The Renaissance of Transcervical Balloon Catheters for Cervical Ripening and Labour Induction

Renaissance des transzervikalen Ballonkatheters zur Zervixreifung und Geburtseinleitung

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Key words

- labour induction
- balloon catheter
- prostaglandins
- effectiveness
- safety

Schlüsselwörter

- Geburtseinleitung
- Ballonkatheter
- Prostaglandine
- Effektivität
- Sicherheit

Abstract

Due to rising rates of labour induction in industrialised countries, safe and effective methods of induction have once again become a focus of interest and research. Prostaglandins are effective for cervical ripening and induction of uterine contractions. They do, however, cause overstimulation of the uterus in up to 20% of cases, sometimes causing changes in fetal heart rate. Transcervical balloon catheters provide an alternative to prostaglandins for labour induction and have been used for this purpose for almost 50 years. This induction method has experienced a recent renaissance in clinical practice that is reflected in an annually rising number of publications on its use. Balloon catheters allow gentle ripening of the cervix without causing uterine overstimulation. The two catheters available are the Foley catheter (off-label use) and the double balloon catheter, which is licensed for use in induction of labour. Both are as effective as prostaglandins, and do not increase the risk of infection to mother or child. Catheter induction also requires less monitoring compared to prostaglandins resulting in improved patient satisfaction. Balloon catheters provide a useful and promising option to achieve vaginal delivery despite failed prostaglandin induction. Intravenous oxytocin is nevertheless required in up to 85% of cases for adequate induction/augmentation of contractions. Balloon catheters, vaginal PGE₂ and misoprostol are equally effective in the context of an unripe/unfavourable cervix, the rate of uterine hyperstimulation being significantly lower, and the need for oxytocin significantly higher for catheters. Balloon catheters are increasingly being used in combination or sequentially with oral/vaginal misoprostol, although there is currently inadequate published data on the subject. International guidelines recommend the use of balloon catheters for labour in-

Zusammenfassung

duction with an unripe cervix (also following previous caesarean section) as an alternative to prostaglandins, particularly when these are not available or are contraindicated.

**Introduction**

In industrialised countries rates of induction of labour have almost doubled in the past 10 years, e.g. the current induction rate in the Netherlands is 33% [1] and in Germany (2013) 22% of which 98% were medical inductions [2].

The advantage of the prostaglandin E₂ analogue misoprostol and prostaglandin E₂ (PGE₂) is their efficiency (e.g. rate of vaginal deliveries in 24 hours) when the cervix is unfavourable (Bishop score BS < 6). This is a result of pharmacological synergism between cervix ripening and myometrium stimulating effects [3], the two effects being clinically indistinguishable from one another.

The main disadvantage of prostaglandins is a variable rate (3–20%) of associated uterine hyperstimulation, which may cause changes in fetal heart rate and thus constitutes a risk factor for fetal hypoxia (e.g. in the context of IUGR with reduced placental reserves) [4].

When the cervix is unfavourable induction of uterine contractions does not accelerate the progress of labour; it worsens fetoplacental perfusion during contractions and patient satisfaction is reduced e.g. through induction of painful contractions. A commentary from the Lancet notes that increasing numbers of clinicians favour the strategy of commencing induction of contractions only once the cervix is ripe [5].

Thus in recent years NO-donors and mechanical induction methods (balloon catheters and cervical dilators such as Lamical or Dilapan-S) have been the focus of interest (see reviews in [6–8]).

NO-donors are currently not recommended in international guidelines due to insufficient literature on their use.

Placement of a transcervical balloon catheter induces cervical ripening without causing significant uterine contractions or systemic side effects in mothers [7,8]. Therefore much less monitoring is required during labour compared to prostaglandin induction.

It has been postulated that mechanical stretching by the catheter balloon causes increased release of endogenous prostaglandins e.g. from myometrium and amniotic cells [9], which in turn cause cervical ripening. A recent prospective study found that cervical ripening was triggered by a local inflammatory reaction; significantly raised levels of interleukin-6 and interleukin-8, metalloproteinase-8, hyaluronic acid synthetase and NO synthetase were found on immunohistochemistry of cervical tissue following balloon insertion [10].

Balloon catheters have been used for labour induction as far back as the 1890s. Embrey and Mollison rediscovered the method in 1967 using it in combination with extramniotic prostaglandins (see review in [11]). Since then numerous studies have been performed worldwide, mostly using the Foley catheter.

Developed by Atad in 1990, the double balloon catheter was expected to provide improved results. It was hoped that the simultaneous application of pressure to the inner and outer cervical openings would cause even more effective cervical ripening compared to the single balloon catheter. The double balloon catheter is now commercially available and licensed for cervical ripening (labour induction) and may be in place for up to 12 hours; prostaglandins, current or planned, and low-lying placenta/placenta praevia are some of the contraindications to its use. Important to note is that according to the manufacturer’s warning, the safety and effectiveness of the double balloon catheter for cervical ripening has not been shown in the context of previous isthmus-transverse caesarean section and its use is therefore contraindicated after previous caesarean section. This problem is the subject of a subsequent, independent publication of the authors and will therefore not be discussed further here.

