Mechanical Methods for the Induction of Labour After Previous Caesarean Section – An Updated, Evidence-based Review

Mechanische Methoden zur Geburtseinleitung nach vorangegangener Sectio – eine aktualisierte, evidenzbasierte Übersicht

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ABSTRACT

There are currently no up-to-date evidence-based recommendations on the preferred method to induce labour after previous Caesarean section, especially for patients with unripe cervix, as randomised controlled studies are lacking. Intravenous oxytocin and misoprostol are contraindicated in these women because of the high risk of uterine rupture. In women with ripe cervix (Bishop Score > 6), intravenous administration of oxytocin is an effective procedure with comparable rates of uterine rupture to those with spontaneous onset of labour. Vaginal prostaglandin E_2 (PGE_2) and mechanical methods (balloon catheters, hygroscopic cervical dilators) are effective methods to induce labour in pregnant women with unripe cervix and previous Caesarean section. According to current guidelines, the administration of PGE_2 is associated with a higher rate of uterine rupture compared to balloon catheters. Balloon catheters are therefore a suitable alternative to PGE_2 to induce labour after previous Caesarean section, even though this is an off-label use. In addition to two meta-analyses published in 2016, 12 mostly retrospective cohort/observational studies with low to moderate levels of evidence have been published on mechanical methods of cervical ripening after previous Caesarean section. But because of the significant heterogeneity of the studies, substantial differences in

study design, and insufficient numbers of pregnant women included in the studies, it is not possible to make any evidence-based recommendations based on these studies. According to a recent meta-analysis, the average rate using balloon catheters is approximately 53 % and the average rate after spontaneous onset of labour is 72 %. The uterine rupture rate was 0.2–0.9 % for vaginal PGE_2 and 0.56–0.94 % for balloon catheters and is therefore comparable to the uterine rupture rate associated with spontaneous onset of labour. According to the product informations, hygroscopic cervical dilators (Dilapan-S) are currently the only method which is not contraindicated for cervical ripening/induction of labour in women with previous Caesarean section, although data are insufficient. Well-designed, randomised, controlled studies with sufficient case numbers comparing balloon catheters and hygroscopic cervical dilators with mechanical methods and vaginal prostaglandin E_2/oral misoprostol are therefore necessary to allow proper decision-making.

ZUSAMMENFASSUNG

Bisher gibt es keine evidenzbasierten Empfehlungen, welche Methode zur Geburtseinleitung nach vorangegangener Sectio, insbesondere bei unreifer Zervix, zu bevorzugen ist, da randomisierte, kontrollierte Studien fehlen. Oxytocin intravenös und Misoprostol sind bei diesen Schwangeren aufgrund des erhöhten Rupturrisikos kontraindiziert. Bei reifer Zervix (Bishop Score > 6) ist die intravenöse Gabe von Oxytocin ein effektives Verfahren mit vergleichbaren Raten an Uterusrupturen wie beim Abwarten spontaner Wehen. Vaginales Prostaglandin E_2 (PGE_2) und mechanische Methoden (Ballonkatheter, hygroskopische Zervixdilatatoren) sind effektive Methoden zur Geburtseinleitung nach Sectio bei unreifer Zervix. Nach aktuellen Leitlinien ist die Gabe von PGE_2 im Vergleich zu Ballonkathetern mit einer höheren Rate an Uterusrupturen assoziiert. Daher stellen Ballonkatheter eine geeignete Alternative zu PGE_2 zur Geburtseinleitung nach Sectio dar, ungeachtet ihres Off-Label Use. Nach 2 Metaanalysen 2016 sind 12 weitere meist retrospektive Kohorten-/Beobachtungsstudien mit niedriger bis mäßiger Evidenz zu mechanischen Methoden der Zervixreifung nach vorangegangener Sectio publiziert worden. Allerdings lassen sich aufgrund der erheblichen Heterogenität zwischen den Studien, erheblichen Unterschieden im Studiendesign und der unzureichenden Zahl eingeschlossener Schwangerer keine evidenzbasierten Empfehlungen aus diesen Untersuchungen ableiten. Nach einer aktuellen Metaanalyse liegt die Rate vaginaler Geburten nach vaginalem PGE_2 bei im Mittel 66 %, unseren Untersuchungen zufolge bei Anwendung von Ballonkathetern und unreifer Zervix bei durchschnittlich 53 % und bei Schwangeren mit Abwarten spontaner Wehen bei im Mittel 72 %. Die Frequenz an Uterusrupturen beträgt mit vaginalem PGE_2 0,2–0,9 % und mit Ballonkathetern 0,56–0,94 % und ist damit der nach Abwarten spontaner Wehen vergleichbar. Hygroskopische Zervixdilatatoren (Dilapan-S) sind unter Berücksichtigung von Produktinformationen die derzeit einzige „erlaubte“ Methode zur Zervixreifung/Geburtseinleitung nach Sectio, allerdings ist die diesbezügliche Datenlage völlig unzureichend. Zur Entscheidungsfindung sind daher gut konzipierte randomisierte, kontrollierte Studien mit adäquater Fallzahl zum Vergleich von Ballonkathetern und hygroskopischen Zervixdilatatoren einerseits und mechanischen Methoden und vaginalem Prostaglandin E_2/oralem Misoprostol andererseits erforderlich.

