Artificial rupture of membranes was performed when the cervix was ≥3 cm dilated. Tachysystole was identified if >6 contractions in 10 minutes were noted for two consecutive 10-minute periods. Hypertonus was noted if a single contraction lasted ≥2 minutes. Hyperstimulation was defined as the presence of tachysystole or hypertonus that was associated with the new onset of prolonged or late fetal heart rate decelerations. Terbutaline 0.25 µg was administered subcutaneously for cases of hyperstimulation, when the deceleration did not respond to the discontinuation of oxytocin. Chorioamnionitis was defined as a temperature of ≥100.4°F (38.0°C) at any time during the course of labor induction.

Data were analyzed with intent to treat. The primary outcome measure was the rate of vaginal delivery. The intervals between induction to active phase labor, active phase to delivery, and induction to delivery were also evaluated. Statistical analysis was accomplished with use of SPSS 11.0 (SPSS Inc, Chicago, Ill). Analysis of variance (ANOVA) and Kruskal-Wallis tests were used for analysis of continuous variables; χ² and Fisher exact tests were used for categoric data. All tests were two-sided, and statistical significance was defined as a probability value of <.05. An a priori sample size calculation determined that 126 patients (42 patients per group) would be needed to detect a 30% difference in the rate of successful vaginal delivery with 80% power and an α error of .05.

Results

A total of 146 patients were enrolled (Figure): 49 patients (33.6%) were assigned to the misoprostol group, 54 patients (37%) were assigned to the Foley group, and 43 patients (29.5%) were assigned to the combination group. There were a total of 12 protocol deviations: 1 deviation in the misoprostol group, 5 deviations in the Foley group, and 6 deviations in the combination group. Most of the protocol deviations were due to the inability to place the Foley catheter (4 patients) and misoprostol administration in an interval other than that described by the study protocol (4 patients). Three patients in the Foley group required a second cervical ripening agent,
and 1 patient in the combination group was found to be 3 cm dilated immediately after Foley placement and thus did not receive misoprostol. In addition, 1 patient was removed from the study (Foley group) because of worsening gestational hypertension.

The demographic characteristics were similar among the three groups (Table I). There were no statistically significant differences in maternal age, ethnicity, gravidity, parity, gestational age, number of previous vaginal deliveries, and Bishop score on admission. The indications for induction were similar among the groups, with postdates, gestational hypertension, and oligohydramnios accounting for 80% of the inductions.

As shown in Table II, there was no statistically significant difference in vaginal delivery rates (63.3% in the misoprostol group, 57.4% in the Foley group, and 58.1% in the combination group; P = .81). A subanalysis of nulliparous patients showed no statistically significant difference in the rate of vaginal delivery (16/33 [48%] in the misoprostol group; 16/33 [48%] in the Foley group, and

Table I. Demographic data and labor characteristics

<table>
<thead>
<tr>
<th></th>
<th>Misoprostol (n = 49)</th>
<th>Foley catheter (n = 54)</th>
<th>Combination (n = 43)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal age (y)</td>
<td>26.3 ± 6.82</td>
<td>26.5 ± 5.98</td>
<td>26.4 ± 6.61</td>
<td>.99</td>
</tr>
<tr>
<td>Gestational age (w)</td>
<td>39.8 ± 2.33</td>
<td>40.0 ± 2.11</td>
<td>39.9 ± 2.50</td>
<td>.81</td>
</tr>
<tr>
<td>Nulliparity</td>
<td>33 (67.3%)</td>
<td>33 (61.1%)</td>
<td>31 (72.1%)</td>
<td>.52</td>
</tr>
<tr>
<td>Prior vaginal delivery</td>
<td>16 (32.7%)</td>
<td>21 (38.9%)</td>
<td>12 (27.9%)</td>
<td>.52</td>
</tr>
<tr>
<td>Bishop score</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-2</td>
<td>12</td>
<td>13</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>3-4</td>
<td>21</td>
<td>24</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>5-6</td>
<td>12</td>
<td>15</td>
<td>12</td>
<td>.93</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>21 (42.9%)</td>
<td>15 (27.8%)</td>
<td>17 (39.5%)</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>18 (36.7%)</td>
<td>25 (46.3%)</td>
<td>17 (39.5%)</td>
<td></td>
</tr>
<tr>
<td>African American</td>
<td>6 (12.2%)</td>
<td>8 (14.8%)</td>
<td>5 (11.7%)</td>
<td></td>
</tr>
<tr>
<td>Asian/other</td>
<td>4 (8.2%)</td>
<td>6 (11.1%)</td>
<td>4 (9.3%)</td>
<td>.83</td>
</tr>
</tbody>
</table>

*ANOVA and Kruskal-Wallis tests for continuous variables, χ² test for categorical variables.
There was also no statistically significant difference in the rate of vaginal delivery among multiparous patients (15/16 [94%] in the misoprostol group, 15/21 [71%] in the Foley group, and 11/12 [92%] in the combination group; \( P = .13 \)).

