Thieme

Effect of Premature Rupture of Membranes on Induction of Labor: A Historical Cohort Study

Einfluss des vorzeitigen Blasensprungs auf den Erfolg der Geburtseinleitung: eine historische Kohortenstudie

Authors
Sven Kehl[1], Christel Weiss[2], Ulf Dammer[1], Friederike Baier[1], Florian Faschingbauer[1], Matthias W. Beckmann[1], Marc Sütterlin[3], Jutta Pretscher[1]

Affiliations
1 Frauenklinik, Universitätsklinikum Erlangen, Erlangen, Germany
2 Abteilung für Medizinische Statistik, Biomathematik und Informationsverarbeitung, Universitätsmedizin Mannheim, Universität Heidelberg, Mannheim, Germany
3 Frauenklinik, Universitätsmedizin Mannheim, Mannheim, Germany

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Correspondence
Prof. Dr. Sven Kehl
Universitätsklinikum Erlangen, Frauenklinik
Universitätsstraße 21–23, 91054 Erlangen, Germany
sven.kehl@gmail.com

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ABSTRACT

Objective The aim of this study was to assess the influence of premature rupture of membranes (PROM) on the induction of labor.

Material and Method This historical cohort study analyzed 1861 inductions of labor at term using misoprostol which occurred between 2010 and 2015. Exclusion criteria included intrauterine fetal death, previous cesarean section, and fetal structural or chromosomal anomalies. Induction of labor for PROM (PROM group) was compared to induction for other indications (no-PROM group); the primary outcome measure was the cesarean section rate.

Results The cesarean section rate for the PROM group was significantly lower (21.9% vs. 26.3%, $p = 0.029$). The induction-to-delivery interval was shorter (mean: 972 [854–6734] min vs. 1741 [97–10834] min, $p < 0.0001$) and the rates of vaginal birth within 24 hours (80.9 vs. 52.0%, $p = 0.0001$) and 48 hours (98.4 vs. 85.3%, $p = 0.0001$) were higher in the PROM group. The impact of PROM on the cesarean section rate was not significant in multivariate analysis; however, PROM was found to have the greatest effect on the induction-to-delivery interval ($p < 0.0001$).

Conclusion Premature rupture of membranes significantly affects various outcome measures when delivery is induced, particularly the induction-to-delivery interval.

ZUSAMMENFASSUNG

Ziel Ziel dieser Arbeit war es herauszufinden, inwieweit ein vorzeitiger Blasensprung (PROM) den Erfolg einer Geburtseinleitung beeinflusst.

Material und Methode In dieser historischen Kohortenstudie wurden 1861 Geburtseinleitungen am Termin mit Misoprostol zwischen 2010 und 2015 analysiert. Zu den Ausschlusskriterien gehörten unter anderem ein intrauteriner Fruchttod, eine vorherige Sectio caesarea oder strukturelle respektive chromosomale Anomalien. Geburtseinleitungen wegen eines PROM (PROM-Gruppe) wurden mit Geburtseinleitungen aus anderen Indikationen (Kein-PROM-Gruppe) verglichen; der primäre Zielparameter war die Kaiserschnitt-Rate.

Ergebnis In der PROM-Gruppe war die Rate an Kaiserschnitten signifikant geringer (21,9 vs. 26,3 %, p = 0,029). Zudem waren in der PROM-Gruppe das Einleitung-Geburt-Intervall kürzer (Mittelwert 972 [854–6734] min vs. 1741 [97–10 834] min, p < 0,0001) und die Raten an vaginalen Geburten innerhalb von 24 Stunden (80,9 vs. 52,0 %, p = 0,0001) und 48 Stunden (98,4 vs. 85,3 %, p = 0,0001) höher. Mittels einer multivariablen Analyse wurde der Einfluss auf die Kaiserschnitt-Rate zwar nicht bestätigt, es konnte jedoch gezeigt werden, dass der PROM den stärksten Einfluss auf das Einleitung-Geburt-Intervall hat (p < 0,0001).

