Induction of labour : Foley catheter revisited

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FOLEY CATHETER OR PGE2 INSERTS FOR INDUCTION OF LABOUR AT TERM: AN OPEN-LABEL RANDOMISED CONTROLLED TRIAL (PROBAAT-P TRIAL) AND SYSTEMATIC REVIEW OF LITERATURE

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ABSTRACT

Objective: To assess safety and effectiveness of transcervical Foley catheter compared to vaginal prostaglandin E2 inserts for term induction of labour.

Study Design: We conducted an open label randomised controlled trial in five hospitals in the Netherlands. Women with a singleton term pregnancy in cephalic presentation, intact membranes, unfavourable cervix, and no prior caesarean section were enrolled.

Participants were randomly allocated by a web-based randomisation system to induction of labour with a 30cc Foley catheter or 10 mg slow-release vaginal prostaglandin E2 inserts in a 1:1 ratio. Due to the nature of the intervention this study was not blinded. The primary outcome was caesarean section rate. Secondary outcomes were maternal and neonatal morbidity and time from intervention to birth. Additionally, we did a systematic review and meta-analysis of similar studies.

Results: We analysed 226 women, 107 received a Foley catheter and 119 inserts. Caesarean section rates were comparable (20% versus 22%, RR 0.90, 95% CI 0.54 to 1.50). Secondary outcomes showed no differences. We observed no serious maternal or neonatal morbidity.

Meta-analysis showed comparable caesarean section rates, but significantly fewer cases of hyperstimulation during the ripening phase when a Foley catheter was used.

Conclusions: We found, in this relatively small study, no differences in effectiveness and safety of induction of labour with a Foley catheter and 10 mg slow release vaginal prostaglandin E2 inserts. Meta-analysis confirmed a comparable caesarean section rate, and showed fewer cases of hyperstimulation when a Foley catheter was used.

INTRODUCTION

Induction of labour is a common obstetric intervention. The percentage of induced labour ranges from 20 to 30% of all deliveries, but varies globally.[1-3] A substantial proportion of women in whom labour is induced has an unfavourable cervix at the start of induction. In these women, the risk of caesarean section is increased, and therefore cervical ripening is required.[4] The optimal method for ripening the cervix is still uncertain. A variety of methods, including mechanical and pharmacological, is available for cervical ripening. Prostaglandin E2 preparations (Prostin®, Cervidil®, Propess®), are method of choice in many countries.[5-9]

We recently reported that in women with an unfavourable cervix at term, induction of labour with a Foley catheter is as effective as induction of labour with vaginal prostaglandin E2 gel, with fewer side-effects.[10] When comparing mechanical methods with prostaglandin preparations, it is important to take into account the type of prostaglandin, dose and route of administration.[11] Little is known about the direct comparison of slow-release vaginal prostaglandin E2 inserts and Foley catheters.[12] Previous research mainly focused on the comparison of prostaglandin E2 inserts with other prostaglandin preparations, showing comparable effectiveness in terms of caesarean deliveries and comparable side-effects.[13,14] We hypothesise that prostaglandin E2 inserts may be safer than the prostaglandin E2 gel, as they can be removed in case of uterine hyperstimulation. In view of this, a direct comparison between induction of labour with prostaglandin E2 inserts and Foley catheters is needed. Therefore, in a similar study design as the PROBAAT study comparing Foley-catheter to Prostaglandins E2 gel,[10] we evaluated the effectiveness and safety of induction with Foley-catheter compared to 10 mg slow-release vaginal prostaglandin E2 inserts. Additionally, to gather as much information as possible on this comparison, we undertook a systematic review en meta-analysis.

MATERIALS AND METHODS

The present study was an open-label randomised controlled trial, performed according to the protocol of our recently published PROBAAT trial.[10] The protocol was designed to evaluate Foley catheters versus prostaglandins, predominantly prostaglandin E2 gel. The hospitals could use the prostaglandin they were used to, in order to improve participation and recruitment rates, facilitate logistics and given the restricted financial budget. As vaginal prostaglandin E2 gel was the most frequently used method for induction of labour in women with an unfavourable cervix in the Netherlands, the goal of the main study (PROBAAT study) was to investigate the effectiveness and safety of Foley catheter versus prostaglandin E2 gel. We performed the current study comparing 10mg slow release vaginal prostaglandin E2 inserts (PROBAAT-P) parallel to the main PROBAAT study, and according to a parallel protocol, together with a study comparing Foley catheter to vaginal misoprostol (PROBAAT M). The results of the latter study will be published

elsewhere. At the time of the study, slow release prostaglandin E2 inserts were only used in five hospitals in the Netherlands.

