Title:

Double balloon catheter (+oxytocin) versus dinoprostone vaginal insert for term rupture of membranes: a randomized controlled trial (RUBAPRO)

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ABSTRACT

Objective: To demonstrate that a double balloon catheter combined with oxytocin decreases time between induction of labour and delivery (TID) as compared to a vaginal dinoprostone insert in cases of PROM at term.

Design: Prospective, randomized, controlled trial.

Setting: French university hospital

Population: Patients undergoing labour induction for PROM at term with unfavorable cervix.

Methods: We compared the double balloon catheter over a period of 12 hours with adjunction of oxytocin 6 hours after catheter insertion, versus dinoprostone vaginal insert. After device ablation, cervical ripening continued only with oxytocin.

Main outcome measures: The primary outcome was TID. Secondary outcomes concerned delivery mode, maternal and fetal outcome and were adjusted for parity.

Results: 40 patients per group were randomized. Each group had similar baseline characteristics. The study failed to demonstrate reduced TID (16.2 vs 20.2 hours, ES = 0.16 (-0.27 to 0.60), *p*=0.12) in catheter group versus dinoprostone except in nulliparous women (17.0 vs 26.5 hours, ES = 0.62 (0.10 to 1.14), *p*=0.006). The rate of vaginal delivery <24h significantly increased with combined induction (88.5% vs 66.6%, *p*=0.03). No statistical difference was observed concerning caesarean rate (12.5% vs 17.5%, p>0.05), chorioamnionitis (0% vs 2.5%, p=1), postpartum endometritis, maternal or neonatal outcomes. Procedure-related pain and tolerance to devices were found to be similar for the two methods.

Conclusion: The double balloon catheter combined with oxytocin is an alternative for cervical ripening in case of PROM at term, and may reduce TID in nulliparous women.

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Keywords: premature rupture of membranes, labour induction, unfavorable cervix, cervical ripening balloon, nulliparous.

Clinical trial registration: EudraCT number: 2017-002687-41; clinicaltrials.gov: NCT03310333.

Tweetable abstract: Double balloon combined with oxytocin reduces time to delivery as compared to vaginal dinoprostone in case of PROM at term in nulliparous.

INTRODUCTION

Premature rupture of membranes (PROM) at term, a complication in 8% of pregnancies[1], is associated with risk of chorioamnionitis and neonatal sepsis, which increase with PROM duration [2,3]. Spontaneous labour occurs in 60-70% of these patients within 24 hours[2–4], however when no effective uterine contraction occurs, induction of labour (IOL) is the optimal strategy for women with PROM at term according to recommendations by French and American Colleges of Obstetricians and Gynecologists.[5,6]

Prostaglandins and oxytocin are frequently used for cervical ripening in cases of PROM[7], and reported to be of similar efficacy when there is unfavourable cervix[7]. Mechanical induction using a balloon is generally considered as effective as a vaginal dinoprostone, though less effective than low-dose vaginal misoprostol, despite improved levels of safety. Studies comparing a mechanical device (Foley catheter) for IOL in cases of PROM versus prostaglandins or oxytocin have reported similar time intervals from induction to delivery, and no differences concerning maternal or neonatal infections, with the exception of one retrospective study that revealed quicker deliveries associated with a Foley catheter[8–11]. In multiparous women with intact membranes, the simultaneous use of a cervical ripening balloon and oxytocin led to higher rates of delivery within 24 hours and a shorter induction-to-delivery interval without adverse maternal or neonatal outcomes[12]. Two trials conducted in women with PROM at 34 or more gestational weeks, reported that the combined use of a Foley catheter and oxytocine was not found to shorten the time to delivery compared with oxytocine alone, with one of the trials indicating a likely increase in the incidence of clinical chorioamnionitis [9,10].

Since the optimal method for IOL in cases of PROM at term is currently unknown, the main objective of this study was to determine whether the use of a double balloon catheter combined with oxytocin would lead to a reduction in time between IOL and delivery (TID) when compared to a vaginal dinoprostone insert. The secondary objective was to compare maternofetal outcomes for each induction strategy, and to investigate the association between parity and choice of strategy.