Expulsion of the double balloon catheter usually occurs at a cervical dilation of about 4 cm.

In recent years there has been a veritable renaissance of balloon catheter use for labour induction with almost two thirds of the literature on the subject from the past 15 years having been published in the last 5 years. Combinations of medical and mechanical methods have been studied in particular. This review article aims to provide an overview of the current evidence on labour induction using balloon catheters.

**Implementation in Clinical Practice**

**Comparison of Foley catheter vs. double balloon catheter**

We identified 4 randomised trials comparing Foley and double balloon catheters for labour induction [12–15]. The results are somewhat contradictory (see Table 1). In 3 studies the Foley catheter was shown to have significant advantages [12,14,15], in two other studies the double balloon catheter was more effective [13,16]. Taking all available data into account, no significant difference between the two catheters has been clearly demonstrated. All studies note the better cost-effectiveness of the Foley catheter; the double balloon catheter has the major advantage of being licensed for labour induction.

**Balloon filling**

The filling volume of the double balloon is up to 80 ml. Various trials have studied the effectiveness of different filling volumes when using the Foley catheter. Three randomised studies compared a filling volume of 30 ml with 60 ml [17] and 80 ml [18,19] (see Table 2). All three studies were included in a recently published systematic review and meta-analysis by Berndt et al. [20]. Although there was no significant difference in caesarean section rate (RR 0.82; 95% CI 0.48–1.41) the likelihood of a favourable cervix (not uniformly defined) was greater with larger filling volumes (RR 1.72; 95% CI 1.46–2.04), and the rate of women not delivered within 24 hours was significantly reduced (RR 0.70; 95% CI 0.54–0.90). Another randomised study examined whether traction to the Foley catheter influences rate of cervical dilatation (filling volume 30 ml, weighted traction using a 1000 ml fluid-filled bag; n = 60). Time to cervical opening was significantly reduced in the weighted traction group (by approx. 3 hours) without an increased rate of pain perception following balloon insertion [21]. In the above mentioned study by Kashanian et al. [19], 500-ml–weighted traction had no additional effect (see Table 2).

**Premature rupture of membranes**

Balloon catheters are not used or are removed when membranes rupture prematurely; alternatively the catheter remains in situ for a maximum of 24 hours.
### Table 1  Randomised controlled trials of Foley catheter vs. double balloon catheter.

<table>
<thead>
<tr>
<th>Lead author</th>
<th>Year</th>
<th>n</th>
<th>Foley catheter (F)</th>
<th>Double balloon catheter (DB)</th>
<th>Significant findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pennell CE</td>
<td>2009</td>
<td>320</td>
<td>Filling vol.: 30 ml in situ time 12 h</td>
<td>80 ml 12 h or PGE2 vaginal gel</td>
<td>Induction to delivery time (h, median) F: 23.2 DB: 24.5 PGE2: 23.8 p = 0.043</td>
</tr>
<tr>
<td>Solt I</td>
<td>2009*</td>
<td>200</td>
<td>n/a</td>
<td>n/a</td>
<td>Perceived as painful (pain score ≥ 4) (%) F: 36 DB: 55 PGE2: 63 p &lt; 0.001</td>
</tr>
<tr>
<td>Salim R</td>
<td>2011</td>
<td>293</td>
<td>Filling vol.: 60 ml in situ time 12 h</td>
<td>80 ml 12 h</td>
<td>Caesarean section rate in nulliparae (%) F: 40 DB: 20 p = 0.02</td>
</tr>
<tr>
<td>Mei-Dan E</td>
<td>2012</td>
<td>188</td>
<td>Filling vol.: 30 ml in situ time 12 h + extraamniotic NaCl 50 ml/h</td>
<td>80 ml 12 h</td>
<td>Balloon removal to delivery time (nulliparae) (h) F: 22.6 DB: 14.6 p = 0.05</td>
</tr>
<tr>
<td>Mei-Dan E</td>
<td>2014</td>
<td>186</td>
<td>Filling vol.: 30 ml in situ time 12 h + extraamniotic NaCl 50 ml/h</td>
<td>80 ml 12 h + extraamniotic NaCl 50 ml/h</td>
<td>Bishop score after balloon removal (nulliparae) F: 3.4 ± 2.0 DB: 4.4 ± 1.9 p = 0.02</td>
</tr>
</tbody>
</table>

