OBSTETRICS

A randomized trial of Foley Bulb for Labor Induction in Premature Rupture of Membranes in Nulliparas (FLIP)

Jennifer M. H. Amorosa, MD; Joanne Stone, MD; Stephanie H. Factor, MD, MPH; Whitney Booker, MD; Meredith Newland; Angela Bianco, MD

BACKGROUND: In premature rupture of membranes (PROM), the risk of chorioamnionitis increases with increasing duration of membrane rupture. Decreasing the time from PROM to delivery is associated with lower rates of maternal infection. The American College of Obstetricians and Gynecologists suggests that all women with PROM who do not have a contraindication to vaginal delivery have their labor induced instead of being managed expectantly. Although the use of oxytocin for labor induction has been demonstrated to decrease the time to delivery compared with expectant management, no studies have evaluated the effectiveness of cervical ripening with a Foley bulb to additionally decrease the time to delivery.

OBJECTIVE: To determine whether simultaneous use of an intracervical Foley bulb and oxytocin decreases time from induction start to delivery in nulliparous patients with PROM compared with the use of oxytocin alone.

STUDY DESIGN: A randomized trial was conducted from August 2014 to February 2016 that compared the use of concurrent Foley bulb/oxytocin vs oxytocin alone in nulliparous patients ≥34 weeks' gestational undergoing labor induction for PROM. Our primary outcome was time from induction to delivery. Secondary outcomes were mode of delivery, tachysystole, chorioamnionitis, postpartum hemorrhage, Apgar scores, and admission to the neonatal intensive care unit.

RESULTS: A total of 128 women were randomized. Baseline characteristics were similar between groups. We found no difference in induction-to-delivery time between women induced with concurrent Foley bulb/oxytocin vs oxytocin alone (median time 13.0 hours [interquartile 10.7, 16.1] compared with 10.8 hours [interquartile range 7.8, 16.6], respectively, $P = .09$). There were no significant differences in mode of delivery, rates of postpartum hemorrhage, chorioamnionitis, or epidural use. Both groups had similar rates of tachysystole as well as total oxytocin dose. There were no differences in neonatal birth weight, Apgar scores, cord gases, or admissions to the neonatal intensive care unit.

CONCLUSION: This is the first randomized trial to compare concurrent Foley bulb/oxytocin vs oxytocin alone in nulliparous patients undergoing induction of labor for PROM. We found no difference in time from induction to delivery in patients induced with concurrent Foley bulb/oxytocin vs oxytocin alone. In nulliparous patients with PROM, this study suggests that addition of a Foley bulb to oxytocin does not decrease the time from induction start to delivery.

Key words: Foley bulb, induction of labor, labor induction, nulliparous, premature rupture of membranes, PROM

Premature rupture of membranes (PROM) or rupture of membranes before the onset of labor affects 8% of pregnancies.[1] The risk of chorioamnionitis increases with increasing duration of membrane rupture, and multiple studies have demonstrated that decreasing the time from PROM to delivery is associated with lower rates of maternal infection.[2-5] Therefore, the American College of Obstetricians and Gynecologists suggests that all women with PROM who do not have a contraindication to vaginal delivery have their labor induced instead of being managed expectantly.[6] Although the use of oxytocin for labor induction has been demonstrated to decrease the time to delivery compared with expectant management, no studies have evaluated the effectiveness of cervical ripening with the use of a Foley bulb to additionally decrease the time to delivery.

The use of 2 induction agents concurrently compared with the use of one has been demonstrated to decrease time to delivery in pregnant women without PROM. Connolly et al[7] in their study of women undergoing induction found a decreased time to delivery among women receiving concurrent Foley bulb and oxytocin compared with sequential Foley bulb followed by oxytocin. In a 4-arm study of women undergoing induction, Levine et al[8] compared time to delivery among women assigned to 4 different induction protocols: (1) concurrent Foley bulb and misoprostol; (2) concurrent Foley bulb and oxytocin; (3) misoprostol alone; and (4) Foley bulb alone. The groups with concurrent administration of 2 agents had shorter time to delivery than the groups with sequential administration of agents. The use of concurrent Foley bulb and oxytocin has never been studied in women with PROM.

The purpose of this study was to determine whether simultaneous use of an intracervical Foley bulb inflated to 60 cc and oxytocin decreases the time from induction start to delivery in nulliparous patients with PROM compared with the use of oxytocin alone.

Materials and Methods

This was a single-center, nonblinded, randomized clinical trial in which we compared the efficacy of Foley bulb plus oxytocin vs oxytocin alone in patients with PROM. The study was approved by the Icahn School of Medicine at Mount Sinai Medical Center's Institutional