Introduction

Given the globally increasing rates of Caesarean sections and the increasing rates of labour inductions, the obstetric procedures used in subsequent pregnancies are particularly important. In Germany, previous Caesarean delivery is the most common indication for repeat C-section, with 31.8 % of C-sections carried out for this reason [1].

Induction of labour is medically indicated in 18–27 % of these women [2] and the numbers are still rising. A 2017 Cochrane analysis (8 randomised controlled studies, n = 707) was unable to make any evidence-based recommendations about the most suitable method to induce labour after previous Caesarean section because of the heterogeneity of the included studies and the limited number of cases [3].

In addition to other factors (e.g., maternal age, body mass index, previous Caesarean section), the efficacy of the methods used to induce labour and the risk of uterine rupture depend on whether the patient had a previous vaginal delivery and on the degree of cervical ripening before starting induction [4, 5, 6, 7].

The rate of vaginal deliveries in women with unripe cervix (Bishop Score [BS] < 6) without a previous vaginal delivery is only 45 % but is 77 % in women with a previous vaginal delivery [4, 6]. The rate of uterine rupture has shown to be significantly lower for women with a previous vaginal delivery compared to those without (0.8 vs. 1.5 %) [4]. Depending on the method used to induce labour, the rupture rate in women with unripe cervix is 3 to 4 times higher than that in women with ripe cervix [4, 8, 9].

The induction of labour after previous Caesarean section in women with unripe cervix is therefore particularly challenging for obstetricians.

According to the manufacturer's product information, the use of prostaglandin E_2 (PGE_2) in this setting is contraindicated because of the increased risk of uterine rupture, as is the use of misoprostol (overview in [10]). Intravenous administration of oxytocin to induce labour should only be used in cases with ripe cervix [11].

Pregnant women must be informed in detail about the risks and benefits of inducing labour after previous Caesarean section, and written consent is required [11].

As the efficacy of mechanical methods to induce labour is comparable to the efficacy of PGE_2 [12], the benefits of using balloon catheters or hygroscopic cervical dilators (Dilapan-S) are a significantly lower rate of uterine hyperstimulation (PGE_2: 3–20 %, balloon catheter: 0–2.7 %) [13, 14], lower monitoring costs (CTG) during the cervical ripening period, lower overall costs, and the option of carrying out cervical ripening on an outpatient basis [15], although in cases with previous Caesarean section this should only be done in the context of clinical studies. According to current guidelines, the risk of uterine rupture is significantly lower when using balloon catheters compared to using vaginal PGE_2 [6, 11, 16, 17]; however, the risk of rupture after PGE_2 reported in the guidelines is based on "historical" studies [18, 19, 20].

It should be noted that mechanical methods require the additional administration of intravenous oxytocin to induce/augment labour more often (mean: 70 %) [21] compared to using PGE_2 to induce labour (mean: 40 %) [22].

The maternal risk of infection following the use of balloon catheters is no higher than the risk of infection when using vaginal PGE_2 [23].

Foley catheters have not been generally approved for cervical ripening/induction of labour; double-balloon catheters have been approved, however, their use is contraindicated for labour induction in women with a previous Caesarean section when considering product informations. Cervical ripening with the Dilapan-S dilator is not contraindicated after previous Caesarean section, however, according to our recent PubMed search there are only 2 prospective studies on this issue conducted by the same working group [24, 25].

A number of further studies have been published since our meta-analysis of 2016 [21], and they highlight the importance of re-evaluating the efficacy and safety of mechanical methods to induce labour after previous Caesarean section in order to develop evidence-based recommendations for clinical practice.