* published as abstract only

### Table 2  Randomised controlled trials comparing various filling volumes.

<table>
<thead>
<tr>
<th>Lead author</th>
<th>Year</th>
<th>n</th>
<th>Standard filling volume (SF)</th>
<th>Greater filling volume (GF)</th>
<th>Significant results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levy R</td>
<td>2004</td>
<td>203</td>
<td>30 ml</td>
<td>80 ml</td>
<td>Cervical dilatation ≥ 3 cm to cervical ripening (%) SF: 52.4 GF: 76.0 p &lt; 0.001</td>
</tr>
<tr>
<td>Kashani-M</td>
<td>2009</td>
<td>270</td>
<td>30 ml with traction</td>
<td>80 ml without traction</td>
<td>Vaginal delivery rate in 24 h in nullipara (%) SF: 49.0 GF: 71.4 p &lt; 0.05</td>
</tr>
<tr>
<td>Delaney S</td>
<td>2010</td>
<td>192</td>
<td>30 ml</td>
<td>60 ml</td>
<td>Oxytocin augmentation in nullipara (%) SF: 90.4 GF: 69.3 p &lt; 0.05</td>
</tr>
<tr>
<td>Delaney S</td>
<td>2010</td>
<td>192</td>
<td>30 ml</td>
<td>60 ml</td>
<td>Bishop score ≥ 9 (%) SF: 38.9 GF: 83.3 p &lt; 0.001</td>
</tr>
<tr>
<td>Delaney S</td>
<td>2010</td>
<td>192</td>
<td>30 ml</td>
<td>60 ml</td>
<td>Vaginal deliveries (%) SF: 83.3 GF: 90.0 p &lt; 0.001</td>
</tr>
<tr>
<td>Delaney S</td>
<td>2010</td>
<td>192</td>
<td>30 ml</td>
<td>60 ml</td>
<td>Vaginal delivery rate in 24 h (%) SF: 14.0 GF: 26.0 p &lt; 0.04</td>
</tr>
<tr>
<td>Delaney S</td>
<td>2010</td>
<td>192</td>
<td>30 ml</td>
<td>60 ml</td>
<td>Cervical dilatation at balloon expulsion SF: 3 cm GF: 4 cm p &lt; 0.01</td>
</tr>
</tbody>
</table>
for a maximum of 12 hours during the 1st stage of labour [8]. The Foley catheter (filling volume 30 ml) was compared to vaginal misoprostol (25 µg 4-hourly or 50 µg 6-hourly) in a retrospective observational study of 122 pregnant women with premature rupture of membranes ≥ 36 SSW [22]. The median induction to delivery time was significantly shorter for the Foley catheter group (736 vs. 1354 min) though use of oxytocin for augmentation of labour was significantly higher; caesarean section rates were comparable (36.3 vs. 39.4%). The incidence of chorioamnionitis (defined as intrapartum fever with need for antibiotics or anatomical/pathological evidence of chorioamnionitis) was significantly lower in Foley catheter patients (11.5%) compared to those receiving vaginal misoprostol (27.3%); notably, it is well known that frequent vaginal manipulations increase the risk of infection.

A recent retrospective cohort study of 129 women with premature rupture of membranes close to term showed the rate of chorioamnionitis (not defined by the authors) non-significantly higher; caesarean section rates were comparable (36.3 vs. 39.4%). The incidence of chorioamnionitis (defined as intra partum fever with need for antibiotics or anatomical/pathological evidence of chorioamnionitis) was significantly lower in Foley catheter patients (11.5%) compared to those receiving vaginal misoprostol (27.3%); notably, it is well known that frequent vaginal manipulations increase the risk of infection.

In conclusion it can be assumed that the placement of a balloon catheter is not associated with increased infection risk, particularly when compared to repeated vaginal application of prostaglandins.

### Risk of infection

Whether the placement of a “foreign body” into the uterus increases the risk of infection or not is currently a topic of debate, the evidence being astoundingly sparse and contradictory. Recent review articles either do not mention infection risk at all [6, 7] or quote the two meta-analyses noted below. According to available literature there has not been a single reported case of serious infection or sepsis associated with balloon catheters used for labour induction, though it should be noted that studies have been conducted almost exclusively on women with intact membranes [8].

The meta-analysis by Heinemann et al. 2008 [25] that included 30 randomised controlled trials (n = 4468) comparing the Foley catheter to medical methods of induction found a significantly increased rate of maternal infections (7.6 vs. 5.0%, pooled OR: 1.50; 95% CI 1.07–2.09). Infection was defined as fever, endometritis or chorioamnionitis. The rate of chorioamnionitis was significantly raised (7.6 vs. 3.7%, pooled OR: 2.05; 95% CI 1.22–3.44), rates of endomyometritis non-significantly raised (5.1 vs. 3.2%, pooled OR: 1.42; 95% CI 0.74–2.97). There are no randomised studies of prophylactic antibiotic use in this context to date. The 2012 Cochrane review (33 trials using the Foley catheter) concluded that in view of the limited number of trials and differing criteria for infections, there is no evidence that balloon catheters increase infection risk. The authors do warn though, that the results should be interpreted with caution [26].

