Vaginal prostaglandin-E2 suppository versus extra-amniotic Foley catheter to induce labor: a randomized clinical trial

Running title: Prostaglandin-E2 vs. Foley catheter to induce labor

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Abstrict: The aim of the present study was to compare the effect of vaginal prostaglandin-E2 suppository with the insertion of Foley catheter in extra amniotic space to induce labor. In a randomized clinical trial study the effect of vaginal prostaglandin-E2 suppository was compared with insertion of Foley catheter in extra amniotic space. The study participants were 44 nulliparous pregnant women presenting with term pregnancy in their 38-42 weeks of gestation. The mean time interval between induction and vaginal delivery was 12.8 hours for extra-amniotic Foley catheter and 12 hours for vaginal prostaglandin-E2 group without statistical significance. Mean time to effective uterine contractions was 8.22(2.6) hours in extra-amniotic Foley catheter group versus 9(4) hours in vaginal prostaglandin-E2 group without statistically significant difference. Mean Bishop's score six hours after induction was 6.22(1.8) in extra-amniotic Foley catheter group versus 4.6(2.5) in vaginal prostaglandin-E2 group and the difference was statistically significant ($P < 0.05$). Mean time from induction to a Bishop's score above 7, mean oxytocin dose, and mean neonatal APGAR score didn't statistically differ between the groups. The women in extra-amniotic Foley catheter group were 1.6 times more likely to have vaginal delivery compared to those in vaginal prostaglandin-E2 group(Risk ratio=1.64, 95% CI: 1.03-2.59). **Conclusions:** In our study, vaginal prostaglandin-E2 suppository and extra-amniotic Foley catheter appeared to be comparable for labor induction. Considering the fact that extra-amniotic Foley catheter has advantages such as simplicity, low cost, reversibility, and lack of systemic or serious side effects, it may be preferred by clinicians.

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Introduction:

The cervix when it is unripe may impede labor induction. Both mechanical and medical cervical ripening can be done to achieve this. Numerous studies have shown locally applied prostaglandins (PG), to increase cervical compliance and dilation(Sherman et al. 2001). Numerous studies are available that have assessed Both PG-E1 and PG-E2 some comparing these two with each other or compared different forms of them or compared them with other pharmacological formulations(Chaudhuri et al. 2011;Kunt et al. 2010;Mostafa-Gharebaghi, Mansourfar, & Sadeghi-Bazargani 2010;Osman et al. 2006;Rabl et al. 2002;Sifakis et al. 2007). Irrespective of their administration modalities PGs also stimulate the myometrium resulting in uterine contractions that may possibly lead to hyper-stimulation(Husslein 1991;Sherman, Frenkel, Pansky, Caspi, Bukovsky, & Langer 2001). A challenge would be to find alternatives lacking such a side effect. Mechanical methods have gained attention in this regard. Such methods may be effective on cervical ripening through dilating and stretching the lower uterine segment and cervix and at the same time are not associated with uterine contractions. Studies have been done in recent years to assess efficacy of extra-amniotic Foley catheter compared to PGs sometimes with controversial results. Although most previous research have been supporting of their acceptable efficacy and posed a non-inferiority hypothesis, due to small sample sizes of most of them and taking into account the protocol variations of the studies, there is need for the accumulation of more studies from different settings in order to form a strong body of evidence to prove it as an appropriate alternative to PGs(Afolabi, Oyeneyin, & Ogedengbe 2005;Al-Taani 2004;Chung et al. 2003;Gelisen et al. 2005;Niromanesh, Mosavi-Jarrahi, & Samkhaniani 2003;Owolabi, Kuti, & Ogunlola 2005;Sadeghi-Bazargani & Sedghipour 2012;Sciscione et al. 2001;Sherman, Frenkel, Pansky, Caspi, Bukovsky, & Langer 2001). The aim of the present study was to compare the effect of vaginal prostaglandin-E2 with the insertion of Foley catheter in extra amniotic space to induce labor.

Methods:

In a randomized clinical trial study the effect of vaginal prostaglandin-E2 suppository was compared with insertion of Foley catheter in extra amniotic space

on labor induction. Study was conducted over the years 2007-2008 in Alzahra and Taleghani University hospitals in Tabriz, Iran. The study participants were 44 nulliparous pregnant women presenting with term pregnancy in their 38-42 weeks of gestation. The gestational age was assessed based on LMP and ultrasonography results. The participants were planned for pregnancy termination while suffering inappropriate cervix having a Bishop's score <= 40. They were randomly allocated to receive either vaginal prostaglandin-E2 suppository or extra-amniotic Foley catheter in two groups of 22 patients each, the sample size was estimated using Cohen's table assuming α=0.05, effect size = 0.7 and V=1.99.

Allocation was done by the obstetrician in labor room after assessing the Bishop's score. Vaginal prostaglandin-E2 was administered in a dose of 3 mg E2 suppository inserted at posterior fornix. In second group foley catheter was inserted in sterile conditions into the extra amniotic space and filled with 30 ml of normal saline. Regardless of the treatment type in each group, in case effective labor contractions were not started after six hours, the labor was induced using oxytocin infusion. The outcomes of interest in this trial included Bishop's score, uterine contractions, need for oxytocin, delivery type, APGAR score and complications. The exclusion criteria were as follows:

1. Vaginal bleeding
2. Probable chorioamnionitis and cervical infectious secretions.
3. Vaginal delivery contraindications
4. Fetal heart rate abnormalities
5. Previous uterus scar
6. Severe preeclampsia
7. Contra indications of using prostaglandins

Data were entered into computer and analyzed using SPSS 11.5 statistical software package. t-test, chi-square test and Mann-Whitney-U test were used to analyze data. A p value <0.05 was considered statistically significant. Study was approved by committee of ethics in Tabriz University of medical sciences.