Schlussfolgerung Das Vorliegen eines vorzeitigen Blasensprungs beeinflusst bei einer Geburtseinleitung signifikant verschiedene Zielparameter, insbesondere das Einleitung-Geburt-Intervall.

Introduction

Premature rupture of membranes (PROM) after week 37 + 0 of gestation occurs in around 8–10 % of all births [1]. In around 40 % of cases, regular contractions only start after more than 24 hours.

Induction of labor is indicated in the absence of contractions as it reduces maternal and infant infection rates and may obviate the need to transfer the infant to a children's hospital post partum. It is also associated with higher satisfaction levels and no increase in cesarean section rates [2, 3].

A number of options are available to induce labor; medications to induce labor include oxytocin and prostaglandins, and a balloon catheter may be used for mechanical induction. The pharmaceutical information for prostaglandin E2 medication states that all forms of treatment after rupture of the "chorioamniotic membrane" should proceed "with care", without expanding on the possible problems that could occur. Administration of the synthetic prostaglandin E1 analog misoprostol is the most effective medication to induce labor [4 – 7], and its use after PROM has been studied in detail [5, 8 – 12]. Although previous studies did not find higher infection rates following the use of balloon catheters [13], they are not commonly used. Moreover, inducing labor with a balloon catheter is not beneficial compared to the administration of misoprostol alone – and should therefore not be used in this context [14]. As vaginal applications are generally associated with a higher risk of infection, oral administration (misoprostol) appears to be the preferred method of administration [15].

There are numerous studies on the efficacy of various procedures to induce labor, but these studies often ignore the fact that the occurrence of PROM itself could be a decisive factor influencing the induction of labor.

The aim of this study was therefore to investigate to what extent premature rupture of membranes affects the induction of labor.

Material and Method

This historical cohort study analyzed the induction of labor using misoprostol in singleton term pregnancies delivered at the University Gynecology Hospitals of Erlangen (2011–2015) and Mannheim (2010–2013).

Inclusion and exclusion criteria

Exclusion criteria included fetal breech presentation, intrauterine fetal death, previous cesarean section, and the presence of fetal structural or chromosomal anomalies. The induction of labor with mechanical procedures such as balloon catheters was not included in the analysis.

Procedure in routine clinical practice

Gestational age was determined based on the last menstrual period; presumed gestational age was then reviewed using the crown-rump length measured in the first trimester of pregnancy and corrected where necessary [16]. Induction of labor for PROM was compared with induction of labor for other indications. Rupture of membranes was diagnosed clinically using the standard in-house guidelines of the participating hospital or – if clinical findings were ambiguous – based on the detection of biomarkers (e.g. insulin-like growth factor-binding protein 1 [IGFBP-1]). Antibiotic prophylaxis with penicillin or clindamycin for patients allergic or intolerant to penicillin was initiated at twelve hours after PROM and administered until delivery of the infant. Prophylactic antibiotics were only administered immediately if Group B streptococci were detected.

In the group who had labor induction for PROM, induction of labor started at 12–24 hours after rupture of membranes. The Bishop score was determined before inducing labor with misoprostol. Misoprostol was administered orally. The initial dose was 50 µg, with repeat doses administered after four and eight hours in the absence of contractions. On the second day of labor induction, oral misoprostol was increased to 100 µg per dose, with a maximum of three administrations over a 24 hour period and a minimum interval of four hours between each administration. On the third day, 100 µg misoprostol tablets were administered vaginally.

Outcome measures

The primary outcome measure was the cesarean section rate. Secondary outcome measures included the induction-to-delivery interval, the number of vaginal births within 24 and 48 hours, the number of unsuccessful inductions of labor (defined as no birth within 72 hours), the total dose of misoprostol, umbilical cord blood pH and base excess (BE), and Apgar score at five minutes. The number of neonatal infections and of transfers of neonates to children's hospitals and the incidence of puerperal endometritis were also reviewed.