Comparison of Induction of Labour with Balloon Catheters versus Spontaneous Onset of Labour

A retrospective cohort study from Finland [26] evaluated 361 pregnant women with unripe cervix (BS < 6) and previous Caesarean section who underwent induction of labour with a Foley catheter followed by amniotomy/intravenous administration of oxytocin once the cervix is ripe; women whose cervix was still unripe were given oral (50 µg every 4 h) or vaginal misoprostol (25 µg every 4–6 h). This group was compared to 1198 women with spontaneous onset of labour. The primary endpoints of the study were the rates of repeat Caesarean sections and of severe maternal complications. The rate of repeat C-sections after the use of balloon catheters was 38 % while the rate following spontaneous onset of labour was 20.2 % (p = 0.001); the rates of complete uterine rupture were 0.3 and 0.8 %, respectively (p = 0.47), and the rates of suture dehiscence were 2.2 and 1.0 %, respectively (p = 0.10). There were no significant differences in perinatal outcomes. The retrospective study design (LoE III), significant differences in number of cases and the significantly higher risk profile of women treated with balloon catheters (selection bias) limit the validity of this study. It should be noted that despite the oral/vaginal administration of misoprostol during the subsequent induction of labour, the rate of complete uterine rupture was lower than the rate in patients with spontaneous onset of labour (▶ **Table 1**).

Comparison of Induction of Labour with Balloon Catheter vs. Intravenous Oxytocin

There are a total of 3 recent studies on this topic (cf. ▶ **Table 1**).

It is debatable whether it is appropriate to compare the induction of labour using a Foley catheter or a double-balloon catheter left in place for up to 24 hours in women with unripe cervix (BS < 6) with the induction of labour using intravenous oxytocin in women with ripe cervix (BS ≥ 6); moreover, the evidence level of this retrospective cohort study is low (LoE III) [27]. As the degree of cervical ripening has a significant impact on the method's efficacy and the risk of uterine rupture, both methods cannot be compared. It is therefore unsurprising that the vaginal delivery rate (primary endpoint) for women with ripe cervix who received oxytocin was higher (63.9 %) than the rate for women with unripe cervix treated with balloon catheters (45.8 %). There was no difference between groups with regard to the frequency of uterine rupture.

The results of another retrospective cohort study (LoE III) which compared double-balloon catheters vs. intravenous oxytocin administration in women with unripe cervix is shown in ▶ **Table 1** [29]. Although the study investigated women with unripe cervix, the rate of vaginal deliveries following the intravenous administration of oxytocin was surprisingly higher (70.7 %) compared to the rate when using balloon catheters (50 %); there was no statistically significant difference with regard to the risk of uterine rupture [29].

A randomised controlled multicentre study compared induction of labour with the Foley catheter (n = 101, left in place for 12 h) in women with previous Caesarean section and unripe cervix (BS ≤ 4) to labour induction with intravenous oxytocin at increasing doses (n = 103) ([35], LoE Ib). Endpoint of the study was the rate of vaginal deliveries, which was significantly higher following the use of balloon catheters (50.0 %) compared to the administration of intravenous oxytocin (37 %); there were no signficant differences in uterine rupture rates or perinatal outcomes between groups (▶ **Table 1**). This again raises the question why the authors used oxytocin in cases with (very) unripe cervix contrary to guideline recommendations and the product information. The low rate of vaginal deliveries with oxytocin underlines this assumption.

▶**Table 1** Balloon catheters for the induction of labour after previous Caesarean section in women with unripe cervix: studies 2016–2021.