METHODS AND ANALYSIS

This study was a prospective, monocentric, randomized, controlled clinical trial with two parallel arms comparing induction via double balloon catheter (+ oxytocin) with vaginal dinoprostone insert, in cases of PROM at term. The protocol was in accordance with the Declaration of Helsinki and was approved by the Ethics Committee on August 22th, 2017 (Comité de Protection des Personnes Sud Méditerranée IV N°ID-RCB: 2017-A00811-52) and by the National Agency for Medicines and Health Products Safety on November 17th, 2017 (ANSM: 170440RS-22). The trial was registered at http://www.clinicaltrials.gov under the registration number NCT03310333.

Participants

Women with a live, singleton gestation at term (37 or more weeks of gestation) with PROM, an unfavorable cervical examination (Bishop score < 6), and no contraindication to labour who presented at the University Hospital of Clermont-Ferrand, France between February 2018 and March 2019, were approached for study participation. Patients underwent spontaneously rupture of membranes at least 12 hours before randomization and were registered on the French healthcare system. Spontaneous rupture of membranes

was defined as amniotic fluid leakage with pooling or a positive detection of Insulin-like Growth Factor Binding Protein 1 (IGFBP-1) in cervicovaginal secretions revealed by an immunochromatographic test (ActimProm® test, Alere, France), in case of doubt of PROM.

Maternal exclusion criteria included those in active labour, suspected intraamniotic infection, detection of group B *Streptococcus* on any vaginal or urinary sample during the current or any previous pregnancy, placental abruption or significant hemorrhage, any prior uterine surgery including caesarean delivery, any contraindication to vaginal delivery, human immunodeficiency virus or herpetic genital lesions. Fetal exclusion criteria were non-cephalic presentation, severe fetal anomalies, intrauterine fetal demise, growth restriction < 3rd percentile with Doppler anomalies and non-reassuring fetal heart rate (FHR) tracing.

Study procedures

Women meeting all inclusion criteria and presenting no exclusion criteria were invited to participate and those who gave written informed consent were enrolled and randomized. Randomization was conducted using Research Electronic Data Capture (REDCap) software and was carried out in random-sized blocks with stratification on parity (nulliparous vs parous)[13]. Details of the randomization algorithm were known to the data manager alone.

Participants were randomly allocated to the double balloon catheter (+ oxytocin) or vaginal dinoprostone insert groups. A course of prophylactic antibiotics—amoxicillin, or clindamycin in case of allergy—was administered upon recruitment and up to time of delivery to prevent chorioamnionitis. The double balloon device used was the Cook® Cervical Ripening Balloon, (Cook Medical Europe, Ireland, reference: J-CRBS-184000). The catheter was inserted following the manufacturer's instructions[14]. Each balloon was filled with 80 mL of saline solution and the device remained in place for 12 hours. Oxytocin was started six

hours after device insertion, with epidural analgesia following patient wishes. Cervical assessment was performed after catheter removal (H12), or earlier if the patient experienced severe pain or spontaneous expulsion of the device. Oxytocin was continued according to uterine contractions after catheter loss or removal. In the second group, the vaginal dinoprostone insert (Propess®, Ferring SAS, France) was inserted for a maximum of 24 hours. In cases where the insert was expulsed in the first 12 hours and the patient had no contractions or continued to present an unfavorable cervix, another vaginal system was placed for a maximum further 24 hours. Oxytocin could then be administered 30 min after removal of the vaginal system, with or without epidural analgesia as per patient request. For the two groups, FHR and uterine contractions were monitored 30 minutes before and two hours after device placement, then every six hours until device extraction or expulsion, or entry into labour and continuously for patients receiving oxytocin. Patient pain levels were assessed every six hours until device removal by a midwife, who also monitored temperature and blood pressure in accordance with the recommendations[15]. The management of obstructed labour, FHR abnormalities and final delivery method was at the discretion of the physician on duty. After delivery, placenta samples were collected and maternal satisfaction recorded before discharge. Data regarding potential maternofetal infections were recorded until the end of hospitalization and used in the analysis. No additional visits after discharge were scheduled. The nature of the intervention rendered impossible the blinding of physicians, midwives or patients. The protocol was published on the BMJ open website[16] and the main study stages are described in Figure 1.

