Foley Catheter Compared With the Controlled-Release Dinoprostone Insert
A Randomized Controlled Trial

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OBJECTIVE: To assess efficacy of the Foley catheter compared with the dinoprostone vaginal insert for beginning labor inductions at or near term.

METHODS: We performed a multicenter randomized controlled trial. We enrolled women at 36 weeks of gestation or greater with a singleton live fetus in cephalic presentation, intact membranes, an unfavorable cervix (dilation less than 3 cm; if 2 cm, less than 80% effaced), and no contraindication to labor or either study agent. Women were allocated to either a cervical Foley catheter inflated to 30 mL or dinoprostone for up to 12 hours. Oxytocin was allowed only after study agent removal. The primary outcome was time from agent placement to delivery. Secondary outcomes included delivery by 24 hours, vaginal delivery by 24 hours, time to vaginal delivery, cesarean delivery rate, and rate of tachysystole. Analysis was by intent-to-treat.

RESULTS: We enrolled 376 patients, 185 allocated to Foley catheter and 191 to dinoprostone. In the Foley catheter group, time to delivery was shorter (median 21.6 compared with 26.6 hours; \( P = .003 \)), more patients delivered within 24 hours (56% compared with 40%; \( P = .003 \)), more delivered vaginally within 24 hours (44% compared with 30%; \( P = .004 \)), and time to vaginal delivery was shorter (median 20.1 compared with 24.3 hours; \( P = .005 \)). The cesarean delivery rates were 29% compared with 39% (\( P = .07 \)). Uterine tachysystole occurred in 0% compared with 3% (\( P = .06 \)).

CONCLUSION: Starting labor inductions with a Foley catheter, compared with the dinoprostone vaginal insert, results in a shorter time to delivery and a higher proportion of women delivered and delivered vaginally within 24 hours. Cesarean delivery rates were not statistically significantly different.


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Labor induction is iatrogenic initiation of labor to achieve vaginal delivery. Inductions may be undertaken for medical and obstetric indications or to electively time birth. Today in the United States, almost one-fourth of pregnant women have a labor induction. When the cervix is unfavorable, exogenous oxytocin is less successful. Therefore, cervical ripening agents are used.

Approaches to cervical ripening include mechanical (eg, Foley catheter) and pharmacologic (synthetic prostaglandins) methods. Compared with oxytocin alone, the Foley catheter is associated with a decreased risk of cesarean delivery. Dinoprostone (prostaglandin E2) is available as a gel and a controlled-release vaginal insert. The insert releases 0.3 mg/hour of dinoprostone over 12 hours (Cervidil package insert). A recent trial compared the Foley catheter with dinoprostone gel. In that study, the vaginal delivery rate was similar between groups, but the Foley catheter had fewer
maternal and neonatal side effects. A recent systematic review and meta-analysis comparing the dinoprostone insert with repeated prostaglandin administration (dinoprostone or misoprostol) concluded that the insert is superior as a result of a lower cesarean delivery rate and less oxytocin use.6

When the current study was initiated, there were no studies comparing the Foley catheter and the dinoprostone insert (PubMed and clinicaltrials.gov searches August 15, 2009, using the terms “Foley,” “labor induction,” and “prostaglandin E2 vaginal insert”). The purpose of our study was to compare these two methods for beginning labor inductions in the setting of an unfavorable cervix.

MATERIALS AND METHODS
We conducted a multicenter randomized controlled trial. Women were enrolled at Banner Good Samaritan Medical Center in Phoenix, Arizona, Banner Desert Medical Center in Mesa, Arizona, and at the University of Alabama in Birmingham, Alabama. The third site was added after one of the authors (R.K.E.) moved to that institution.