Author/year	n	Balloon/filling volume	Vaginal delivery rate (%)	Uterine rupture (n/%)	Oxytocin (%)	Comparison group
Kruit 2017 [26]	361	Foley: 50 ml	62	1/0.3 SD: 8/2.2	85.7	Spontaneous onset of labour: n = 1198 Vaginal delivery: 79.8 % (S) Uterine rupture: 0.8 % (NS) SD: 1.0 % (NS) Intra-/postpartum infection: 6.1 vs. 1.8 % 5.3 vs. 1.3 % (S)
Radan 2017 [27]	107	Foley: 60 ml DB: up to 80 ml	45.8	1/0.9 SD: 5/4.7	n/s	Oxytocin with BS ≥ 6, n = 72 Vaginal delivery: 63.9 % (S) Uterine rupture: 1.4 % (NS) SD: 5.6 % (NS)
De Bonrostro-Torralba 2017 [28]	418	DB: 80 ml	51.4	5/1.2	72.2	None
Shah 2017 [29]	69	DB: 80 ml	50.0	0	Primary: 100 %	Oxytocin IV: n = 150 Vaginal delivery: 70.7 % (S) Uterine rupture: 1.3 % (NS)
Vital 2018 [30]	105	DB: 80 ml	43.8	0	n/s	None
Wallström 2018 [31]	335	Foley: 50 ml	69.0	7/2.1	88.4 (S)	▪ Vaginal PGE_2 gel: n = 281 – vaginal delivery: 57.1 % (S) – uterine rupture: 5 % (S) ▪ Oral misoprostol: n = 295 – vaginal delivery: 69.2 % (NS) – uterine rupture: 2 % (NS)
Atia 2018 [32]	108	Foley: 50 ml	39.8	0	No oxytocin	None
Boisen 2019 [33]	304	DB: 80 ml	50.3	3/1.0 SD: 3/1.0	n/s	Unsuccessful induction of labour with PGE_2/misoprostol → DB (n = 58) without previous Caesarean section
Boujenah 2019 [34]	59	DB: 80 ml	50.8	1/1.7	64	None
Sarreau 2019 [35]	101	Foley: 50 ml	50.0	0/0 SD: 2/2	n/s	IV Oxytocin: n = 103 Vaginal delivery: 37 % (S) Uterine rupture: 0 (NS) SD: 0.98 % (NS)
Huisman 2019 [36]	993	Foley: 30–50 ml DB: 60–80 ml	56.4	11/1.1 SD: 7/0.7	77.5	Elective repeat Caesarean section: n = 321 ▪ uterine rupture: 0.3 %, SD: 0.96 ▪ overall maternal morbidity: 7.8 vs. 4.5 % (NS)
Korb 2020 [37]	117	DB: 10–80 ml	57.3	0/0 SD: 2/1.7	76.9	Intracervical PGE_2 → vaginal misoprostol: n = 127 ▪ vaginal delivery: 57.5 % (NS) ▪ uterine rupture: 0.7 % (NS), SD: 1.5 % (NS) ▪ oxytocin: 55.1 % (S)
Overall:	3077		52.2[+]	29/0.94 % without SD	77.5	

[+] Excluding the study by Atia et al. 2018 (no oxytocin): 53.3 %
Abbreviations: DB: double balloon; n/s: not specified; SD: uterine suture dehiscence; S/NS: significant or not significant versus the comparison group

Balloon Catheter for Induction of Labour with no Comparison Group (cf. ▶ **Table 1**)

Three retrospective cohort/observational studies used double-balloon catheters (filling volume 80 ml, time left in place for 12–24 h) to induce labour in women with previous Caesarean section and unripe cervix (BS < 5); intravenous oxytocin was applied to induce/augment labour once the cervix was ripe (BS ≥ 6). Primary endpoints of the studies were the vaginal delivery rate [28, 34] and an improved BS [30]. The respective vaginal delivery rates were 51.4 %, 43,8 % and 50.8 % [28, 30, 34]. During and after placement of the catheter, regular contractions leading to birth occurred in 20.8 and 15.2 % of pregnant women, respectively [28, 30]. Additional findings of these studies (e.g., uterine rupture, oxytocin administration) are shown in ▶ **Table 1**. In the study by Vital et al. [30], 70.5 % of pregnant women had a BS ≥ 6 (primary endpoint) after removal of the catheter. Multivariate regression analysis showed that an initial mean BS of 4 and a BS ≥ 6 after catheter removal were significant predictive parameters for vaginal delivery.

None of the studies provide information on uterine hyperstimulation. Quite apart from the low levels of evidence (LoE III), these studies are not helpful to determine the most appropriate method for labour induction in women with a previous Caesarean section as they lack proper comparison groups.

A cohort study from Saudi Arabia investigated how effective Foley catheters (filling volume 50 ml, time left in place for 12–24 h) followed by amniotomy once the cervix is ripe and without the additional administration of uterotonic drugs are at inducing labour in women with previous Caesarean section and unripe cervix [32]. The vaginal delivery rate (primary study endpoint) was 39.8 %, the rate of uterine rupture was 0. No uterine hyperstimulation and no uterine rupture occurred with the balloon catheters. This study is relevant for women rejecting uterotonic drugs for further labour induction.

Comparison of Induction of Labour with Balloon Catheter vs. Prostaglandins

There are 3 recent retrospective cohort studies (LoE III) on this topic, each with a completely different study design, making it impossible to compare their respective findings.