Results:

Of all the 44 pregnant women enrolled to this study, one had zero Bishop's score, 11 had Bishop's score equal to 2 and the Bishop's score for 25 and 7 women were 3 and 4 respectively. 29 pregnancies were terminated through normal vaginal delivery and 15 cesarean sections (CS) were performed. The reason for CS deliveries was fatal bradicardia in five cases, meconium staining in three cases and delayed labor in seven cases.

Mean gestational age was 39(SD:1.44) weeks in extra-amniotic Foley catheter group and 39.3(SD:1.6) weeks in vaginal prostaglandin-E2 group. The observed difference was not statistically significant. The mean time interval between induction and vaginal delivery was 12.8 hours for extra-amniotic Foley catheter and 12 hours for vaginal prostaglandin-E2 group without statistical significance. Mean time to effective uterine contractions was 8.22(2.6) hours in extra-amniotic Foley catheter group versus 9(4) hours in vaginal prostaglandin-E2 group without statistically significant difference. Mean Bishop's score six hours after induction was 6.22(1.8) in extra-amniotic Foley catheter group versus 4.6(2.5) in vaginal prostaglandin-E2 group and the difference was statistically significant($P < 0.05$). Mean time from induction to a Bishop's score above 7 was 8.3 hours in extra-amniotic Foley catheter group versus 9.5 in vaginal prostaglandin-E2 group. Mean oxytocin dose to continue delivery induction was 6055 units in extra-amniotic Foley catheter group compared to 7400 units in vaginal prostaglandin-E2 group without statistical significance. Mean neonatal APGAR score was 8.95 in extra-amniotic Foley catheter group versus 8.86 in vaginal prostaglandin-E2 group without statistical significance. The women in extra-amniotic Foley catheter group were 1.6 times more likely to have vaginal delivery compared to those in vaginal prostaglandin-E2 group(Risk ratio=1.64, 95% CI: 1.03-2.59). The reasons for cesarean section were as fetal bradycardia, meconium staining, and CPD. The gestational age was positively correlated with time to Bishop's score above 7 and mean time to effective uterine contractions. It was reversely correlated with oxytocin dose.

Discussion

Cervical ripening induced by E-prostaglandinsis associated with enzymatic collagen degradation and increased water content in the cervical extracellular matrix. Therefore regardless of their efficacy on labor induction through ripening the cervix, PGs also stimulate the myometrium resulting in uterine contractions that may possibly lead to hyper-stimulation(Husslein 1991;Sherman, Frenkel, Pansky, Caspi, Bukovsky, & Langer 2001). This is while mechanical methods if equally effective on cervical ripening through dilating and stretching the lower uterine segment and cervix and usually are not associated with uterine contractions. So if consistent evidence on their accumulates on their efficacy may be a reasonable alternative to prostaglandins or as an adjunct to them for possible higher efficacy.

In our study the women in extra-amniotic Foley catheter group were 1.6 times more likely to have vaginal delivery compared to those in vaginal prostaglandin-E2 group. A previous Iranian study comparing extra-amniotic Foley catheter with vaginal prostaglandin-E2 had similarly found the vaginal

delivery to be more common in extra-amniotic Foley catheter but with borderline statistical significance(Moini et al. 2003). Controversially one study had found higher rates of caesarean section following extra-amniotic Foley catheter than with PGE2 (29% and 10%, respectively)(Lyndrup et al. 1994). But generally the main body of literature has not been conclusive to support a difference in efficacy of the extra-amniotic Foley catheter versus locally applied prostaglandins on vaginal delivery rates(Adeniji et al. 2005;Afolabi, Oyeneyin, & Ogedengbe 2005;Al-Taani 2004;Gelisen, Caliskan, Dilbaz, Ozdas, Dilbaz, Ozdas, & Haberal 2005;Owolabi, Kuti, & Ogunlola 2005;Sciscione, Nguyen, Manley, Pollock, Maas, & Colmorgen 2001). In present study mean Bishop's score six hours after induction was higher in extra-amniotic Foley catheter group versus vaginal prostaglandin-E2 group and the difference was statistically significant. This is supportive of internal consistency on our previous finding on higher vaginal delivery rate in extra-amniotic Foley catheter group. Owolabi et al. Found significant change in the Bishop's score in both groups but without inter group differences(Owolabi, Kuti, & Ogunlola 2005).

Niromanesh et al. Found the Bishop's scores mean after ripening to be 6.6 and 6.7 for the Foley catheter and prostaglandin groups, respectively but without statistical significance(Niromanesh, Mosavi-Jarrahi, & Samkhaniani 2003). Sciscione et al. Also didn't find statistically significant differences between groups in change in Bishop score(Sciscione, Nguyen, Manley, Pollock, Maas, & Colmorgen 2001). Some studies have also tried to assess combined prostaglandin and extra-amniotic Foley catheter not finding them combined treatment to have higher efficacy either(Chung, Huang, Rumney, Garite, & Nageotte 2003). In a study by there were fewer cesarean deliveries among women with balloon and PGE2 ripening compared with balloon and saline, and a 50% reduction in cesareans for halted progression in the PGE2 group, but those differences did not reach statistical significance(Sherman, Frenkel, Pansky, Caspi, Bukovsky, & Langer 2001).

In our study, vaginal prostaglandin-E2 and extra-amniotic Foley catheter appeared to be comparable for labor induction. Considering the fact that extra-amniotic Foley catheter has advantages such as simplicity, low cost, reversibility, and lack of systemic or serious side effects, it may be preferred by clinicians.

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