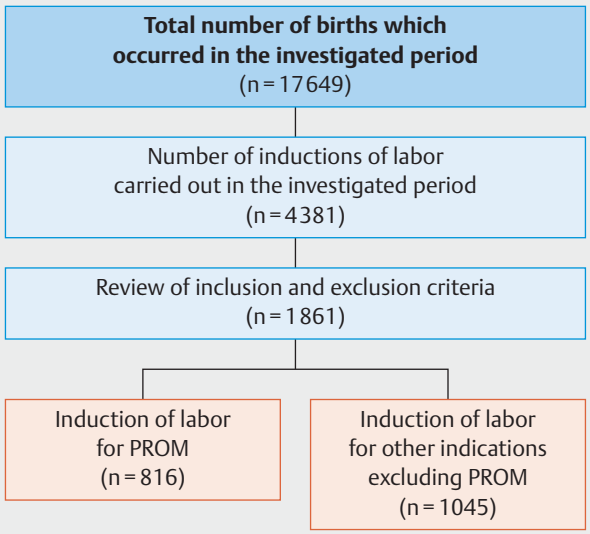
Statistical analysis

All statistical calculations and analyses were done with the statistical software package SAS, Release 9.3 (SAS Institute Inc., Cary, North Carolina, USA). Absolute and relative frequencies are shown for nominally scaled variables; nearly normally distributed quanti-

tative variables are presented as means and standard deviation. The median and the two min/max values are given for ordinally scaled and quantitatively discrete variables, instead of the mean.

χ^2-test or (if the necessary conditions were not fulfilled) Fisher's exact test were used to compare nominally scaled variables between the two groups. Comparisons of the means of two groups were done using t-test for two unpaired samples. Mann-Whitney U-test was used for ordinally scaled or discrete quantitative variables. All tests were 2-tailed. The results were considered significant if the p-value was less than 0.05.

For the primary outcome measure "cesarean section", the odds ratios and associated p-values of every potential moderating factor were determined by logistic regression analysis. Similarly, the secondary outcome measure "induction-to-delivery interval" was analyzed using linear regression, and the regression coefficient and p-value of every moderating variable were calculated. Multivariate regression analysis was done to analyze several moderating factors simultaneously. Parameters were integrated into the respective statistical model up to a significance level of 0.05 using the option "Selection = Forward".



▶ **Fig. 1** Flow chart with information on the total number of births and inductions of labor in the investigated cohort during the study period, after taking the inclusion and exclusion criteria into account.

Results

A total of 17649 births occurred in the study period; 4381 of them were induced (24.8%). After taking the inclusion and exclusion criteria into account, 1861 cases were included in this study (▶ **Fig. 1**). Misoprostol was administered to 816 women to induce labor for PROM (PROM group) and administered to 1045 women to induce labor for other indications (no-PROM group).

Demographic data

Demographic data are presented in ▶ **Table 1**. There were significant differences relating to various parameters between the two groups: the women in the PROM group were older (30.7 ± 5.2 years vs. 30.1 ± 5.6, p = 0.0196) and had a lower BMI (29.0 ± 5.3 vs. 30.5 ± 5.4, p < 0.0001). Gestational age and infant birth weight were lower in the PROM group at delivery (276.4 ± 7.4 vs. 283.3 ± 7.4, p < 0.0001; 3350.6 ± 417.8 vs. 3507 ± 473.2, p < 0.0001). Rates of gestational diabetes (9.6 vs. 15.9%, p < 0.0001), hypertensive disorders of pregnancy (1.7 vs. 7.7%, p < 0.0001) and intrauterine growth retardation/placental insufficiency (1.7 vs. 4.6%, p = 0.0006) were lower for the women in the PROM group.

▶ **Table 1** Demographic data of the study group with premature rupture of membranes (PROM) and the study group without premature rupture of membranes (no PROM).