A Swedish cohort study compared the induction of labour using a Foley catheter (n = 335, filling volume 50 ml, time left in place up to 10 h) in women with unripe cervix (BS ≤ 5) and previous Caesarean delivery at ≥ 34 weeks of gestation with the induction of labour using oral misoprostol (25 µg every 2 h until the onset of painful contractions, n = 295) or the administration of 1–2 mg vaginal PGE_2 gel (3 applications at intervals of 6 h, n = 281) [31]. Primary study endpoint was the uterine rupture rate, which was significantly higher following vaginal PGE_2 than after placement of a Foley catheter or oral misoprostol; the efficacy of the latter two methods was comparable (▶ **Table 1**). The limitations of this study are the retrospective analysis of data obtained from coded patient files (potential coding errors), the lack of randomisation, and a selection bias based on the initial mean BS (balloon catheter: BS = 4, vaginal PGE_2: BS = 2.4, oral misoprostol: BS = 2.9, p < 0.001).

Another retrospective cohort study [33] compared using a double-balloon catheter (mean time left in place 18 h) to induce labour in 304 women with previous Caesarean delivery and unripe cervix (BS ≤ 5) with the induction of labour in 58 pregnant women without previous C-section who underwent placement of a double-balloon catheter following prior unsuccessful attempts to induce labour with oral (25 µg every 2 h) or vaginal (50 µg every 4 h) misoprostol over a period of 48 hours when amniotomy was not possible. The results of this study are shown in ▶ **Table 1**. The clinically relevant finding of this study was the observation that the use of a double-balloon catheter after an unsuccessful attempt to induce labour with misoprostol still resulted in a vaginal delivery in 51.7 % of cases; otherwise, the study design should be viewed critically as it compared women with to women without a previous Caesarean section. Hence, the comparison of both groups is questionable.

A retrospective data analysis by Korb et al. [37] evaluated the induction of labour in pregnant women with prior Caesarean delivery and unripe cervix (BS < 6) using a double-balloon catheter (time left in place up to 24 h) followed by the administration of oxytocin (n = 117) and compared this group with another group of women who underwent complex procedures to induce labour (n = 127): 0.5 mg intracervical PGE_2 gel/day for 3 days, followed by 25–50 µg vaginal misoprostol/day until day 7.

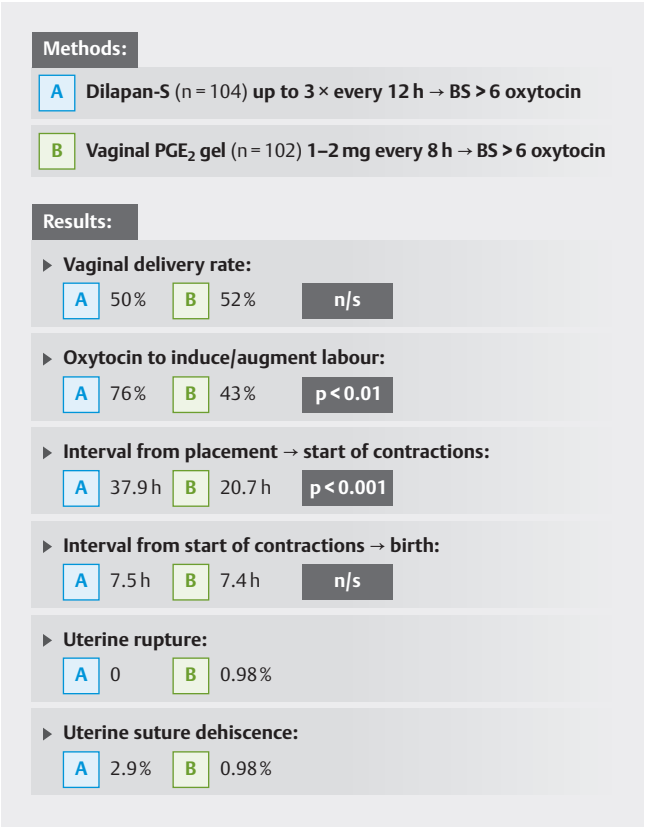
The primary endpoint of this study was the rate of Caesarean deliveries. Caesarean section rates did not differ significantly between groups (42.5 vs. 42.7 %), nor did the rates of uterine rupture (▶ **Table 1**).