Outcomes data were either documented on an ongoing basis by the labour and delivery team or obtained from medical records by research personnel not involved with data analysis. The primary outcome was the period of time between induction (time of

induction device insertion) and delivery (time of birth). Secondary outcomes included time between PROM and the start of induction, delivery rate within the first 24 hours, duration of induction device placement; spontaneous or assisted vaginal delivery rate, rate of caesarean section and indications; postpartum haemorrhage rate (blood loss>500 mL), Bishop score or measure of dilatation on catheter loss or removal , rate of balloon expulsion within 12 hours of placement, rate of oxytocine cessation, balloon or vaginal dinoprostone insert ablation due to suboptimal FHR, epidural analgesia rate, time taken to achieve active labour and full dilatation, pain levels assessed using the Visual Analog Scale of Pain Intensity (VASPI) at time of placement, every 6 hours and after ablation, uterine hyperstimulation rate, fever during labour rate, rate of chorioamnionitis based on Newton's criteria, rate of materno-fetal infection, endometritis, histological chorioamnionitis and positive bacteriological culture. Neonatal outcomes included birth weight, lactates, rate of Apgar score <7 at 5 min, umbilical artery pH<7.15 and neonatal intensive care unit admission.

Statistical analysis and sample size calculations

Sample size estimation was based on data from our center and from results reported by Mackeen et al [10]. To highlight a clinical and relevant absolute difference of 9 hours, 26 patients per group were needed for a two-sided type I error of 5% and a statistical power of 90%. However, to ensure satisfactory statistical power for secondary outcomes, 40 patients per group were required.

Data storage and management were performed following international guidelines. Results from intermediate analysis and all records concerning transfer of participating patients or their newborns to intensive care or reanimation units were examined by an

independent Data Monitoring Safety Committee. Intermediate safety analyses were conducted for caesarean section and chorioamnionitis rates.

All analyses were conducted with Stata software (version 13, StataCorp, College Station, US) in accordance with the International Conference on Harmonization Good Clinical Practice guidelines. All statistical tests were performed with a type I error at 5%, and primary analysis was based on intention to treat (ITT). Continuous variables were presented as means and SD, or as medians and quartiles [interquartile range], according to the statistical distribution. Normality was studied using the Shapiro-Wilk test. Comparison of the primary outcome between randomized groups was performed using the non-parametric Mann-Whitney test, as t-test assumptions were not met. Homoscedasticity was checked using the Fisher-Snedecor test. The result was also expressed using effect-size (ES) and 95% confidence interval (95% CI) after logarithmic transformation. The primary outcome was also treated as censored data associated with a favourable outcome (uncomplicated delivery, without caesarean section). The estimation was carried out using the Kaplan-Meier method and comparison between randomized groups using the log-rank test.

The Student's t-test and Mann-Whitney test were applied for other quantitative parameters, with Chi-squared and Fisher's exact tests used for categorical parameters. When appropriate, results were expressed using absolute differences and 95% confidence intervals.

On the basis of clinical relevance and European Medicines Agency and Consolidated Standards of Reporting Trials recommendations, subgroup analysis according to parity was performed after investigation of the interaction *parity × randomization* group.