	PROM (n = 816)	no PROM (n = 1045)	p-value
Age (years)	30.7 ± 5.2	30.1 ± 5.6	0.0196
Maternal height (cm)	166.6 ± 6.7	166.4 ± 6.6	0.5986
Maternal weight (kg)	82.3 ± 15.0	85.0 ± 16.0	0.0002
Body mass index	29.0 ± 5.3	30.5 ± 5.4	< 0.0001
Gravidity	1 (1–7)	2 (1–14)	< 0.0001
Parity	0 (0–4)	0 (0–9)	< 0.0001
Gestational age (days)	276.4 ± 7.4	283.3 ± 7.4	< 0.0001
Birth weight (g)	3350.6 ± 417.8	3507.5 ± 473.2	< 0.0001
Bishop score	2 (0–6)	2 (0–6)	0.0095
Gestational diabetes	78 (9.6%)	166 (15.9%)	< 0.0001
Hypertensive disorders of pregnancy	14 (1.7%)	80 (7.7%)	< 0.0001
Intrauterine growth retardation. placental insufficiency	14 (1.7%)	48 (4.6%)	0.0006

p < 0.05 is considered statistically significant

▶ **Table 2** Indications for the induction of pregnancy if there was no premature rupture of membranes.

Indications	no PROM
Overdue pregnancy	556 (53.2%)
Gestational diabetes	109 (10.4%)
Patient's request	88 (8.4%)
Anhydramnios, oligohydramnios	58 (5.6%)
Suspicion of fetal macrosomia	39 (3.7%)
Decreased fetal movement	20 (1.9%)
Intrauterine growth retardation, placental insufficiency, pathological Doppler sonography	36 (3.4%)
Hypertensive disorders of pregnancy (HDP)	61 (5.8%)
Suspicious/pathological CTG	28 (2.7%)
Cholestasis of pregnancy (ICP)	11 (1.1%)
Other	39 (3.7%)

CTG: cardiotocography

Indications for the induction of labor

▶ **Table 2** lists the indications for the induction of labor for the women in the no-PROM group. The most common indications were overdue pregnancy (53.2%), gestational diabetes (10.4%), and patient's request with no medical reason (8.4%).

Outcome measures

The outcome parameters for both groups are shown in ▶ **Table 3**. The cesarean section rate, i.e. the primary outcome measure, was significantly lower for the PROM group (21.9 vs. 26.3%, p = 0.0391). Likewise, the induction-to-delivery interval for the PROM group was shorter (972 ± 727 [854–6734] vs. 1741 ± 1335 [97–10 834] min, p < 0.0001) and the rate of vaginal births within 24 hours (80.9 vs. 52.0%, p = 0.0001) and 48 hours (98.4 vs. 85.3%, p = 0.0001) was higher. There were fewer unsuccessful inductions when labor was induced because of PROM (0.5 vs. 5.6%, p = 0.0001). Fewer doses of misoprostol were required in the PROM group (1 [1–10] vs. 3 [1–10], p < 0.0001) and the total dose of misoprostol was lower (50 [50–750] vs. 150 µg [50–2500],

▶ **Table 3** Outcome measures for the two study groups (PROM und and no PROM).