Of the patients who achieved successful vaginal delivery, there was no statistically significant difference in the interval between induction to active phase, active phase to delivery, or induction to delivery (Table III). However, a shorter induction to active phase interval was noted in the patients who received combination therapy compared with those who received misoprostol or Foley catheter alone (\( P = .17 \)).

Labor management was comparable among the three groups (Table IV). There was no difference in the use of oxytocin or epidural anesthesia during labor. However, tachysystole, hyperstimulation, and the use of terbutaline occurred more frequently in the misoprostol group compared with the Foley group and the combination group. Additionally, there was an increased rate of chorioamnionitis in the combination group, but this did not reach statistical significance. There was no difference in the rate of meconium-stained amniotic fluid or endometritis. Neonatal outcomes (including birth weight, Apgar scores, and rate of admission to the neonatal intensive care unit) were similar among the groups (Table V).

**Comment**

The induction of labor often results in a prolonged labor and increases the rate of cesarean delivery, both of which are associated with increased maternal and neonatal morbidity. Ripening of an unfavorable cervix has become an integral part of the labor induction process. The best method of cervical ripening remains controversial; no one method has proved to be superior.

Several studies have been performed that compared the efficacy of combining mechanical and pharmacologic methods for cervical ripening. Sullivan et al\(^\text{10}\) described the combination of Foley balloon with intracervical prostaglandin E\(_2\) gel as being more effective in improving the Bishop score and led to fewer failed inductions compared with prostaglandin E\(_2\) gel alone. Perry et al\(^\text{11}\) demonstrated a shortened induction to vaginal delivery interval and a greater number of vaginal deliveries in patients who received intracervical Foley catheter with intravaginal dinoprostone compared with those patients who received intravaginal misoprostol alone. In contrast, Rust et al\(^\text{12}\) found that the addition of mechanical...
Table V. Neonatal outcomes*

<table>
<thead>
<tr>
<th>Misoprostol</th>
<th>Foley catheter</th>
<th>Combination</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight (g)</td>
<td>3332 ± 750</td>
<td>3299 ± 608</td>
<td>3495 ± 577</td>
</tr>
<tr>
<td>1-min Apgar score ≤7</td>
<td>12 (24.5%)</td>
<td>17 (31.5%)</td>
<td>9 (19.9%)</td>
</tr>
<tr>
<td>5-min Apgar score ≤8</td>
<td>5 (10.2%)</td>
<td>9 (16.7%)</td>
<td>4 (9.3%)</td>
</tr>
<tr>
<td>Neonatal admission</td>
<td>5 (10.2%)</td>
<td>5 (9.3%)</td>
<td>2 (4.7%)</td>
</tr>
</tbody>
</table>

*ANOVA and χ² tests.

Ripening did not improve the total ripening-to-delivery time or cesarean delivery rate compared with intravaginal misoprostol alone. None of these studies prospectively compared the combination of prostaglandin and Foley catheter therapy with either Foley catheter or prostaglandin alone to affect the rate of vaginal delivery.

In our study, intravaginal misoprostol and intracervical Foley catheter appear to be comparable for preinduction cervical ripening. Further, the combination of the two methods did not provide additional efficacy. No improvement in the rate of vaginal delivery was noted, nor was there any difference found in the interval from induction to delivery. However, the interval between induction to active labor, designated as ≥4-cm dilatation of the cervix, was shortened in the combination group compared with either the Foley or misoprostol groups, although this was not statistically significant. There was also a higher incidence of chorioamnionitis in the combination group (P = .07). This difference may be due to an increased risk of ascending infection, potentially attributable to multiple cervical examinations for misoprostol administration in the presence of the Foley catheter within the uterus and vagina.

Patients who received misoprostol alone had a higher incidence of tachysystole, hyperstimulation, and need for terbutaline, as compared with patients who received Foley catheter alone or in combination with misoprostol. The difference between the two groups that received misoprostol may have been due to a greater number of doses administered to patients in the misoprostol group as compared with the combination group. However, this difference did not reach statistical significance (P = .06).

In conclusion, among the three methods that were studied, no single technique for cervical ripening proved to be superior. Our study was potentially limited by selection bias because the physicians and patients were not blinded from method of induction. Further investigation, perhaps with a larger sample size, may be warranted. This would be of potential value in the assessment of our observed trend toward a shorter latency period, yet higher rate of chorioamnionitis, that was seen in patients who received combination therapy. Importantly, the finding of a particularly high cesarean delivery rate (46/97 [47%]) among our nulliparous patients who underwent induction should be taken into consideration before choosing to induce such a patient. In addition, because misoprostol alone was shown to be associated with a higher incidence of tachysystole, hyperstimulation, and the use of terbutaline, induction with Foley catheter alone or in combination with misoprostol may be a reasonable alternative for patients who are at increased risk of nonassuring fetal heart rate patterns during labor.

REFERENCES