The protocol was approved by the Ethics committee of the Academic Medical Centre Amsterdam (MEC 08/310), and the institutional review boards of participating hospitals. The trial was registered with the Netherlands Trial Register (NTR 1646).

Participants

Women over 18 years of age with a term pregnancy, requiring induction of labour at term with an unfavourable cervix (Bishop score <6) were eligible for the study. Prior caesarean delivery, non-vertex presentation of the fetus, ruptured membranes, a hypersensitivity for one of the products used for induction, or a lethal congenital anomaly of the fetus were exclusion criteria.

Outcomes

The main outcome was mode of delivery. Secondary outcomes included maternal and neonatal morbidity and time from the start of induction to birth.[10]

Sample Size

As described above, this study was performed parallel to the PROBAAT study, within the same timeframe. We randomised for the comparison Foley catheter versus 10 mg slow-release PGE2 inserts until our power in the main study was reached. We did not calculate a separate sample size for the current study. As only a few hospitals used prostaglandin inserts or misoprostol, we estimated that during the time the 812 women were randomised to the pgE2 gel study, we would have approximately 250 women in the prostaglandin insert study, and 150 in the misoprostol study, yielding a total of approximately 1200 participants.

Randomization and blinding

We used a central randomisation list, stratified for centre and parity. Each of the hospitals used only one prostaglandin for the trial: either prostaglandin E2 gel, prostaglandin E2 inserts or misoprostol. They could use the prostaglandin they regularly use, some centres already used Foley catheters, others started using them for this trial. All patients randomised in centres using prostaglandin E2 gel were included in the prostaglandin E2 gel trial (PROBAAT trial), all patients randomised in centres using prostaglandin E2 insert in the current prostaglandin E2 insert trial (PROBAAT-P trial), and all centres using misoprostol in the misoprostol trial (PROBAAT-M trial). Within these centres there was a 1:1 randomisation between Foley catheter and prostaglandin.

Women were informed about the study by their obstetrician, when planned for induction of labour. After informed consent, women were enrolled by the attending physician, midwife or research nurse at the labour ward on the day of induction. Randomization occurred through a computerised program, especially designed for randomised controlled trials. The randomization sequence was computer generated,

and was composed out of variable blocks of 2 and 4. The sequence could not be viewed by the recruiter, nor the trial-coordinator when the trial was ongoing.

Due to the nature of the intervention, neither the caregiver, nor the patient were blinded.

Intervention

The intervention is described in detail in the recently published PROBAAT trial.[10] In summary: In the Foley catheter group a 30 cc catheter was introduced transcervically. The protocol advised to examine women at the same 12-hour intervals as women in the prostaglandin E2 insert group. Women in the prostaglandin E2 insert group were treated with a 10 mg slow release (0.3 mg/hour) vaginal insert, which was placed in the posterior vaginal fornix. The insert was left in place for 12 hours, or until active labour started. If after 12 hours active labour had not commenced, and the Bishop score was <6 women were examined the next morning. If needed, a second insert was placed.

In both groups, if upon examination the cervix was found to be favourable (Bishop score ≥6), amniotomy was performed and oxytocin augmentation was started when contractions or progress were deemed inadequate. Continuous fetal monitoring by CTG was started after amniotomy.

Induction was generally started in the morning. If after two days cervical ripening the cervix was unfavourable for amniotomy, a day of rest was advised, followed by two days of ripening with the same method. If after these four days of ripening the cervix was still unfavourable, further management was decided on by the patient's obstetrician.

Statistical Methods

Data were analysed according to the intention-to-treat principle, and the statistical methods are described in detail in the PROBAAT trial.[10] Normally distributed data are presented as means with standard deviation; skewed distributions are presented as medians with interquartile ranges (IQR). For categorical data the treatment effect is presented as relative risks (RR) with 95% confidence intervals. For time to delivery data Kaplan-Meier survival curves were constructed and Log-rank tests and according p-values calculated. Calculation of the percentages was based on the number of valid observations. Calculations were done in SPSS 18.0).[15]

Meta-analysis

We searched the Cochrane Collaboration's Trial Registry from January 1st 1966 to January 15th 2013. Additionally we searched Medline and EMBASE from January 2012 till January 2013, because the Cochrane collaboration's trial registry is updated 4 times a year (search date January 15th 2013). The following search terms were used:

'(Balloon Dilation OR mechanical methods OR mechanical method OR mechanical dilation OR mechanical dilatation OR mechanical dilations

OR mechanical dilatations OR balloon OR foley* OR Catheterization OR Catheterisation OR catheter OR catheters OR catheter*) AND (propess OR cervidil OR dinoprostone OR prostaglandins OR prostaglandin E2 OR "prostaglandin E(2)" OR prostaglandin E2alpha OR prostaglandin E2ethanolamide OR "PGE(2)" OR PGE2 OR PGE2alpha OR PGE2ethanolamide OR prostamide E2)'