Women were eligible for the study if they were to undergo induction of labor at 36 weeks of gestation or greater, were carrying a live singleton fetus in cephalic presentation, and had an unfavorable cervix (less than 3 cm dilated; if 2 cm dilated, less than 80% effaced). Women were excluded from consideration for the trial if they were younger than 18 years old, could not provide informed consent in English, or had uterine contractions more frequent than every 5 minutes, ruptured membranes, a prior cesarean delivery or any other prior uterine incision, a temperature of 38°C or higher, lethal fetal anomalies (no plan for fetal heart rate monitoring during labor, no plan for cesarean delivery for fetal indications, or both), placenta previa or any other contraindication to vaginal delivery, suspected placental abruption or undiagnosed bleeding characterized as more than “spotting,” a category II or III fetal heart rate pattern, human immunodeficiency virus infection or any other immune dysfunction, or an allergy to either study agent (latex or dinoprostone). Women were also excluded if they had previously received any agent in the current pregnancy for cervical ripening or labor induction. The study was approved by the institutional review boards of Banner Good Samaritan Medical Center and the University of Alabama at Birmingham.

Women who met the enrollment criteria for the study were approached for entry into the trial. Those who provided informed consent were allocated by an online randomization system (Clinical Trials Management System; http://nuthalapaty.net/ctms) either to placement of a transcervical Foley catheter or the controlled-release dinoprostone vaginal insert in a one-to-one ratio in blocks of 10. The Arizona sites were allocated collectively. There was a separate allocation for the Alabama site. As a result of the nature of the agents used in each of the two arms of the study, blinding was not feasible. However, allocation was unknown to all parties until randomization occurred. After randomization, women allocated to the Foley catheter were placed in a lithotomy position and a 16-Fr Foley catheter with a 30-mL balloon was introduced past the internal cervical os into the lower uterine segment but outside the chorioamnion. The balloon was inflated with 30 mL of sterile water, pulled back against the internal os, and the Foley catheter was taped to the inside of the maternal thigh under minimal tension, as has been described by others.7-9 If Foley catheter placement was unsuccessful, care was at the discretion of the attending physician (repeat attempt or another agent). The Foley catheter was removed if any one of the following occurred: 1) expulsion; 2) nonreassuring fetal heart rate tracing mandating evaluation for membrane rupture and placement of internal monitors; 3) tachysystole (more than five contractions per 10-minute window averaged over 30 minutes); 4) spontaneous membrane rupture; or 5) if 12 hours elapsed since placement. The dinoprostone insert was placed in the posterior vaginal fornix and was removed for any of items 1–5. Women remained recumbent for 30 minutes after agent placement and, except for trips to the restroom, underwent continuous monitoring of uterine contractions and fetal heart rate. Oxytocin (by standard intravenous protocol for the specific hospital) was allowed only after study agent removal. Otherwise, labor management was at the discretion of the attending physician. Antibiotics were administered if indicated for prophylaxis against early-onset neonatal infection with group B streptococci or for treatment of chorioamnionitis. Cesarean delivery was performed, per the discretion of the attending physician, for standard maternal or fetal indications.

The primary outcome variable was time from first attempt at study agent placement to delivery. Secondary outcomes included the proportions of patients delivered by 12 hours, delivered by 24 hours, delivered vaginally by 12 hours, and delivered vaginally by 24 hours. Other outcomes included rates of tachysystole, clinical chorioamnionitis (defined as a temperature of 38°C or higher and one or more of the following: maternal heart rate more than 100 beats per minute, baseline fetal heart rate more than 160 beats per minute, uterine tenderness,
purulent or foul-smelling cervical discharge), endometritis (defined as a postpartum temperature of 38°C or higher on two or more occasions and no other apparent source of fever), other postpartum complications, and cesarean delivery. Early neonatal outcomes also were assessed. In addition to the primary analysis, we conducted prespecified secondary analyses stratifying women by parity and by body mass index (BMI, calculated as weight [kg]/[height (m)]^2) categories. Analysis of outcome variables was done by intent-to-treat.