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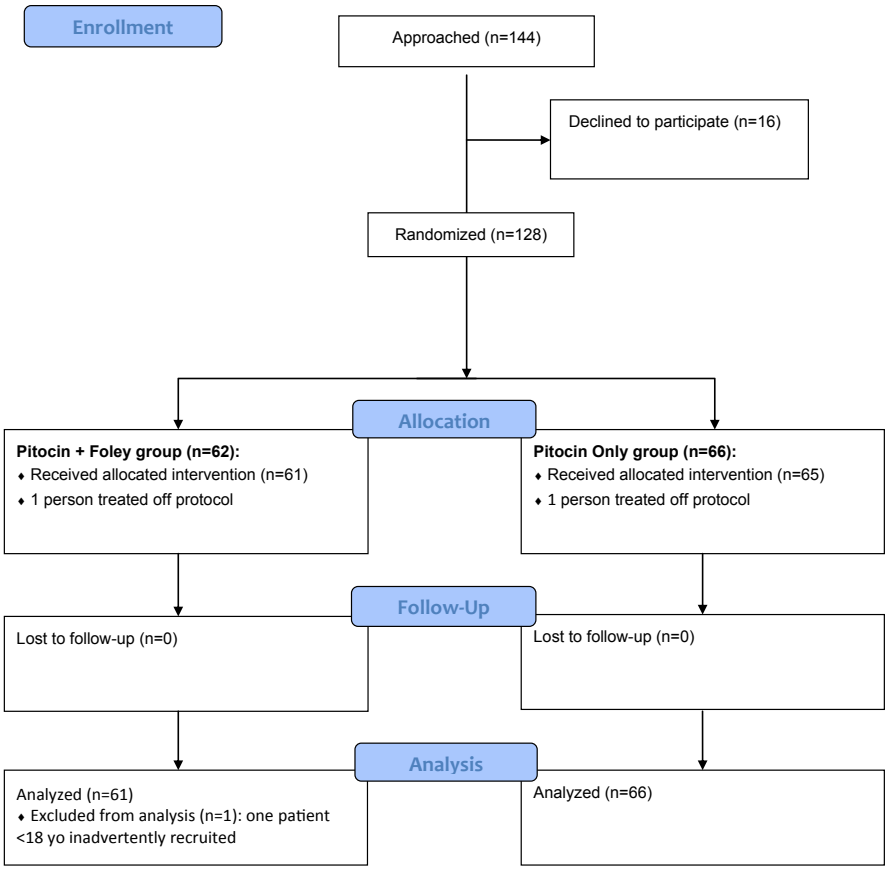
Review Board and was registered with the clinical trials registry (ClinicalTrials.gov #NCT02098421). Women age 18 and older with a viable cephalic singleton gestation of 34 weeks' gestational age or greater who presented with PROM between August 2014 and February 2016 were evaluated for participation by labor floor providers. Patients were eligible for participation if their cervix was dilated less than 3 cm or, if the primary provider wished to defer the initial cervical examination because of ruptured membrane status, the patient was having contractions less than 3 times every 10 minutes. Patients were ineligible to participate if they had a multifetal gestation, a known anomalous fetus, a fetus with malpresentation, a latex allergy, unexplained vaginal bleeding or contraindication to vaginal delivery (such as a placenta previa), had received latency antibiotics, had had previous uterine surgery (including previous cesarean delivery or myomectomy), or were in spontaneous labor (regular uterine contractions with cervical change). If eligible patients indicated that they were interested in hearing more about the study, they were approached by a member of the research team, who explained the study and obtained informed consent from agreeable patients.

FIGURE 1
Study enrollment, allocation, and analysis



Flow chart demonstrating patient recruitment through analysis.

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Once the patient consented to participate in the study, participants were randomized to receive either concurrent Foley bulb and oxytocin or oxytocin alone. The randomization envelopes were prepared before the start of the study by the use of a random numbers generator from OpenEPi, Version 3 (http://www.OpenEpi.com). Cards allocating patients to either "oxytocin plus Foley" or "oxytocin alone" were placed in sequentially numbered, sealed opaque envelopes. After signing consent, participants were given the next ordered envelope.

Patients in the Foley bulb and oxytocin group had a 16-F, 30-cc Foley bulb inserted digitally or under direct visualization with the aid of a sterile speculum. The Foley was threaded through the internal cervical os and filled with 60 mL of normal saline. The diameter of the Foley balloon with this volume of saline is ~4 cm. The catheter of the Foley bulb was then taped to the patient's thigh under tension. Oxytocin was started within 1 hour of Foley bulb placement. In the oxytocin alone group, oxytocin was started as soon as possible after consent was obtained.

In both groups, oxytocin was titrated according to our institution's standard induction protocol in which the oxytocin infusion is started at 2 mU/min. This dose is doubled every 30 minutes to a maximum dose of 16 mU/min (2—4—8—16) and then may be increased by 2 mU/min every 30 minutes to a maximum dose of 30 mU/min or until regular uterine contractions occur. Fetal heart rate and contraction patterns are monitored continuously in all patients receiving oxytocin. Further labor management was at the discretion of the private provider.

Demographic characteristics, pregnancy history, labor course, delivery data, and neonatal outcomes were collected via patient interview and/or chart review by the study team. After each delivery, the fetal heart rate tracing was reviewed for periods of tachysystole (>5 uterine contractions in 10 minutes, averaged over 30 minutes).

The primary outcome measure was time from start of induction to delivery. Secondary outcomes included mode of delivery, tachysystole, chorioamnionitis, postpartum hemorrhage, neonatal Apgar scores, and admission to the neonatal intensive care unit (NICU).

The sample size was estimated a priori based on the primary outcome. We assumed a normal distribution of