Randomised controlled trials comparing Foley catheter to 10 mg slow-release vaginal prostaglandin E2 inserts in third trimester cervical ripening with a viable fetus in cephalic presentation and intact membranes were eligible. As we believe that different forms of application (e.g. tablets, gel, inserts) and dosages have different effects and side-effects, all other forms and dosages of prostaglandin E2 were not included in the current meta-analysis. We did not apply any language restrictions, nor did we exclude studies that only appeared as an abstract. Studies were excluded if they did not report any of the predefined outcome measures. We attempted to contact the authors of studies that were only reported as abstract or did not report the predefined outcome measures. Two reviewers (MJ, ME) assessed all studies identified by the search independently, in case of disagreement, a third assessor was consulted (KB).

Methodological quality of the studies was assessed using the Cochrane collaboration's tool for assessment of studies.[16] Studies were not excluded based on their methodological quality, but a sensitivity analysis based on study quality was planned, excluding poor quality studies.

Treatment outcomes that were sought were all the outcomes that are also reported in the current trial. Caesarean section rate was the primary outcome. As we sought dichotomous data only, the data are presented as a summary risk ration (RR), with 95% confidence interval (95%CI). Heterogeneity was assessed using the T^2, I^2, and Chi^2 statistics. If I^2 >30% and either T^2 >0, or the P value <0.10 in the Chi^2 test for heterogeneity, we regarded heterogeneity as substantial. We used a fixed-effect model for combining data where it was reasonable to assume that studies were estimating the same underlying treatment effect. When statistical heterogeneity was substantial, we used a random-effects model for pooling. All statistic analyses were carried out in Review manager software.[17]

RESULTS

Trial Results

Between February 2009 and May 2010, 226 women were included in the trial, of which 107 were allocated to induction of labour with a transcervical Foley catheter and 119 to prostaglandin E2 insert. Two woman allocated to Foley catheter and four women in the Prostaglandin insert group did not receive any intervention, as they had a BS >6 at induction, in five cases Foley catheter insertion was unsuccessful. In nine women in the Foley catheter group and six women in the prostaglandin insert group the study protocol was discontinued for a variety of reasons (Figure1). All women were analysed according to intention to treat. There

were no missing values for the primary outcome. Umbilical cord pH was missing in 34% (76/226) of cases, and the number of missing values was evenly distributed in both groups. All other secondary outcomes had less than 1% missing.

Baseline characteristics were comparable between the groups (Table 1.) and representative for the population of Dutch women with induced labour.[18] One