Patients’ medical records were reviewed no less than 30 days after delivery. Demographic, intrapartum, and outcome data were entered into a computerized spreadsheet. Patient characteristics and outcomes were compared between the two study groups using two-sample t tests for continuous measures and \( \chi^2 \) tests of association for categorical measures. The Wilcoxon rank-sum test and Fisher’s exact test were used as respective alternatives where appropriate. Tests of trend were conducted using analysis of variance with linear contrasts and Jonckheere-Terpstra tests for continuous outcomes and Cochran-Mantel-Haenszel tests for categorical outcomes. Over the course of the trial, a subset of participants was discharged before delivery. We thus examined the median time to delivery for all participants with the outlier-robust Wilcoxon rank-sum test as well as the mean time to delivery (excluding those discharged undelivered) using the Student’s t test. Those discharged home undelivered were also excluded in the analysis of cesarean compared with vaginal delivery. For time-to-event analyses, primary study outcomes for these participants were censored at the time of discharge. Tests of significance were conducted using the log-rank test and cumulative probability plots were constructed (1-Kaplan–Meier). All data management and analysis was done using SAS 9.2. All tests of significance were two-tailed and used a .05 level of significance.

Based on data published previously, we estimated a mean time from agent placement to delivery of 24 hours in the dinoprostone group and a standard deviation of 15 hours in both study groups.\(^8-12\) Based on a two-group t test with a two-sided \( \alpha \) level of 0.05, the total sample size was determined to be 352 (176 in each group). This sample size allowed for greater than 90% power to detect a clinically significant mean decrease in time to delivery of 6 hours (to 18 hours) in the Foley catheter group. In addition, allowing for a 25% cesarean delivery rate, this sample size provided 90% power to detect a 6-hour decrease in time to delivery when restricted to women who delivered vaginally \( (n=264, 132 \text{ in each group}) \).

A data safety monitoring board was assembled before the initiation of the study. The data safety monitoring board was comprised of an independent obstetrician–gynecologist, a statistician, and a bioethicist. In addition to monitoring for serious adverse events, the data safety monitoring board conducted an interim analysis for superiority and futility after outcome data were available for 100 patients. Using the O’Brien-Fleming method, the \( P \) value for stopping the study resulting from superiority was <.005, leaving the \( \alpha \) for determining superiority at the end of the trial at 0.0477. A conditional power less than 0.20 was used as a stopping rule for futility. Neither threshold was reached in those analyses, so the trial continued to its conclusion.

RESULTS

We enrolled 376 patients, of whom 185 were allocated to a Foley catheter and 191 to dinoprostone. There were 326 patients enrolled in Arizona from July 6, 2010, to February 9, 2013, and 50 patients enrolled in Alabama from November 6, 2012, to February 22, 2013. Nine women (five Foley catheter and four dinoprostone) did not deliver during the first induction attempt (initial hospitalization). See Figure 1 for patient distribution. Demographic data and baseline obstetric characteristics of the study patients are presented in Table 1; no significant differences were observed.

![Fig. 1. Patient distribution.](Edwards. Foley Catheter Compared With the Dinoprostone Insert. Obstet Gynecol 2014.)
Median time from agent placement to delivery was shorter in the Foley catheter group (21.6 compared with 26.6 hours; \(P=.003\)). Excluding those discharged before delivery, the mean time from agent placement to delivery also was shorter in the Foley catheter group (25.3 compared with 30.5 hours; \(P=.003\)). Figure 2 shows the cumulative probability plots for time to delivery for women in the Foley catheter and dinoprostone insert groups, demonstrating graphically that time to delivery was shorter in the Foley catheter group. The median time from agent placement to vaginal delivery also was shorter in the Foley catheter group (20.1 compared with 24.3 hours; \(P=.005\)). Other secondary maternal outcomes are shown in Table 2. There were no cases of bowel ileus or obstruction, pneumonia, venous thromboembolism, intraperitoneal hematoma, intraperitoneal abscess, pyelonephritis, maternal admission to the intensive care unit, or maternal death. There was one case of cystitis in each group (\(P>.99\)). Initial placement of study agent was unsuccessful for 28 (15%) patients in the Foley catheter group compared with three (2%) in the dinoprostone insert group (\(P<.001\)).

As shown in Table 3, there were no significant differences between the Foley catheter and dinoprostone insert groups with respect to neonatal outcomes. There were two neonatal deaths in the study. Both of these neonates were born to women randomized to the dinoprostone insert group, and both of them died as a result of complications related to prenatally diagnosed congenital diaphragmatic hernias and unrelated to the labor induction.