Induction/augmentation of labour was required significantly more often after placement of a balloon catheter than after the application of PGE_2 (76.9 vs. 55.1 %; p < 0.001), and the rate of postpartum bleeding (blood loss > 500 ml) was significantly higher (12 % vs. 2.4 %; p = 0.004). There were no significant differences in neonatal outcomes. Despite the low level of evidence (LoE III), this raises the question whether such a procedure to induce labour over several days can be implemented in clinical practice; moreover, notwithstanding the low rate of uterine rupture of 0.7 %, the vaginal application of misoprostol is in contrast with current guideline recommendations.

Comparison of Labour Induction Using Balloon Catheters and Elective Repeat Caesarean Section

A prospective multicentre study [36] compared the efficacy and safety of inducing labour in women with previous Caesarean section and unripe cervix (no information about the BS) using a Foley catheter (time left in place 12–24 h) or a double-balloon catheter followed by intravenous oxytocin once the cervix is ripe with the outcomes of pregnant women who underwent primary repeat Caesarean section (LoE IIb).

Primary endpoint of the study was composite maternal morbidity. With maternal morbidity rates of 7.4 vs. 4.5 %, there was no significant difference between groups (aOR 1.58; 95 % CI: 0.88–



▶ **Fig. 1** Fig. Osmotic cervical dilator vs. vaginal PGE_2 for cervical ripening after previous Caesarean delivery (data from [25]).
BS = Bishop Score

2.96). There were also no significant differences between groups with regard to the rates of uterine rupture (▶ **Table 1**), maternal infection, severe postpartum bleeding, and perinatal/neonatal outcomes. Because the differences between groups were not significant, the authors of the study no longer carry out primary repeat Caesarean section unless there is an additional medical indication. Apart from the lack of randomisation, points of criticism include significant selection bias due to the considerably higher risk profiles of the pregnant women who underwent primary repeat Caesarean section (e.g., older maternal age, higher rate of maternal co-morbidities) and the more than 3 times higher number of cases in the induction of labour group.

Hygroscopic Cervical Dilator (Dilapan-S) for Cervical Ripening/Induction of Labour after Previous Caesarean Delivery

In contrast to the extensive data on balloon catheters, a recent PubMed search showed that data on hygroscopic cervical dilators is extremely limited. An initial study by our working group published in 2017 [24] was continued [25]; as far as we know, this is the only study to investigate the use of the Dilapan-S dilator in women after previous Caesarean delivery.

A total of 104 pregnant women with previous Caesarean section and unripe cervix (BS ≤ 5) were included in a prospective observational study in which up to 5 Dilapan-S rods were placed in the cervical canal with a time left in place of 12 h; placement was repeated if required. Once the BS was ≥ 6, the women were administered intravenous oxytocin/underwent amniotomy. The results of this cohort were compared with those from a "historical" study group (a retrospective analysis of 102 pregnant women with unripe cervix) who received 1–2 mg vaginal PGE_2 gel every 8 h (maximum 3 applications/24 h). After the BS had increased to > 6, patients received intravenous oxytocin; the primary endpoint of this study was the rate of vaginal deliveries. The results are shown in ▶ **Fig. 1**. There were no differences in perinatal outcomes. The main limitations of this study are the lack of randomisation, the comparison between prospectively collected data and retrospectively collected data (LoE III), and the lack of data on the initial BS, the indications for labour induction, maternal infectious morbidity and the rate of uterine hyperstimulation.

Discussion

Despite a Cochrane analysis in 2017 [3], several meta-analyses/systematic reviews [21, 38, 39] and the publication of 12 additional, mostly retrospective, cohort or observational studies since 2016 (▶ **Table 1**), it is still unclear which method should be recommended to induce labour in women with previous Caesarean section based on the method's efficacy and safety. Important criteria which should guide clinical practice are the rate of vaginal deliveries and the incidence of uterine rupture. Uterine rupture is the most serious complication which occurs during the induction of labour in women with previous Caesarean section and rupture is also associated with hypoxic-ischaemic encephalopathy (mean frequency: 6.2 %) [16].

The higher rate of uterine rupture associated with PGE_2 (compared to the onset of spontaneous labour or the use of mechanical induction methods) reported in "historical" studies has affected the recommendations made in guidelines and led to PGE_2 being contraindicated in product information leaflets. But following a recent meta-analysis (45 studies) which reported a pooled incidence of uterine ruptures of 0.2–0.9 % [22], this contraindication should be revisited. There are currently no randomised controlled studies (RCT) comparing the outcomes after vaginal PGE_2 with those of mechanical methods used to induce labour in women with previous Caesarean section [3]. A currently recruiting prospective randomised study which aims to compare the outcomes of using a Foley catheter to induce labour in women with previous Caesarean section and unripe cervix (BS ≤ 5) with the results of inducing labour using vaginal tablets containing 3 mg PGE_2 could shed more light on the issue [40]. However, it is unlikely that the number of planned pregnant women (50 in each group) will reach statistical power as regards the risk of uterine rupture.