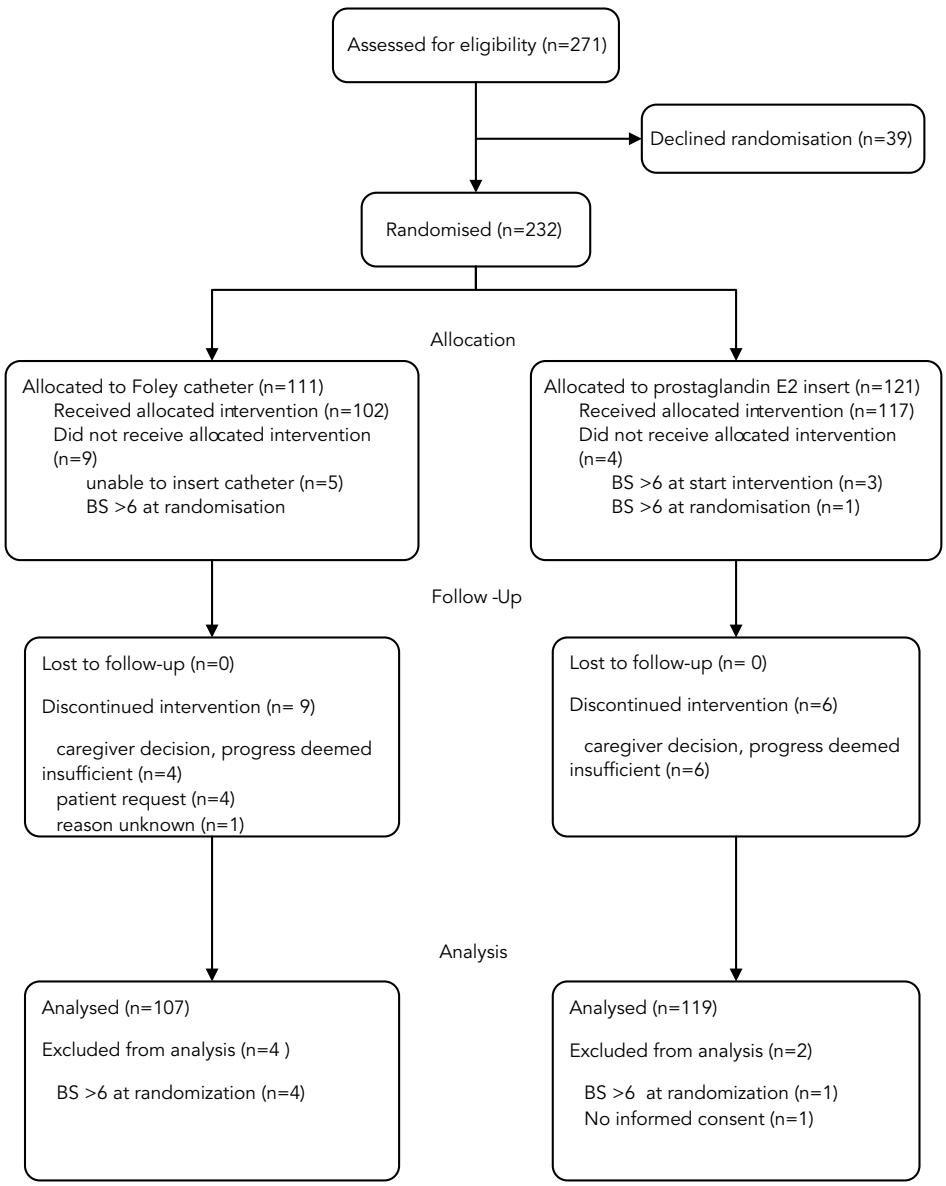

Figure 1. Patient flow diagram

woman in the Foley catheter group and three women in the prostaglandin insert group had a failed induction. Caesarean section rates were did not differ between the groups: 20% [n=21/107] versus 22% [n=26/119] in the Foley and prostaglandin insert group, respectively (RR 0.90, 95% CI 0.54-1.50).

A similar effect was shown after adjustment for stratified randomization (RR 0.85, 95% CI 0.52 -1.40). A comparable number of caesarean sections was performed for failure to progress during the first stage of labour (Table 2). The number of caesarean deliveries due to fetal distress did not differ between the groups (Table 2). The median time from start of the intervention to birth was 28 hours (IQR 18-41) in the Foley catheter group and 27 hours (IQR 16-48) in the Prostaglandin insert group (Table 2). Labour was augmented with oxytocin significantly more often when a Foley catheter was used (78% [n=83/107] vs. 66% [n=78/119]; RR 1.18, 95% CI 1.00-1.40) (Table 2).

We did not record any cases of serious maternal or neonatal adverse events (Table 3). Hyperstimulation was not statistically different between the groups (2% [n=2/107] vs. 2% [n=2/119]; RR 1.11, 95% CI 0.16-7.76). Hyperstimulation

Table 1. Baseline Characteristics

Maternal age (years)[a]	30.5 (4.0)	31.7 (5.2)
Ethnic origin		
Caucasian	83 (78%)	94 (79%)
Non-Caucasian	12 (11%)	7 (6%)
Unknown	12 (11%)	18 (15%)
BMI[b, c]	25.4 (22.2-28.3)	24.4 (21.6-27.5)
Parity		
0	77 (72%)	83 (70%)
1	19 (18%)	28 (24%)
≥2	11 (10%)	8 (7%)
Bishop score		
0	18 (17%)	19 (16%)
1	33 (31%)	28 (24%)
2	27 (25%)	40 (34%)
3	17 (16%)	19 (16%)
4	9 (8%)	8 (7%)
5	3 (3%)	5 (4%)
Gestational age (weeks)	39.1 (38.1-40.7)	39.8 (38.4-41.2)
Indications for induction of labour[d]		
Hypertensive disorders	51 (48%)	34 (29%)
Post term pregnancy	20 (19%)	28 (24%)
IUGR	8 (8%)	7 (6%)
Psychosocial = elective	17 (16%)	27 (23%)
Insulin dependent diabetes	7 (7%)	7 (6%)
Oligohydramnios	7 (7%)	11 (9%)
Other	12 (11%)	17 (14%)

[a]mean+ SD, [b]median+ IQR, [c]14% missing values, [d]more than one indication possible