A detailed analysis of the infectious morbidity within the trials included was not performed in the Cochrane review. Interestingly, a recent multicentre study from the Netherlands showed that placement of an intrauterine pressure catheter did not increase infection risk up to 3 weeks postpartum when compared to external tocodynamometry (8.8 vs. 10.4% respectively [27]).

Another large Dutch multicentre trial (n = 824) compared the Foley catheter to vaginal PGE2 gel [28]. Suspected intrapartum infection (defined as body temperature ≥ 38°C and commencement of broad spectrum antibiotics) was diagnosed in 1% of patients with Foley catheter and 3% with vaginal PGE2 (p = 0.035), and the rate of neonatal admission was significantly higher following PGE2 (20 vs. 12%, p = 0.002, Table 3).

In conclusion it can be assumed that the placement of a balloon catheter is not associated with increased infection risk, particularly when compared to repeated vaginal application of prostaglandins.

### Failed induction with prostaglandin/misoprostol

Notwithstanding differing definitions of the term “failed induction” [26, 29, 30], balloon catheters are a promising option in this setting, though research evidence is insufficient. 75% of women delivered vaginally when a Foley catheter was used following failed induction with 3 mg PGE2 vaginal tablet (no evidence of labour onset after 2–3 applications) [31], and after failure of 50 µg vaginal misoprostol – applied 6-hourly to the unripe cervix (no evidence of labour onset after 24 hours) – 93 of 112 women (83%) delivered vaginally [32].

In our view, women who have failed induction with prostaglandins and who still wish to deliver vaginally should be offered further induction with a balloon catheter. The decision should be made together with the patient and on an individual basis, considering all potential risks and benefits.

### Patient satisfaction

Patient satisfaction with balloon catheters vs. medical induction is not addressed in existing reviews/meta-analyses [7,8,26,33,34] or current guidelines. Only Penell et al. 2009 [12], whose pre-

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### Table 3  Labour induction: Foley catheter vs. vaginal PGE2 gel: PROBAAT-study (randomised, controlled, multicentre, n = 824) [28].

<table>
<thead>
<tr>
<th>Criteria (selected)</th>
<th>0.5 mg PGE2 vaginal gel (n = 408)</th>
<th>Foley catheter (n = 412)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caesarean section rate (%)</td>
<td>20</td>
<td>23</td>
<td>NS</td>
</tr>
<tr>
<td>Caesarean due to failure to progress in the 1st stage of labour (%)</td>
<td>8</td>
<td>12</td>
<td>0.021</td>
</tr>
<tr>
<td>Operative delivery due to fetal distress (%)</td>
<td>18</td>
<td>12</td>
<td>0.0218</td>
</tr>
<tr>
<td>Induction to delivery time (median, h)</td>
<td>18</td>
<td>29</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Oxytocin augmentation (%)</td>
<td>59</td>
<td>86</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Uterine hyperstimulation (tachysystole/contractions lasting &gt; 3 min) (%)</td>
<td>3</td>
<td>2</td>
<td>NS</td>
</tr>
<tr>
<td>Uterine rupture/perforation (n)</td>
<td>2</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>Suspected maternal infection (intrapartum fever and commencement of antibiotics) (%)</td>
<td>3</td>
<td>1</td>
<td>0.035</td>
</tr>
<tr>
<td>Neonatal admission (%)</td>
<td>20</td>
<td>12</td>
<td>0.0019</td>
</tr>
</tbody>
</table>

NS = not significant
viously mentioned randomised study was included in the 2012 Cochrane review [22], state finding no significant difference in overall satisfaction among women induced with Foley catheter, double balloon catheter or PGE2 vaginal gel. A very recent comparative study of double balloon catheter and 10 mg PGE2 vaginal insert in oligohydramnios at term has come to a similar conclusion: Although balloon catheter placement was significantly more unpleasant than the vaginal insert, no significant difference was found in patient satisfaction between the two methods [35].

Patient satisfaction was the focus of a prospective, randomised trial in which oral misoprostol alone was compared to a combination of oral misoprostol plus double balloon catheter for labour induction in 122 women [36]. Findings were as follows: There was no significant difference in patient satisfaction between the two methods; women were not bothered by the insertion of the double balloon catheter or its presence subsequently; significantly more women in the combination group would choose the same method of induction in a subsequent pregnancy or would recommend it to others; the birth experience, assessed using a standardized questionnaire on postpartum mental state which provides a total score for birth experience (Salmon’s item list), was positive in both groups but significantly better in the combination group compared to misoprostol alone.

A pre-publication study from Israel [37] found that patient satisfaction (calculated using a 10 point scale) was significantly lower in obese pregnant women (body mass index > 30) compared to non-obese women (BMI ≤ 30, 5.95 ± 3.14 vs. 7.85 ± 2.7; p = 0.009). It has been recognised that this important criterion of labour induction with balloon catheters compared to other methods needs further research and two recent randomised studies (oral misoprostol vs. Foley catheter) in the Netherlands [38] and the USA [39] address the issue.