▶**Table 2** Use of balloon catheters for cervical ripening/induction of labour after previous Caesarean delivery. Results of prospective/retrospective studies; there are no randomised controlled studies.

Author/year	Study	N	Vaginal deliveries (%)	Oxytocin (%)	Uterine rupture (%)
Kehl S, Rath W 2016 [21]	meta-analysis	1406	56.4	68.4	0.7
Lamourdedieu C 2016 [39]	meta-analysis	1278	58	n/s	0.62
Boujenah J 2019 [34]	systematic review	2936	54	n/s	0.56
This review	systematic review (from 2016–2021)	3077	53.3	77.5	0.94

According to meta-analyses/systematic reviews, the mean rate of complete uterine rupture following the use of balloon catheters is between 0.56 and 0.7% (▶ **Table 2**); in our systematic review it is 0.94% (▶ **Table 1**). This does not differ significantly from the rates associated with vaginal PGE_2 [22] or the rates associated with the onset of spontaneous labour which are reported to be 0.4–0.9% [5, 6, 16, 41]. In a recent comprehensive prospective cohort study of women with previous Caesarean section [42], multivariate regression analysis showed no significant differences in the rates of uterine rupture and uterine suture dehiscence between inducing labour with a Foley catheter and the spontaneous onset of labour (aOR 2.02; 95% CI: 0.71–5.78 and aOR 1.32; 95% CI: 0.37–4.72). Uterine rupture after placement of a balloon catheter does not usually occur during the cervical ripening period but during intravenous administration of oxytocin [21, 36].

The mean frequency of uterine rupture after intravenous administration of oxytocin to induce labour in women with previous Caesarean section is reported to be 1.4% (0.4–2.3%) [5, 41], which is up to 3 times higher than the rates reported after the onset of spontaneous contractions [5, 43]. The risk of rupture is even higher if oxytocin is used to augment labour, irrespective of whether it is used to induce labour (2.2%) or used after spontaneous onset of labour (1.7%) [41]; when PGE_2 and oxytocin are applied sequentially, the risk of rupture is up to 16 times higher [44]. Oxytocin should not be used in women with unripe cervix (BS < 6) because it is not sufficiently effective [35] and is also associated with a 3–4 times higher risk of rupture compared to oxytocin applied in women with ripe cervix [4, 8, 9].

According to current guidelines [6, 11, 16], the use of misoprostol to induce labour in women with previous Caesarean section is contraindicated, as the mean risk of rupture is 6.2% (0–18%) [10]. It should be noted, however, that these figures are based entirely on studies carried out prior to 2004, in which vaginal misoprostol was mostly applied in a single dose of > 50 µg [10]. According to recent studies, the use of oral misoprostol (25 µg every 2 h) does not lead to a significantly higher rate of uterine rupture compared to vaginal PGE_2 and balloon catheters [31, 45]. In this respect randomised controlled studies are urgently needed.

It should be noticed, that studies often do not provide a precise definition of uterine rupture (complete/incomplete, uterine suture dehiscence) [16].

According to meta-analyses, the mean rate of vaginal deliveries after induction with a balloon catheter followed by amniotomy/intravenous oxytocin is 54–58%; the figure in our study is 53.3% (▶ **Table 2**), the mean vaginal delivery rate after vaginal application of PGE_2 was 66% [22], and the mean vaginal delivery rate following the administration of IV oxytocin was 60.7% [41]; this is significantly lower than the mean rate of vaginal deliveries after spontaneous onset of labour which was 72% (60–80%) [4, 43, 46]. Both the risk of rupture and the efficacy of labour induction depend significantly on various independent influencing factors, especially on whether the pregnant woman has had a previous vaginal delivery and on her cervical status (see above). Uterine hyperstimulation occurs significantly less often (0–2.7%) with balloon catheters [14] compared to the application of vaginal PGE_2 (mean rate: 7.2%; 0–25% [22]).