In a prespecified secondary analysis, we stratified results by parity. In the Foley catheter group, 79 women were parous and 106 were nulliparous. In the dinoprostone insert group, 64 women were parous and 127 were nulliparous (\(P=.07\)). For parous women in the Foley catheter and dinoprostone insert groups, respectively, median time from agent placement to delivery was 17.2 compared with 22.9 hours (\(P=.01\)), delivery within 24 hours occurred in 73% compared with 55% (\(P=.02\)), vaginal delivery within 24 hours occurred in 65% compared with 44% (\(P=.01\)), and the cesarean delivery rate was 18% compared with 25% (\(P=.29\)). For nulliparous women in the Foley catheter and dinoprostone insert groups, respectively, differences were in the same direction but not statistically significant—median time from agent placement to delivery was 25.9 compared with 28.3 hours (\(P=.18\)), delivery within 24 hours occurred in 42% compared with 33% (\(P=.14\)), vaginal delivery within 24 hours occurred in 29% compared with 23% (\(P=.27\)), and the cesarean delivery rate was 40% compared with 45% (\(P=.42\)). Tests of interactions indicated no differences in the treatment effects by parity (\(P>.26\) for all outcomes), although the study was not powered to detect these interactions.

We also stratified results by BMI categories of less than 30, 30–39.9, and 40 or greater. In the Foley catheter group, 51 women had BMIs less than 30, 85 had BMIs of 30–39.9, and 48 had BMIs of 40 or greater. In the dinoprostone insert group, 55 women had BMIs less than 30, 82 had BMIs of 30–39.9, and 53 had BMIs of 40 or greater (\(P=.84\)). Table 4 shows outcomes in each treatment group across BMI categories. Figure 3 shows cumulative probability plots for time from agent placement to delivery for each BMI category stratified by treatment group. With increasing BMI, we observed longer durations of labor, fewer deliveries within 24 hours, fewer vaginal deliveries within 24 hours, and more cesarean deliveries in both study groups. Although these relationships between BMI and all outcomes were more marked in the dinoprostone insert group, the study was not...
powered to detect interactions. Nevertheless, the rate of vaginal delivery within 24 hours was found to decline more rapidly with increasing BMI category in the dinoprostone insert group (P<.05). Treating BMI as an ordinal variable, no other tests of interaction were significant (P>.15).

DISCUSSION
This multicenter randomized controlled trial demonstrated that, compared with the dinoprostone vaginal insert, starting inductions of labor for women with an unfavorable cervix with a Foley catheter leads to shorter times to delivery and a higher proportion of patients delivered and delivered vaginally within 24 hours. This shorter induction time was achieved without an increase in the cesarean delivery rate.

Between the initiation of our trial and now, a trial comparing Foley catheter with the dinoprostone vaginal insert was conducted in The Netherlands by Jozwiak and colleagues. There were no outcome
differences between groups in that trial other than a lower rate of "hyperstimulation" in the Foley catheter group. Per the authors’ admission, that trial was underpowered for their primary outcome variable—cesarean delivery rate. In addition, the results of that trial may not be generalizable to many U.S. delivery populations, because more than 75% of the patients in that study were white and more than 75% had BMIs less than 30. Furthermore, only one-third of patients in that study received epidural analgesia. In our study, ethnicity was more heterogeneous, the average BMI was greater than 35, and most women received epidural analgesia, thus making our study seem more generalizable to other obstetric populations in the United States.

Another trial was published by Cromi and colleagues.14 Those authors compared three groups including the dinoprostone insert, Foley catheter left in place for up to 12 hours, and Foley catheter for up to 24 hours. They found that delivery occurred less readily in the group where the Foley catheter was left in place for up to 24 hours than in the other two groups, but there were no significant differences between the other two groups. Neither Foley catheter group had any cases of “uterine hypercontractility.” Like in the trial published by Jozwiak, et al,13 patients had a mean BMI less than 30.