Of relevance to clinical practice is the observation that the insertion of a Foley catheter using a speculum is significantly more often experienced as painful by patients (visual analogue scale) compared to digital insertion. However, once again, overall satisfaction with the method was not affected [40].

**Balloon Catheter vs. Prostaglandin E2**

Balloon catheters alone only lead to effective uterine contractions during cervical ripening 15–33% of the time; in 67–85% of cases intravenous oxytocin (mostly commenced concurrently with balloon insertion or after balloon expulsion using various dosing schedules) is necessary for augmentation of labour [41, 42]. Previous studies/meta-analyses comparing balloon catheters and prostaglandins for labour induction have focussed almost exclusively on differing filling volumes using the Foley catheter.

The most recent Cochrane review, which includes 23 randomised studies, provides an overview of published data on balloon catheter vs. prostaglandins (PGE2 and misoprostol) [26]. The results (Table 4) are in general agreement with a meta-analysis by Vaknin et al. from 2010 [43] as well as two subsequently published randomised controlled trials [12, 44], so that in 2011 Henderson et al. are able to conclude that in nulliparae and multiparae with unfavourable cervix, transcervical balloon catheter is preferable to PGE2 with respect to safety, cost, patient satisfaction and length of labour [45].

<table>
<thead>
<tr>
<th>Table 4</th>
<th>Labour induction: balloon catheter vs. prostaglandins (prostaglandin E2, misoprostol). Results of 2012 Cochrane review [26].</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>tendency to increased rate of women not delivered within 24 h:</strong></td>
<td></td>
</tr>
<tr>
<td>48 vs. 38% (RR 1.26; 95% CI 1.04–1.68)</td>
<td></td>
</tr>
<tr>
<td><strong>no significant difference in caesarean section rate:</strong></td>
<td></td>
</tr>
<tr>
<td>27 vs. 25% (RR 1.01; 95% CI 0.90–1.13)</td>
<td></td>
</tr>
<tr>
<td><strong>no significant difference in cervical ripening (cervix unfavourable after 12–24 h):</strong></td>
<td></td>
</tr>
<tr>
<td>37 vs. 39% (RR 0.96; 95% CI 0.70–1.34)</td>
<td></td>
</tr>
<tr>
<td><strong>significantly higher rate of need for augmentation of labour with oxytocin:</strong></td>
<td></td>
</tr>
<tr>
<td>75 vs. 80% (RR 1.51; 95% CI 1.15–1.97)</td>
<td></td>
</tr>
<tr>
<td><strong>significantly lower rate of uterine hyperstimulation with fetal heart rate changes:</strong></td>
<td></td>
</tr>
<tr>
<td>0.4 vs. 3% (RR 0.19; 95% CI 0.08–0.43)</td>
<td></td>
</tr>
</tbody>
</table>


**Balloon catheter vs. PGE2 vaginal gel**

The largest randomised, controlled trial to date on the subject (PROBAAT-trial) compared the Foley catheter (filling volume 30 ml + amniotomy and i.v. oxytocin on catheter expulsion or BS > 6 dependant on uterine activity) to PGE2 vaginal gel (1 mg initially, repeated after 6 h then twice daily, initial dose in nulliparae 2 mg) in 824 women with unfavourable cervix (BS < 6) [28]. Results are shown in Table 3. The authors of a meta-analysis that takes these results into account as well as the results of two other recent randomised trials using PGE2 vaginal gel in controls [12, 44] conclude the following:

- No significant difference in caesarean section rate, however with Foley catheter caesarean more often indicated because of failure to progress; lower rates due to fetal distress.
- Longer induction to birth times for Foley catheter compared to PGE2, possibly due to delayed commencement of oxytocin/ or amniotomy only after catheter expulsion (e.g. at night) (also compare with [7]).
- With Foley catheter, significantly lower rate of uterine hyperstimulation in the meta-analysis (RR 0.44; 95% CI 0.21–0.9) but not in the PROBAAT-trial (2 vs. 3%, p = 0.36); no significant effect on neonatal outcome (5-minute Apgar score, umbilical cord pH).

The unanimously stated advantages of balloon catheters compared to PGE2 in clinical practice are less need for monitoring during the first stage of labour, simple storage at room temperature and lower cost [6, 7, 24].

The latest cost-effectiveness analysis on the PROBAAT-trial data [46] that included costs of labour ward admission, those for additional medication and regional anaesthesia, for the induction method itself and for the delivery showed no significant differences in cost between Foley catheter and vaginal PGE2 for induction with unfavourable cervix.