The 12 studies on the use of balloon catheters published since 2016 have low to moderate levels of evidence, and analysis of the studies highlighted the following obvious problems: significant heterogeneity between studies (e.g., different study designs, different/no comparison groups, different induction methods), a selection bias (e.g., different initial BS prior to initiating induction, comparisons of study groups with different risk profiles), a lack of statistical power with regard to maternal complications (especially uterine rupture) because of limited case numbers, and often no data about relevant outcome parameters (e.g., induction-to-delivery interval, use of oxytocin, maternal infection, perinatal/neonatal morbidity).

The use of hygroscopic cervical dilators (Dilapan-S) is an alternative mechanical method of cervical ripening [47]. According to AWMF guideline 015/088 [11], this approach is considered safe in women with unripe cervix, and even in women with a previous Caesarean section, where hygroscopic cervical dilators are the only method not beeing contraindicated. It is surprising that according to our recent PubMed search there are only two prospective observational studies on cervical ripening using the Dilapan-S in women with previous Caesarean delivery. Both studies are from the same working group [24, 25] and it is not yet possible to make definite evidence-based recommendations based solely on these studies.

Well-designed, prospective, randomised studies including a sufficient number of patients are needed which compare the use of balloon catheters vs. hygroscopic cervical dilators on the one hand and these mechancial methods vs. vaginal PGE_2/oral misoprostol on the other hand.

Conclusions

Even after evaluating the studies from 2016 to 2021, it is still unclear which induction method should be preferred for women with previous Caesarean section, especially if the cervix is unripe. For a comparative analysis of the different methods used to induce labour after previous Caesarean delivery, the most important parameters are the efficacy of the method (rate of vaginal deliveries) and the risk of uterine rupture, which significantly affects maternal and perinatal/neonatal morbidity and mortality.

Intravenous oxytocin should not be administered to women with unripe cervix because of its lack of efficacy and the increased risk of uterine rupture compared to women with ripe cervix (no increased risk of rupture compared to women with the onset of spontaneous labour); according to the product information, the use of oxytocin in women with unripe cervix is contraindicated. Vaginal PGE_2 and balloon catheter are effective methods to induce labour in women with previous Caesarean delivery, even though randomised controlled studies with sufficient case numbers are lacking. According to meta-analyses/systematic reviews, vaginal delivery in women with unripe cervix can be achieved in more than 50% of cases with the use of balloon catheters and in 66% of women with the use of vaginal PGE_2 while approximately 72% of women have a vaginal delivery after the onset of spontaneous labour. According to current guidelines, the major disadvantage of vaginal PGE_2 compared to mechanical methods is the higher rate of uterine rupture, however, when considering a recent meta-analysis (mean rate of uterine rupture 0.5%) this statement should be re-evaluated and be taken into account in further guidelines. The mean risk of uterine rupture when using balloon catheters is between 0.56 and 0.94% which is within the ranges reported for vaginal PGE_2 and the onset of spontaneous labour (0.4–0.9%). It has to be mentioned that these results only apply to women with a prior transverse lower uterine segment incision. Uterine rupture associated with balloon catheters does commonly not occur during the cervical ripening period but occurs during the time when intravenous oxytocin is administered.

According to the product information, hygroscopic cervical dilators (Dilapan-S) are currently the only method for cervical ripening in women with previous Caesarean delivery which is not contraindicated, however, available data are completely insufficient. However, the data for this is completely inadequate. After some initial promising results, further clinical research will be necessary to determine whether oral misoprostol might be a suitable option to induce labour in women with previous Caesarean section. But until no more data are available, misoprostol remains contraindicated for labour induction in women with previous Caesarean delivery.

The question whether induction of labour, if medically indicated, is preferable to repeat elective Caesarean section also remains unanswered as there is only one recent not randomised study with a moderate evidence [36].

Well-designed, randomised, controlled trials comparing balloon catheter vs. Dilapan-S on the one hand and mechanical methods vs. vaginal PGE_2/low dose oral misoprostol on the other hand are urgently needed to underpin evidence-based recommendations for clinical practice.

Conflict of Interest

Patrick Stelzl has a part-time job agreement as consultant and speaker and is member of the Steering Committee in concerns of the LION ("Labour Induction Outcomes Network") project for Angusta 25 µg tablets from Norgine Pharma GmbH. / Patrick Stelzl hat eine werksvertraglich geregelte nebenberufliche Berater- und Referenten-Tätigkeit und ist Steering Committee Mitglied im Rahmen des LION („Labour Induction Outcomes Network") Projektes für das Einleitungs-Präparat Angusta 25 µg Tabletten von der Firma Norgine Pharma GmbH.

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