The goal of labor inductions is to achieve timely vaginal delivery without adverse effects for mother or neonate. Compared with the dinoprostone vaginal insert, our results suggest that the Foley catheter is superior. The reason that our data differ from those of the other studies described13,14 may be that our study population was more obese. In fact, we did detect a significant interaction between the rate of vaginal delivery within 24 hours and BMI category. Particularly for obese women undergoing labor inductions, the Foley catheter seems to be the better choice.

Our study did not include a formal cost analysis. However, the dinoprostone vaginal insert costs much more than a Foley catheter. Although less costly than the dinoprostone insert, the other clinically available mechanical device for cervical ripening, a double balloon catheter, is more expensive than the Foley catheter.15 There are limited data comparing the Foley catheter with the double balloon device.15,16

Despite being a large randomized controlled trial, our study does have some limitations. As a result of the nature of the interventions, blinding was not possible. Although we think that it is unlikely to have affected the results significantly, this fact could have

<table>
<thead>
<tr>
<th>Table 3. Neonatal Outcome Data</th>
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<td><strong>Outcome</strong></td>
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<tr>
<td>ICU admission</td>
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<td>Birth weight (g)</td>
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<td>1-min Apgar score</td>
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<td>5-min Apgar score</td>
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<td>5-min Apgar score less than 7</td>
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<tr>
<td>Arterial cord pH level less than 7.10*</td>
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<td>Male sex</td>
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<td>Congenital anomaly</td>
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ICU, intensive care unit. Data are n (%), mean±standard deviation, or median (interquartile range) unless otherwise specified.

* There were 77 patients with missing values for arterial cord pH level. Proportions calculated for this variable assume that all patients with missing values had arterial cord pH levels of at least 7.10.

| Table 4. Labor Induction Outcomes Stratified by Body Mass Index Categories |
|-----------------------------|----------------------|----------------------|----------------------|----------------------|
| **Outcome** | **BMI (kg/m²)** | **Less Than 30** | **30–39.9** | **40 or Greater** | **Test of Trend P** |
|-----------------------------|----------------------|----------------------|----------------------|----------------------|
| **Foley catheter** |          |          |          |          |          |
| Time to delivery (h)      | 18.0 (13.3–28.2) | 23.7 (17.5–35.2) | 21.9 (16.7–37.4) | .06          |
| Delivery in 24 h or less | 63                   | 51                   | 56                   | .38          |
| Vaginal delivery in 24 h or less | 51                  | 44                   | 41                   | .86          |
| Cesarean delivery          | 20                   | 31                   | 36                   | .21          |
| **Dinoprostone insert** |          |          |          |          |          |
| Time to delivery (h)      | 22.8 (17.9–30.6) | 27.1 (21.7–43.5) | 29.8 (20.0–41.1) | .007        |
| Delivery in 24 h or less | 55                   | 38                   | 30                   | .01          |
| Vaginal delivery in 24 h or less | 47                  | 26                   | 19                   | .001         |
| Cesarean delivery          | 22                   | 40                   | 55                   | .002         |

BMI, body mass index expressed as kilograms of weight divided by the square of height in meters. Data are median (quartile 1–quartile 3) or % unless otherwise specified.
introduced some unmeasured bias. In addition, the
study was conducted at large hospitals, where the vast
majority of cervical Foley catheters were placed by
obstetrics and gynecology resident physicians. Because
placing a cervical Foley catheter is a procedure that
typically is not within the scope of nursing
practice, the logistics involved in placing the device
may limit its use in some populations. However, at
least in the United States, we would anticipate
physician presence at the start of labor inductions in
the vast majority of cases. Furthermore, the study was
not powered to assess various interactions. Finally, we
conducted multiple statistical analyses. Although
some of the differences found may have occurred by
chance, we think that this fact is unlikely to have
affected the results significantly, because findings were
consistent.

Future studies may further refine the approach to
using the Foley catheter for starting labor inductions
in patients with unfavorable cervices. Among these
refinements might include investigation of main-
taining outpatient status for women while the Foley
catheter is in place. However, potential logistic
issues aside, we think that our data clearly demon-
strate that starting labor inductions with a Foley
catheter should be the standard approach for
women at or near term with intact membranes
and an unfavorable cervix.

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