**Balloon catheter vs. PGE2 vaginal insert**

Four randomised trials together including 824 patients have compared the Foley [47] and double balloon catheters [41, 42, 48] with 10 mg PGE2 vaginal insert (insertion time up to 24 h) for labour induction with unfavourable cervix (Bishop score ≤ 6) (Table 5). Cromi et al. 2011 [47] left the Foley catheter in situ for either 12 or 24 hours and on catheter expulsion gave oxytocin intravenously. There were no significant differences between the methods for caesarean section rate or effectiveness of cervical ripening after 12 and 24 hours; the rate of uterine hyperstimulation was however significantly lower with Foley catheter (0 vs. 6.1%). Rate of vaginal deliveries in 24 hours was only 21% for Fo-
Foley catheter in situ for 24 hours compared to 59.5% for Foley catheter in situ for 12 hours and 48.5% for PGE2 vaginal insert ($p < 0.001$), a clinically relevant finding. The results of the two randomised prospective comparative studies of double balloon catheter vs. 10 mg PGE2 vaginal insert (insertion time up to 24 hours) were in agreement, finding no significant difference in caesarean rate between the methods but a significantly greater need for oxytocin and lower rate of uterine hyperstimulation with the double balloon catheter without affecting neonatal outcome. Rate of vaginal deliveries in 24 hours differed between the two studies: While Cromi et al. 2012 [41] showed a significantly higher rate with the double balloon catheter (68.6 vs. 49.5%), Du et al. 2014 [42] did not (50 vs. 53.2%).

A recently published randomised trial in 62 nulliparae with unfavourable cervix (BS $< 5$) compared the double balloon catheter (filling volume 80 ml, in situ for up to 12 hours, oxytocin intravenously 6 hours after catheter insertion) to a 10 mg PGE2 vaginal insert (insertion time up to 12 hours) [48]. Average induction to delivery time was significantly shorter for the double balloon catheter than for PGE2 vaginal insert (17.9 vs. 26.7 hours) and rate of vaginal deliveries in 24 hours was significantly higher (87.1 vs. 47.4%) with similar caesarean rates (51.6 vs. 54.8%) and no significant differences in neonatal outcome. Uterine hyperstimulation occurred at a rate of 25.8% with PGE2 vaginal insert compared to 0% for the double balloon catheter.

A shortened induction to birth interval is meaningful since it correlates closely with patient satisfaction with the method of induction [49].

### Balloon Catheter vs. Misoprostol

#### Balloon catheter vs. vaginal misoprostol

Numerous studies have investigated the use of Foley catheters (filling volume 30–50 ml) vs. vaginal misoprostol (25 µg 3–6-hourly). A recently published meta-analysis of 10 randomised studies conducted between 2001 and 2012 (n = 1520) summarises the results [50]. More recently data from the 2014 PROBAAT-M study have been published [50] (Table 6). 129 women (BS 0–5) were treated either with Foley catheters (filling volume 30 ml) or with vaginal misoprostol (25 µg 4-hourly, maximum 3 doses/24 h); when the Bishop score was ≥ 6 amniotomy was performed and intravenous oxytocin commenced with dosing according to the strength of contractions. The main findings of the PROBAAT-M study that differ with those of the meta-analysis are a longer induction to delivery time and a non-significantly raised incidence of uterine hyperstimulation for the Foley catheter. The authors offer no explanation for these findings. The findings of the meta-analysis are in general agreement with that of Fox et al. published in 2011 [33] (9 trials, n = 1603), although 4 of these trials used 50 µg vaginal misoprostol 4- to 6-hourly. Interestingly the average induction to delivery time between study groups did not differ significantly (Fox et al.) There was also no significant difference in the incidence of chorioamnionitis (RR 1.13; 95% CI 0.61–2.09).

#### Balloon catheter vs. oral misoprostol

To date there are few trials comparing the Foley catheter to oral misoprostol for labour induction and patient numbers are small.
Advantages of oral misoprostol over the application vaginally – at similar dosage – are lower rates of uterine hyperstimulation, better neonatal outcome (5-minute Apgar < 7), better patient acceptance and lower infection risk through avoidance of vaginal manipulation.

There are currently two studies underway comparing the Foley catheter (filling volume 30 ml) with oral misoprostol (50 µg 4-hourly or 25 µg 2-hourly). Primary endpoints of the first (PROBAAT) study (n = 56), which plans to include 1860 patients, are neonatal outcome (umbilical cord pH ≤ 7.05 or 5-minute Apgar < 7) and postpartum haemorrhage (blood loss ≥ 1000 ml). The single primary endpoint of the second trial, with an intended study population of 620 women with preeclampsia, is vaginal delivery rate in 24 hours [39].

**Combined or Sequential Use of Balloon Catheters and other Uterine Stimulants**

Since balloon catheters cause cervical ripening but in the majority of cases not contractions, they have been combined with numerous other methods of uterine stimulation. The vaginal delivery rate in 24 hours was not increased by intravenous oxytocin commenced simultaneously with Foley catheter insertion during the 1st stage of labour compared to Foley catheter alone (46 vs. 45%) [54]). Also, there was no significant difference in median induction to delivery time between study groups receiving fixed vs. increasing doses of intravenous oxytocin following balloon insertion (23.7 vs. 19.2 hours) [55].