Outcome measures	PROM (n = 816)	no PROM (n = 1045)	p-value
Mode of delivery (n, %)			
▪ spontaneous delivery	529 (64.8%)	659 (63.1%)	0.4314
▪ surgical vaginal delivery	108 (13.2%)	111 (10.6%)	0.0826
▪ cesarean section	179 (21.9%)	275 (26.3%)	0.0290
Induction-to-delivery interval (min)*	972 ± 726.5	1741 ± 1335.0	< 0.0001
Vaginal birth within 24 h (n, %)**	515 (80.9%)	400 (52.0%)	< 0.0001
Vaginal birth within 48 h (n, %)**	627 (98.4%)	657 (85.3%)	< 0.0001
Unsuccessful induction of labor = no vaginal birth within 72 h (n, %)**	3 (0.5%)	43 (5.6%)	< 0.0001
Number of misoprostol doses administered (median, range)*	1 (1–10)	3 (1–100)	< 0.0001
Total dose of misoprostol (µg; median, range)*	50 (50–750)	150 (50–2500)	< 0.0001
Arterial cord blood pH < 7.05 (n, %)	5 (0.6%)	8 (0.8%)	0.6936
Arterial cord blood pH < 7.10 (n, %)	21 (2.6%)	24 (2.3%)	0.7013
BE < −12 (n, %)	4 (0.5%)	13 (1.3%)	0.0872
Apgar score after 5 min (median, range)	10 (5–10)	10 (4–10)	0.1756
Apgar score after 5 min < 7 (n, %)	7 (0.9%)	8 (0.6%)	0.4689
BE < −12 and Apgar score after 5 min < 7 (n, %)	0	1 (0,1%)	1.0000
Pathological CTG (n, %)	167 (20.5%)	258 (24.7%)	0.0313
Pathological fetal blood sampling results (n, %)	3 (0.4%)	5 (0.5%)	1.0000
Epidural analgesia (n, %)	388 (47.1%)	382 (38.0%)	< 0.0001
Oxytocin (n, %)	393 (49.0%)	443 (43.0%)	0.0106
Green amniotic fluid (n, %)	100 (12.3%)	172 (16.5%)	0.0108
Amniotic infection syndrome	7 (0.9%)	6 (0.6%)	0.4659
Postpartum transfer of infant to a children's hospital (n, %)	90 (13.2%)	139 (18.4%)	0.0075
Neonatal infection (n, %)	21 (2.6%)	29 (2.8%)	0.7896
Puerperal endometritis (n, %)	2 (0.3%)	2 (0.2%)	1.0000

BE: base excess

* without cesarean section and unsuccessful induction of labor

** without cesarean section

▶ **Table 4** Outcome measures in the two study groups PROM and no PROM according to parity.

Outcome measures	Primiparae			Multiparae		
	PROM (n = 597)	no PROM (n = 618)	p-value	PROM (n = 219)	no PROM (n = 427)	p-value
Mode of delivery						
▪ spontaneous delivery	328 (54.9%)	293 (47.4%)	0.0056	201 (91.8%)	366 (85.7%)	0.0158
▪ surgical vaginal delivery	99 (16.6%)	96 (15.5%)		9 (4.1%)	15 (3.5%)	
▪ cesarean section	170 (28.5%)	229 (37.1%)		9 (4.1%)	46 (10.8%)	
Induction-to-delivery interval (min)*	1114 ± 734	1976 ± 1379	< 0.0001	684 ± 618	1501 ± 1244	< 0.0001
Vaginal birth within 24 h (n, %)**	321 (75.2%)	165 (42.4%)	< 0.0001	194 (92.4%)	235 (61.7%)	< 0.0001
Vaginal birth within 48 h (n, %)**	418 (97.9%)	322 (82.8%)	< 0.0001	209 (99.5%)	335 (87.9%)	< 0.0001
Unsuccessful induction of labor = no vaginal birth within 72 hours (n, %)**	2 (0.5%)	31 (8.0%)	< 0.0001	1 (0.5%)	12 (3.1%)	0.0390
Number of misoprostol doses (median, range)*	1 (1–9)	3 (1–100)	< 0.0001	1 (1–10)	3 (1–16)	< 0.0001
Total misoprostol dose (µg; median, range)*	50 (50–750)	150 (50–2500)	< 0.0001	50 (50–750)	150 (50–1350)	< 0.0001
Arterial cord blood pH < 7.05 (n, %)	4 (0.7%)	6 (1.0%)	0.7532	1 (0.5%)	2 (0.5%)	1.0000
Arterial cord blood pH < 7.10 (n, %)	18 (3.0%)	20 (3.2%)	0.8209	3 (1.4%)	4 (0.9%)	0.6941
BE < −12 (n, %)	4 (0.7%)	9 (1.5%)	0.1802	0	4 (1.0%)	0.3048
Apgar score after 5 min	10 (5–10)	10 (4–10)	0.0678	10 (5–10)	10 (7–10)	0.2223
Apgar score after 5 min < 7 (n, %)	6 (1.0%)	6 (1.0%)	0.9542	1 (0.5%)	0	0.3401
BE < −12 and Apgar score after 5 min < 7 (n, %)	1 (0.2%)	0	1.0000	0	0	NC
Pathological CTG (n, %)	149 (25.0%)	204 (33.0%)	0.0020	18 (8.2%)	54 (12.7%)	0.0905
Pathological fetal blood sampling results (n, %)	3 (0.5%)	5 (0.8%)	0.7260	0	0	NC
Epidural analgesia (n, %)	333 (55.8%)	304 (50.0%)	0.0455	50 (23.1%)	78 (18.4%)	0.1553
Oxytocin (n, %)	350 (59.5%)	352 (58.2%)	0.6377	43 (20.1%)	91 (21.4%)	0.6992
Green amniotic fluid (n, %)	76 (12.7%)	126 (20.4%)	0.0003	24 (11.0%)	46 (10.8%)	0.9426
Amniotic infection syndrome	6 (1.0%)	6 (1.0%)	0.9520	1 (0.5%)	0	0.3390
Postpartum transfer to a children's hospital (n, %)	78 (15.4%)	98 (22.0%)	0.0085	12 (6.9%)	41 (13.2%)	0.0333
Neonatal infection (n, %)	20 (3.4%)	20 (3.2%)	0.9115	1 (0.5%)	9 (2.1%)	0.1767
Puerperal endometritis (n, %)	2 (0.3%)	1 (0.2%)	0.6183	0	1 (0.2%)	1.0000