Table 2. Mode of delivery

	Foley catheter (N=107)	PGE2 insert (N=119)	RR (95% CI)	p-value
Mode of delivery				
Spontaneous	73 (68%)	73 (61%)	1.11 (0.92-1.35)	0.28
Vaginal instrumental	13 (12%)	20 (17%)	0.72 (0.38-1.38)	0.32
Caesarean section	21 (20%)	26 (22%)	0.90 (0.54-1.50)	0.68
Indication for caesarean section				
Failure to progress in 1st stage	9 (8%)	9 (8%)	1.11 (0.46-2.70)	0.81
Failure to progress in 2nd stage	1 (1%)	4 (3%)	0.28 (0.03-2.45)	0.22
Fetal distress	11 (10%)	12 (10%)	1.01 (0.47-2.21)	0.96
Other	0 (0%)	1 (1%)	NA	1.00[b]
Indication for vaginal instrumental delivery				
Failure to progress in 2nd stage	6 (6%)	9 (8%)	0.74 (0.27-2.01)	0.56
Fetal distress	7 (7%)	10 (8%)	0.78 (0.31-1.97)	0.60
Maternal complication	0	1 (1%)	NA	1.00[b]
Operative deliveries for fetal distress	17 (16%)	22 (19%)	0.86 (0.48-1.53)	0.61
Oxytocin augmentation	83 (78%)	78 (66%)	1.18 (1.00-1.40)	0.046
Time from start intervention to birth (hours)[a]	28 (18-41)	27 (16-48)	NA	0.61

[a]median+ IQR, excluding caesarean section, [b]Fisher's exact test

during ripening only occurred in the prostaglandin group, whereas both cases of hyperstimulation in the Foley catheter group occurred during oxytocin stimulation. Post partum haemorrhage and post partum blood transfusions were not different between the groups, nor were other secondary maternal outcomes (Table 3).

The number of NICU admissions did not differ statistically (4% [n=4/107] vs. 7% [n=8/119]; RR 0.56, 95% CI 0.17-1.79). Among the indications for neonatal admission suspected infection was most frequently noted (Table 3). There was a tendency towards fewer admissions due to suspected asphyxia in the Foley catheter group, although there were no differences in umbilical cord pH (Table 3).

The effect of the induction method on caesarean section rate did not differ statistically between nulliparous and multiparous women (nullipara Foley 24% [n=19/78] vs. prostaglandin E2 30% [n=25/83], multipara Foley 7% [2/29] vs. prostaglandin E2 3% [1/36], p for interaction 0.57).

Meta-analysis results

147 Records were identified in the Cochrane Collaboration's Trial Registry, 16 in PubMed, and 41 in Embase. After removal of duplicates 195 Records remained. 113 records were excluded on basis of title. and another 68 of the remaining 82 were excluded on basis of abstracts . After assessment of the remaining 15 Full text articles, 13 more records were excluded. Reasons for exclusion are presented in Figure 2. Two records remained, one of which used double balloon catheter in

Table 3. Maternal and Neonatal Outcomes

	Foley catheter (N=107)	PGE 2 insert (N=119)	RR (95% CI)	p-value
Analgesics				
Pethidine	15 (17%)	19 (20%)	0.85 (0.46-1.57)	0.61
Epidural	30 (35%)	29 (31%)	1.12 (0.74-1.70)	0.60
Other	0 (0%)	2 (2%)	NA	0.50[b]
Maternal intrapartum infection				
Temp. ≥38 °C during labour	5 (5%)	8 (7%)	0.70 (0.24-2.06)	0.51
Suspected intrapartum infection[a]	3 (3%)	6 (5%)	0.56 (0.14-2.17)	0.51[b]
Post partum haemorrhage (>1000 cc)	8 (8%)	7 (6%)	1.27 (0.48-3.39)	0.63
Post partum blood transfusion (Y/N)	4 (4%)	2 (2%)	2.22 (0.42-11.90)	0.43[b]
Maternal post partum infection	0 (0%)	1 (1%)	NA	1.00[b]
Other maternal complication				
Hyperstimulation	2 (2%)	2 (2%)	1.11 (0.16-7.76)	1.00[b]
Uterine rupture	0 (0%)	0 (0%)	NA	NA
Apgar Score <7				
1 min	8 (8%)	17 (14%)	0.52 (0.24-1.16)	0.10
5 min	4 (4%)	6 (5%)	0.74 (0.22-2.56)	0.7[b]
pH <7.10[c]	6 (8%)	8 (10%)	0.79 (0.29-2.17)	0.65
Neonatal admission				
Ward	19 (18%)	23 (19%)	0.92 (0.53-1.59)	0.76
Intensive care	4 (4%)	8 (7%)	0.56 (0.17-1.79)	0.32
Reason admission				
Suspected infection	5 (5%)	10 (8%)	0.56 (0.20-1.58)	0.26
Asphyxia	1 (1%)	4 (3%)	0.29 (0.03-2.45)	0.37
Dysmaturity	3 (3%)	3 (3%)	1.11 (0.23-5.39)	1.0[b]
Hypoglycaemia	8 (8%)	6 (5%)	1.48 (0.53-4.14)	0.45
IRDS	0 (0%)	0 (0%)	NA	NA
Meconium aspiration	1 (1%)	0 (0%)	NA	0.47[b]
Other/Unknown	10 (9%)	13 (11%)	0.86 (0.39-1.87)	0.70
Length of admission (days) median(IQR)	2 (0-3)	1 (0-3)	NA	0.71