**Balloon Catheter Combined with Extra-amniotic Salt Infusion (EASI)**

A comparative study of the Foley catheter plus extra-amniotic salt infusion vs. double balloon catheter alone showed significant advantages for the combined approach: The time between balloon insertion and expulsion was reduced as was induction to delivery time in the Foley catheter + salt infusion group [15]. A follow-on study by the same investigators [16] compared the Foley and double balloon catheters, both in combination with EASI. The results are summarised in Table 1. On comparison of the double balloon catheter with and without EASI, again significant advantages were found for the combined approach [56]: shorter balloon insertion to delivery time (14.2 vs. 20.45 h, p < 0.001) and a higher rate of balloon expulsion (68.5 vs. 51%, p = 0.04).

**Balloon catheter and misoprostol simultaneously**

More recent randomised trials have focused on the combination of balloon catheter and misoprostol vs. misoprostol alone for labour induction. A 2012 Cochrane review [26] including 8 studies published before January 2012 (n = 1295) summarises this data. Findings were a significantly increased vaginal delivery rate in 24 hours (RR 0.45; 95% CI 0.25–0.71) for the combination method without an effect on the caesarean section rate, as well as a reduced incidence of uterine hyperstimulation (RR 0.59; 95% CI 0.35–0.78) for the combined method. Evidence on the incidence of the uterine hyperstimulation syndrome is however conflicting.

Results of randomised studies since 2012 are shown in Table 7. In their prospective, randomised trial Kehl et al. compared the double balloon catheter (in situ time up to 24 hours) plus oral misoprostol 50 µg (repeated after 4 and 8 hours, increased to 100 µg as required) to oral misoprostol alone in a study population of 122 women [57]. The primary outcome of the study was failure of induction, which was defined as no vaginal delivery within 48 hours. There were significantly fewer induction failures in the control group (9.3 vs. 21.7%, p = 0.07) as well as a significantly shorter median induction to delivery time (15.3 vs. 20.8 hours). In 3 further randomised trials conducted in the past 2 years, the combination of Foley catheter plus vaginal misoprostol (25 µg 4-hourly) vs. vaginal misoprostol alone lead to significantly shorter induction to delivery times, a significant reduction in uterine hyperstimulation and meconium stained liquor and less need for oxytocin [58–60] compared to misoprostol alone. Vaginal misoprostol given 6 hours after Foley catheter insertion was more effective than vaginal misoprostol alone [61] (Table 7). Overall, the combination of balloon catheter and vaginal misoprostol results in a reduction of uterine hyperstimulation (with or without fetal heart rate changes), and no significant differences in chorioamnionitis rates or neonatal outcome when compared to misoprostol alone. However because of low case numbers and the heterogeneity of available trials, the evidence is still insufficient for a general recommendation of the combination approach for clinical practice.

**Balloon catheter and misoprostol sequentially**

Until recently no trial had studied the use of double balloon catheters with sequential oral misoprostol. A multicentre, random-
ised, controlled trial of 326 pregnant women with unfavourable cervix and various induction indications has now been published [62]. Induction was either with double balloon catheter (in situ time up to 12 hours) followed by oral misoprostol 50 µg 24 hours after catheter insertion (repeat doses after 4 and 8 hours with the possibility of increasing dose to 100 µg after 24 hours), or oral misoprostol alone with the same dosing schedule. Primary endpoints were induction to delivery time and vaginal delivery rate in 48 hours. There was a non-significant difference in caesarean section rate (21.6 vs. 29.8%). Independent of parity, the median induction to delivery time for the combination group was significantly longer than for oral misoprostol alone (32.4 hours vs. 22.5 hours; p = 0.004). However this difference was not statistically significant when comparing primiparaea and multiparae. There were no significant differences in vaginal delivery rate in 48 hours (79.5 vs. 84.9%) or need for oxytocin. The number of misoprostol applications was however significantly fewer, and the total misoprostol dose significantly lower in the combination group. The double balloon catheter alone lead to effective contractions in 23.3% of cases. Whether better results would be achieved by giving oral misoprostol immediately after catheter removal or not, remains to be studied.

The 2009 ACOG guidelines [65] recommend the Foley catheter as a sensible and effective alternative to prostaglandins for cervical ripening/labour induction (grade A recommendation). Its use is mentioned an option for outpatient induction. The 2013 Canadian guidelines (SOGC) [66] advocate the balloon catheter as an acceptable method of labour induction following previous caesarean section (I-B) and for outpatient induction (II-B), with the double balloon catheter as second-line option. The guidelines draw attention to the greater need for oxytocin when using balloon catheters as well as lower rates of uterine tachysystole without increased risk of maternal (chorioamnionitis, endometritis) or neonatal infections. In Germany there are no recommendations or guidelines on this subject.