* without cesarean section and unsuccessful induction of labor

** without cesarean section

NC: non-calculable

p < 0.0001). There were significantly fewer pathological CTG patterns (20.5 vs. 24.7%, p = 0.0313), cases of green amniotic fluid (12.3 vs. 16.5%, p = 0.0108), and transfers of infants to the children's hospital (13.2 vs. 18.4%, p = 0.0075) in the PROM group; however, the rates of oxytocin administration (49.0 vs. 43.0%, p = 0.0106) and epidural analgesia (47.1 vs. 38.0%, p < 0.0001) were higher.

Outcome measures according to parity

▶ **Table 4** shows the outcome measures broken down according to parity. The cesarean section rate was lower in the PROM group for both primiparae (28.5 vs. 37.1%, p = 0.0056) and multiparae (4.1 vs. 10.8%, p = 0.0158). The frequencies for cesarean section, spontaneous delivery, and surgical vaginal delivery in the PROM group differed significantly from those of the no PROM group for both primiparae and multiparae (▶ **Table 4**). Similarly, the induction-to-delivery interval was shorter (1114 ± 734 [167–9001] vs. 1977 ± 1379 [288–9001] min, p < 0.0001; 684 ± 618 [54–59 696] vs. 1501 ± 1245 [97–10 834] min, p < 0.0001), the rate of vaginal deliveries within 24 hours (75.2 vs. 42.4%, p < 0.0001; 92.4 vs. 61.7%, p < 0.0001) and 48 hours (97.9 vs. 82.8%, p < 0.0001; 99.5 vs. 87.9%, p < 0.0001) was higher, and the percentage of successful inductions of labor was lower (0.5 vs. 8.0%, p < 0.0001; 0.5 vs. 3.1%, p = 0.0390). Misoprostol was administered less often (1 [1–9] vs. 3 [1–10], p < 0.0001; 1 [1–10] vs. 3 [1–16], p < 0.0001) and the total dose of administered misopros-

▶ **Table 5** Univariate and multiple logistic regression analysis for the primary outcome measure "cesarean section". Parameters with a significance level of up to α = 0.05 were included in the final statistical model.