[a]body temperature during labour ≥38 °C AND start of broad spectrum antibiotics due to suspected infection, [b]Fisher exact test, [c]34% missing values

the catheter group.[12,19] Together with our current trial, three trials were included in meta-analysis. All three trials were of good methodological quality. (Table 4)

Caesarean section rates did not differ between the groups, nor did vaginal instrumental deliveries. Oxytocin was significantly more often used when a Foley catheter was employed; however, hyperstimulation during the ripening phase occurred significantly less often. Epidural analgesia was used more often in the Foley catheter group. No difference was found in other maternal and neonatal outcomes (Table 5).

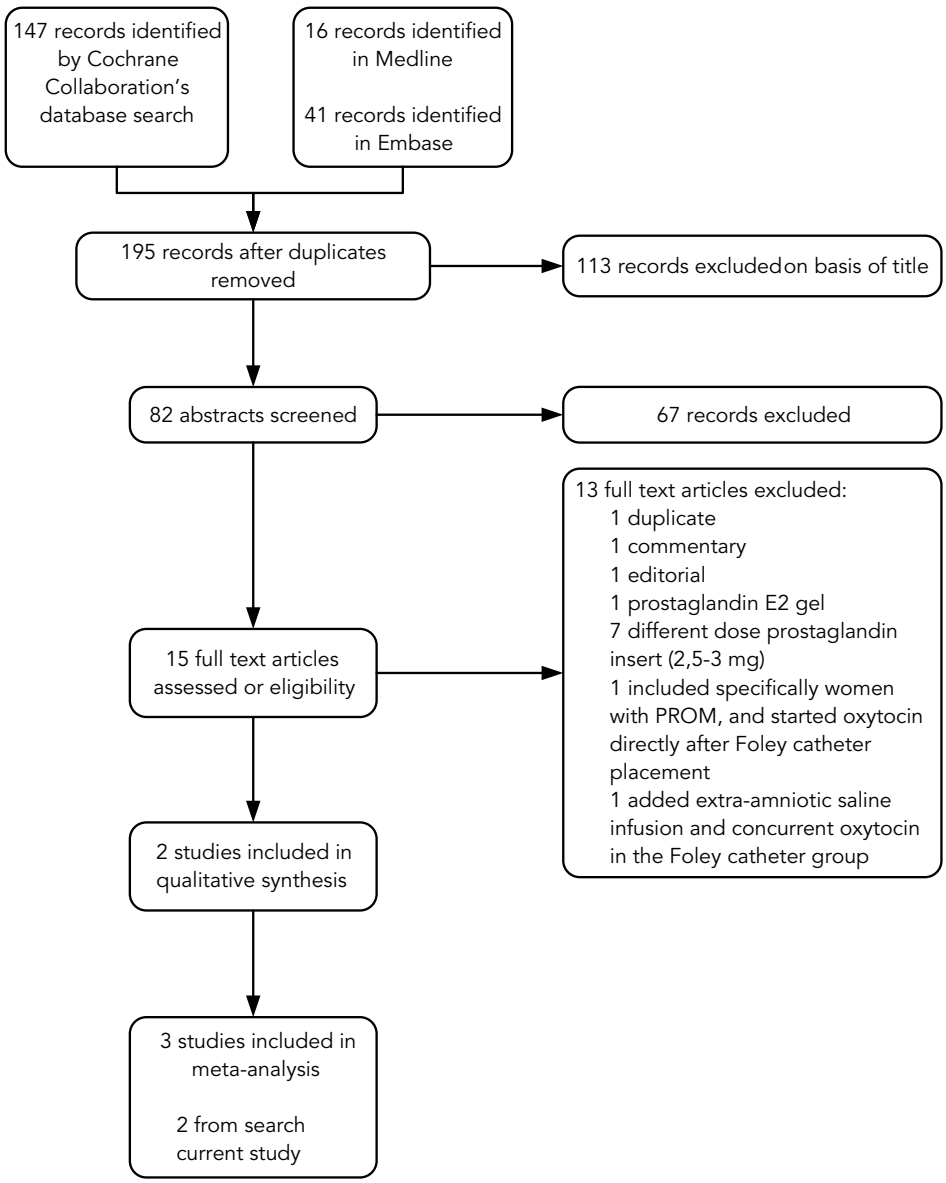

Figure 2. Flow diagram systematic review

COMMENTS

In this relatively small randomised controlled trial, we compared the effectiveness and safety of induction of labour with Foley catheter with prostaglandin E2 insert induction in term women with an unfavourable cervix. The Caesarean section rate