**Conclusion**

Induction of labour using balloon catheters has experienced a renaissance in recent years and the method is now part of many international guidelines. The statistics presented in this paper confirm that, just as with the more established prostaglandins, labour can be successfully induced using balloon catheters. The pros and cons of the balloon catheter compared to prostaglandins are shown in Table 8.

The two catheters available for use are the Foley catheter, which is cheaper, and the double balloon catheter, which has the advantage of being licensed for use in labour induction. Combining medical induction with the use of balloon catheters is a particularly interesting option that results of a number of trials currently underway are expected to provide more detailed information on in future.

**Conflict of Interest**

Sven Kehl: Presentation fee and travel costs (COOK Medical).

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**Table 7** Balloon catheter plus misoprostol vs. misoprostol alone for labour induction with unfavourable cervix. Results of recent randomised, controlled trials.

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Number of patients (n)</th>
<th>Intervention</th>
<th>Control</th>
<th>Significant findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kehl et al. 2011 [57]</td>
<td>122</td>
<td>Double balloon catheter (up to 24h) + 50 µg misoprostol p. o. (dose increase to 100 µg possible)</td>
<td>50 µg misoprostol p. o. (dose increase to 100 µg possible)</td>
<td>Induction to delivery time (median): 15.3 vs. 20.8 hours, Induction failure: 9.3 vs. 21.2%</td>
</tr>
<tr>
<td>Ande et al. 2012 [61]</td>
<td>100</td>
<td>Foley catheter + 50 µg vaginal misoprostol following catheter insertion</td>
<td>50 µg vaginal misoprostol (6-hourly)</td>
<td>Vaginal delivery rate in 12 hours: 92.5 vs. 60% Caesarean section: 20 vs. 40%</td>
</tr>
<tr>
<td>Carbone et al. 2013 [58]</td>
<td>123</td>
<td>Foley catheter + 25 µg vaginal misoprostol (4-hourly)</td>
<td>25 µg vaginal misoprostol (4-hourly)</td>
<td>Induction to delivery time (median): 15.3 vs. 18.3 hours, Cervical dilatation rate (median): 13.7 vs. 17.1 hours</td>
</tr>
<tr>
<td>Ugwu et al. 2013 [59]</td>
<td>150</td>
<td>Foley catheter + 25 µg vaginal misoprostol (4-hourly)</td>
<td>25 µg vaginal misoprostol or Foley catheter alone</td>
<td>1st stage of labour approx. 3 hours shorter, Oxytocin: 40 vs. 17.5 vs. 25.6%</td>
</tr>
<tr>
<td>Lanka et al. 2014 [60]</td>
<td>126</td>
<td>Foley catheter + 25 µg vaginal misoprostol (4-hourly)</td>
<td>25 µg vaginal misoprostol (4-hourly)</td>
<td>Uterine hyperstimulation: 7.9 vs. 39.7%, Meconium stained liquor: 6.3 vs. 27%</td>
</tr>
<tr>
<td>Kehl et al. 2015 [62]</td>
<td>326</td>
<td>Double balloon catheter, after 24 h 50 µg misoprostol p. o. (100 µg possible)</td>
<td>50 µg misoprostol p. o. (100 µg possible)</td>
<td>Induction to delivery time (median): 32.4 vs. 22.5 hours, Total misoprostol dose 100 vs. 200 µg</td>
</tr>
</tbody>
</table>

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**Comment on Current Guidelines**

According to WHO recommendations from 2011 [63] balloon catheters are recommended for labour induction and are approximately as efficient as vaginal prostaglandins (PGE₂, misoprostol) (moderate quality of evidence, strong recommendation). A combination of balloon catheter and oxytocin is recommended as an alternative when prostaglandins (including misoprostol) are not available or are contraindicated (low quality evidence, weak recommendation). The balloon catheter is also mentioned as an option for labour induction after previous caesarean section (no recommendation grade stated). According to the 2008 RCOG guidelines (update 2014 [64]) balloon catheters should not be used routinely for labour induction with unfavourable cervix, and their use after previous caesarean section should be studied in clinical trials.
<table>
<thead>
<tr>
<th>Table 8</th>
<th>Advantages and disadvantages of balloon catheters compared to prostaglandin E2/misoprostol.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pros</strong></td>
<td><strong>Cons</strong></td>
</tr>
<tr>
<td>single application</td>
<td>greater need for oxytocin augmentation</td>
</tr>
<tr>
<td>no uterine hyperstimulation  → less risk to the fetus</td>
<td>potentially increased infection risk compared to oral prostaglandin</td>
</tr>
<tr>
<td>less monitoring required</td>
<td>lower vaginal delivery rate in 24 h* in multiparae</td>
</tr>
<tr>
<td>cheaper than prostaglandin E2</td>
<td></td>
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<tr>
<td>no need for special storage (e.g. cold chain)</td>
<td></td>
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</tbody>
</table>

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