Moderating factor	Univariate analysis		Multiple logistic regression	
	odds ratio	p-value	odds ratio	p-value
Age (years)	1.0000	0.9646	–	–
Maternal height (cm)	0.966	< 0.0001	0.959	< 0.0001
Maternal weight (kg)	1.012	0.0003	–	–
Body mass index	1.061	< 0.0001	1.060	< 0.0001
Gestational age (days)	0.998	0.7432	–	–
Birth weight (g)	1.000	0.8639	–	–
Gravidity	0.653	< 0.0001	0.633	< 0.0001
Parity	0.413	< 0.0001	–	–
Bishop score	0.818	< 0.0001	0.852	< 0.0001
PROM	0.787 (yes vs. no)	0.0292	–	–
Gestational diabetes	1.262 (yes vs. no)	0.1303	–	–
Hypertensive disorders of pregnancy	2.783 (yes vs. no)	< 0.0001	2.063 (yes vs. no)	0.0030
Intrauterine growth retardation, placental insufficiency	2.158 (yes vs. no)	0.0037	–	–

▶ **Table 6** Univariate and multiple linear regression analysis for the secondary outcome measure "induction-to-delivery interval". Parameters with a significance level of up to α = 0.05 were included in the final statistical model. The binary factors PROM, gestational diabetes, and hypertensive disorders of pregnancy had a value of 0 (no) or 1 (yes).

Moderating factor	Univariate analysis		Multiple linear regression	
	regression coefficient	p-value	regression coefficient	p-value
Age (years)	− 6.804	0.2513	–	–
Maternal height (cm)	3.797	0.4224	–	–
Maternal weight (kg)	12.147	< 0.0001	–	–
Body mass index	39.603	< 0.0001	21.391	< 0.0001
Gestational age (days)	23.345	< 0.0001	–	–
Birth weight (g)	0.333	< 0.0001	0.225	0.0012
Gravidity	− 90.404	0.0003	–	–
Parity	− 143.724	< 0.0001	− 213.596	< 0.0001
Bishop score	− 136.677	< 0.0001	− 111.166	< 0.0001
PROM	− 768.939	< 0.0001	− 710.722	< 0.0001
Gestational diabetes	337.895	0.0003	243.398	0.0070
Hypertensive disorders of pregnancy	842.171	0.0002	417.867	0.0102
Intrauterine growth restriction, placental insufficiency	424.003	0.0290	–	–

tol was lower (50 [50–750] vs. 150 µg [50–2500], p < 0.0001; (50 [50–750] vs. 150 µg [50–1350], p < 0.0001). Pathological CTG patterns (25.0 vs. 33.0%, p = 0.0020) and green amniotic fluid (12.7 vs. 20.4%, p = 0.0003) were only lower for primiparae in the PROM group. The epidural analgesia rate was also only significantly higher for the primiparae in the PROM group (55.8 vs. 50.0%, p = 0.0455). The percentage of infants transferred to a children's hospital post partum was lower for both primiparae and multiparae (15.4 vs. 22.0%, p = 0.0085; 6.9 vs. 13.2%, p = 0.0333).

Amniotic infection syndrome (primiparae/multiparae: < 0.5%) and puerperal endometritis (primiparae/multiparae: approx. 0.2%) were very rare events. Neonatal infections were more common for primiparae compared to multiparae (40 [3.3%] vs. 10 [1.5%], p = 0.0270).

Multivariate analysis

The results of multivariate analysis for the outcome measures "cesarean section" and "induction-to-delivery interval" are shown in ▶ **Tables 5** and **6**. As regards the cesarean section rate, it is clear that some factors which were shown to be significant moderating

factors were not included in the multiple model. Whether the mother had PROM was one of them. The reason for not including PROM was that other factors (e.g., gravidity and BMI) had a stronger impact, and the combination of the five factors included in the final model were best suited to explaining the outcome measures. Knowing whether or not the mother had PROM provided no additional relevant information.