Table 4. Characteristics of included studies

Study	Participants	Interventions	Primary Outcome	Risk of bias
Cromi 2011	GA[a] ≥ 34 weeks BS[b] <7 Intact membranes Cephalic presentation	Foley catheter 50 cc[d] for 12 hours n=132 Foley catheter 50 cc[d] for 24 hours n=133 10 mg[c] pge2 insert, up to 24 hours n=132	Vaginal delivery within 24 hours	Low Sequence generation: adequate Allocation concealment: adequate ITT[e]: Yes Reporting bias: no
Cromi 2012	GA[a] ≥ 34 weeks BS[b] <7 membranes Cephalic presentation	Double balloon device 2x 50 cc[d] n=105 10 mg[c] pge2 insert, up to 24 hours n=103	Vaginal delivery within 24 hours	Low Sequence generation: adequate Allocation concealment: adequate ITT[e]: Yes Reporting bias: no
Jozwiak	GA[a] ≥ 37 weeks BS[b]<6 membranes Cephalic presentation	Foley catheter 30 cc[d] n=107 10 mg[c] pge2 insert, up to 24 hours n=119	Caesarean section rate	Low Sequence generation: adequate Allocation concealment: adequate ITT[e]: Yes Reporting bias: no

[a]GA= Gestational age, [b]BS = Bishop Score, [c]mg = milligram, [d]cc=milliliter, [e]ITT=intention-to-treat

was comparable, as was the rate of vaginal instrumental deliveries. Maternal and neonatal secondary outcomes including post partum haemorrhage and pH <7.10 did not differ significantly between the groups, nor did the time from start of the intervention to birth. Although we did not find any differences in primary and secondary outcomes these results should be interpreted cautiously, due to the small numbers. Our results, however, were a valuable contribution to meta-analysis.

In meta-analysis we found comparable caesarean section rates, significantly more oxytocin use and use of epidural analgesia, and a significant reduction in hyperstimulation during the ripening phase when a Foley catheter was used, as compared to 10 mg vaginal prostaglandin E2 inserts.

At the start of this trial there were no published randomised controlled trials on the direct comparison of Foley catheter with 10 mg slow-release vaginal inserts known to us. When performing systematic review of literature, we found one other randomised controlled trial comparing 10 mg prostaglandin inserts with Foley catheter,[12] and one comparing double balloon catheter to 10 mg prostaglandin inserts.[19] We decided to also include this second trial in our meta-analysis, as it has previously been shown, that there are no significant differences in effectiveness or side effects of ripening with double balloon catheter when compared to Foley catheter.[20,21]

In the first trial,[12] Cromi and colleagues investigated the efficacy of 12 hours of ripening with a Foley catheter compared to 24 hours of ripening with a Foley catheter, and ripening with vaginal prostaglandin E2 inserts. The intervention in

Table 5. Meta-analysis results

Outcome	Studies	Total participants	Foley catheter events/total	PGE2 insert events/total	Statistical Method	Effect Estimate RR (95% CI)
Caesarean section	3	699	86/345	93/354	M-H[a], Fixed effect	0.94 [0.73, 1.21]
Hyperstimulation with FHR[b] changes	3	699	0/345	14/354	M-H[a], Fixed effect	0.10 [0.02, 0.52]
Vaginal delivery not achieved within 24 hours	2	473	138/238	120/235	M-H[a], Random effect	0.99 [0.40, 2.45]
Oxytocin augmentation	3	699	281/345	205/354	M-H[a], Random effect	1.41 [1.17, 1.68]
Epidural analgesia	3	699	226/345	163/354	M-H[a], Fixed effect	1.39 [1.23, 1.58]
Vaginal instrumental delivery	3	699	24/345	28/354	M-H[a], Fixed effect	0.91 [0.54, 1.53]
Apgar score <7 at 5 minutes	3	699	5/345	8/354	M-H[a], Fixed effect	0.71 [0.26, 1.97]
pH <7.00	3	699	2/345	3/354	M-H[a], Fixed effect	0.68 [0.12, 4.07]
NICU[c] admission	3	699	17/345	20/354	M-H[a], Fixed effect	0.87 [0.46, 1.64]
Post partum haemorrhage	3	434	16/212	14/222	M-H[a], Fixed effect	1.19 [0.60, 2.38]