However, the secondary outcome measure "induction-to-delivery interval" was strongly affected by PROM. Whether the mother had PROM or not had the greatest impact on this secondary outcome measure compared to all other investigated factors. ▶ **Table 6** shows that when the mother had PROM, the induction-to-delivery interval was shorter by an average of approximately 711 minutes (including all other factors integrated into the final model).

Discussion

This historical cohort study showed that induction of labor for PROM is associated with lower cesarean section rates, a shorter induction-to-delivery interval, and a higher number of births within 24 and 48 hours compared to other indications for the induction of labor. This finding applied to both primiparae and multiparae. In multivariate analysis the effect of PROM was only significant for the induction-to-delivery interval.

This study used oral misoprostol. Misoprostol is the most effective medication for inducing labor; the rate of cesarean sections after misoprostol administration is significantly lower than, for example, after the administration of dinoprostone [4]. A Cochrane analysis done in 2014 found that oral misoprostol was more effective than placebo to induce labor and resulted in fewer cesarean sections, irrespective of whether women had PROM or not [4]. Park et al. reported that primiparae who received dinoprostone or oxytocin to induce labor for PROM had higher cesarean section rates compared to women who did not have PROM [17]. In their meta-analysis Wood et al. investigated whether the induction of labor without PROM led to a higher rate of deliveries by cesarean section. In contrast to the findings in our study presented here, they came to the conclusion that inducing labor when membranes were intact resulted in fewer cesarean sections [18].

In our current study, the induction-to-delivery interval in the PROM group was significantly shorter, even in multivariate analysis, and the rate of unsuccessful inductions (no vaginal birth within 72 hours) was lower. This shorter interval to delivery has already been reported in a number of earlier previous studies [2, 5, 19–21]. The rupture of membranes itself is a trigger for the start of childbirth [22], even if contractions only start more than 24 hours later in around 40 % of women [2].

Misoprostol can safely be used to induce labor after PROM. The rate of pathological CTGs in the PROM group was lower, and there was no difference in the rate of invasive procedures to investigate possible issues (e.g., fetal blood analysis). In their study, Crane et al. also found no difference with regard to the number of fetal blood analyses performed when misoprostol was administered for premature rupture of membranes at term compared to the use of oxytocin [8].

Our study found no difference in the frequency of infant and maternal infections. Amniotic infection syndrome and puerperal endometritis were extremely rare. There was no difference in the rates of neonatal infection between the two groups, but neonatal infection occurred more frequently with primiparae than multiparae. But this could be due to the longer interval until the infant was delivered, as previous studies have reported that a longer interval after PROM is associated with a higher risk of maternal infection [23]. Moreover, vaginal administration also appears to be associated with an increased risk of infection [24], and on the third day of inducing labor, misoprostol was administered vaginally.

The limitation of this study is its retrospective nature. The two comparison groups also differed significantly from one another with regard to certain factors. But, given the differences, these factors did not always appear to be clinically relevant. The strengths of this study are the large number of cases, the study's multicentricity, and the uniform procedure used to induce labor with misoprostol.

This study was able to show that PROM at term has a beneficial effect on inducing labor and results in a shorter induction-to-labor interval. When studies are carried out to assess the efficacy of inducing labor, the information from our study should lead to PROM being taken into account and cases with PROM excluded from the analysis.

Conclusion for Clinical Practice

In summary, the induction of labor with misoprostol in women with premature rupture of membranes leads to a shorter induction-to-delivery interval compared to the induction of labor for other indications. This impact of PROM should be taken into account when studies are carried out to assess the efficacy of methods used to induce labor. The use of misoprostol to induce labor for PROM is safe as it results in fewer pathological CTGs and fewer postpartum transfers of neonates to children's hospitals, and there is no increase in the rates of infant and maternal infection.

Conflict of Interest

The authors declare that they have no conflict of interest.

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