[a]Mantel-Haenszel, [b]Fetal heart rate, [c]Neonatal Intensive Care Unit

this trial differs from our trial, as the maximum ripening time was respectively 12 and 24 hours in all groups, compared to a maximum ripening time of twice 48 hours in the current trial. The primary outcome was also different, as Cromi et al investigated vaginal delivery rate within 24 hours, and we investigated the total caesarean section rate. When analysing the results in meta-analysis, we chose to compare the 24-h Foley catheter and insert group with our results. Cromi et al. reported that both methods have comparable efficacy in terms of vaginal delivery rates, as was shown in our trial. They, however, showed that the rate of caesarean delivery for abnormal fetal heart rate tracing was significantly higher in the vaginal insert group than their 12 h Foley catheter group, this was not different in the 24 h Foley group, and was comparable in our study. They also found that uterine hyperstimulation syndrome occurred significantly more often in the Prostaglandin E2 insert group (6% vs. no cases in the Foley catheter group). In the trial by Cromy et al, comparing double balloon catheter to prostaglandin inserts,[19] caesarean section rates were comparable, but more women delivered vaginally within 24 hours when a double balloon device was used. There was an increase in use of epidural analgesia, and a decrease in hyperstimulation with the double balloon device, with no cases of hyperstimulation during the ripening phase in the balloon catheter group. In our trial we found that two cases of hyperstimulation syndrome occurred during ripening with Prostaglandin E2 inserts and two cases in after oxytocin stimulation in the Foley catheter group. Furthermore, oxytocin was needed more often when a Foley catheter was used in both Cromi trials,[12,19] which is confirmed by our trial. This indicates that the Foley catheter promotes cervical changes without causing contractions, which suggests a decreased need for fetal monitoring during ripening, and a possible reduction of the risk of uterine hyperstimulation. Consequently, although women with caesarean section were excluded from all trials, a Foley catheter could be a good alternative for women with a previous caesarean birth requiring labour induction.[22]

Surprisingly, epidural analgesia was found to be used significantly more often in the balloon group in meta-analysis. This was not seen in our trial. This difference could partly be explained by the fact that women experience more pain when a double balloon catheter is used, when compared to Foley catheter.[20] Furthermore, the use of epidural analgesia overall was much higher in the Cromi trials (respectively 68% and 69% versus 26% in our trial). We do not know how the decision to apply epidural analgesia is made in other countries, and therefore difference in obstetric management could be the cause of the difference in the use of epidural analgesia we found.

Both trials by Cromi and colleagues, used vaginal delivery within 24 hours as a primary outcome. The primary goal of induction is a safe, uncomplicated vaginal delivery, which is likely to be preferred by women over a race against the clock. Therefore, in our opinion, delivery within 24 hours is a less appropriate primary outcome. Caesarean section rate and maternal and neonatal morbidity are more

important. Pooling of our current results with the above mentioned trials resulted in comparable caesarean section rates, and a reduction in hyperstimulation during the ripening phase. A pH <7.00 was reported in few cases, and was not different between the groups when pooled. Post partum haemorrhage was also not different (table 5).

We did not investigate patient satisfaction, which is a drawback of this study. There are no other studies on this comparison investigating women's satisfaction with the methods known to us. Therefore, we can only presume that the absence of contractions during ripening with a Foley catheter with equal efficacy and fewer side effects as prostaglandin inserts, is preferred by pregnant women and their physicians. Further advantages of Foley catheters are the wide availability, easy storage and low cost, when compared to prostaglandin E2 preparations.

Blinding was not conceivable due to the nature of the intervention. The knowledge of the method of cervical ripening may have influenced caregivers in their decision making. We do not know in which way this could have influenced the decision. Especially since the clinical decision of performing a caesarean section is a complex one with many factors involved. We believe that the non-blinded nature of the trial did not cause significant bias.

From the recent trials comparing mechanical methods for induction of labour with prostaglandins[10,20,23] we can learn that the different type, dosages, and administration routes of prostaglandins act differently, and as a result direct comparisons in large randomised trials are needed.

Nowadays vaginal prostaglandins are the most widely used agents in induction of labour in women with an unfavourable cervix in the USA and UK. The optimal method for induction of labour in these women is still uncertain, as prostaglandin analogues were introduced in the 1980s, without appropriately powered RCTs to prove efficacy and safety. Our trial and meta-analysis show that induction of labour with a Foley catheter leads to comparable caesarean section rates as vaginal prostaglandin E2 inserts, with less hyperstimulation during the ripening phase.

Future research, in adequately powered trials, should focus on the comparison of Foley catheters with other Prostaglandin preparations, such as Misoprostol, and the use of Foley catheters in women with a previous caesarean birth.

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