RESULTS

Participant characteristics

From February 2018 to March 2019, we randomized 80 patients, with 40 allocated to each group. A flow chart presenting patient recruitment is shown in Figure 2. There were no withdrawals or patients lost to follow up and both groups were similar with regard to demographic and antenatal characteristics (Table 1). All patients received the device allocated by randomization with the exception of one patient who received a double balloon and spontaneously went into labour immediately after randomization. The median interval between PROM and IOL was similar between the two groups (25.9 [22.8; 29.4] vs 26.8 [24.0; 29.4] hours, *p*=0.46) (Table 2). Using intention to treat, the study failed to demonstrate reduced TID (16.2 vs 20.2 hours, ES = 0.16 (-0.27 to 0.60), *p*=0.12) but treatment by double balloon catheter (+ oxytocin) was found to be associated with a significantly higher rate of delivery <24h (90% vs 57.5%, absolute difference = 33% (15 to 50), *p*=0.001) and vaginal delivery<24h (88.5% vs 66.6%, absolute difference = 22% (3 to 41), *p*=0.03)(Figure 3). In nulliparous women ripened using a double balloon catheter (+ oxytocin), the study found reduced TID (17.0 vs 26.5 hours, ES = 0.62 (0.10 to 1.14), *p*=0.006), a significantly higher rate of delivery <24h (89.6% vs 41.4%, absolute difference = 48% (27 to 69), p=0.001), vaginal delivery <24h (87.5% vs 50%, absolute difference = 38% (13 to 62), *p*=0.01) and shorter induction to active labour time (10.0 [7.5; 12.5] vs 14.7 [9.7; 23.6] hours, ES = 0.69 (0.03 to 1.31) *p*=0.03), however the reduction in delay between induction and full cervical dilatation did not reach significance (14.5 [12.2; 19.1] vs 19.9 [13.1; 29.5] hours, ES = 0.45 (-0.13 to1.02), *p*=0.06)(Table 2). Ripening device removal or oxytocin discontinuation for abnormal FHR rates were similar between the two groups as for rates of uterine hyperstimulation and caesarean section (12.5% vs 17.5%, *p*=0.75). Despite oxytocin quantities being significantly higher in the double balloon catheter (+ oxytocin) group, no differences were found in

postpartum haemorrhage rates (Table 3) or neonatal outcomes. (Table 4). We observed no postpartum endometritis, only one materno-fetal infection and no significant differences concerning clinical, bacteriological or histological chorioamnionitis (Table 5). Device placement was significantly less painful for the dinoprostone vaginal insert (VASPI: 4.6 ± 2.9 vs 2.9 ± 2.5, ES = 0.58 (0.10 to 1.06), *p*=0.02). However, after the placement phase, reported pain levels were significantly lower in the double balloon catheter (+oxytocin) group. A majority of patients responded positively to the question "Would you agree to use the same cervical ripening device during a future delivery?" (Table 6).

DISCUSSION

Main Findings

The RUBAPRO trial failed to demonstrate that the association of a double balloon catheter with oxytocin decreased TID, compared to a vaginal dinoprostone insert except in nulliparous women, for whom a difference of 9 hours was observed. Delivery <24h and vaginal delivery <24h rates however increased in the double balloon catheter (+oxytocin) group for the entire study population.

Interpretation

A double balloon catheter and oxytocin combined, appeared more efficient for nulliparous women who were in the majority in both groups (29/40 patients in each group), in line with other trials studying ripening of PROM at term[8,10,17]. The few studies that have investigated the efficiency and safety of IOL for PROM using mechanical devices, at or near term, describe similar TID when compared to other methods[7–10], with the exception of

Mackeen et al[17] who reported significantly decreased TID when comparing the Foley catheter versus misoprostol in a retrospective bicentric study. To our knowledge no previous study has reported on the use of a double balloon catheter or compared use of a mechanical device with vaginal dinoprostone insert in a PROM-related context .

In other indications however, several authors have compared IOL by double balloon catheter with adjunction of oxytocin versus dinoprostone or oxytocin[18,19]. They observed lower TID, and a higher rate of delivery <24h in the group with combined catheter and oxytocin. A recent meta-analysis has also demonstrated that simultaneous use of oxytocin with a Foley catheter could shorten induction to delivery time and increase deliveries within 12 to 24 hours[20]. The adjunction of oxytocin is likely to favour a synergistic action. As concomitant administration of prostaglandin and oxytocin is strictly forbidden to prevent risk of tachysystolia or uterine hyperstimulation[21], oxytocin may be administrated earlier when used in combination with mechanical devices, positively impacting the period of time before birth. Finally, the combination of catheter plus oxytocin has not been shown to impact rates of caesarean section, postpartum hemorrhage, or neonatal complications[19,22,2319,22,2321,24,2521,24,25].

Clinical implications

Our study demonstrated that a double balloon catheter combined with oxytocin could be an alternative to a dinoprostone vaginal insert for cervical ripening in cases of PROM with unfavorable cervix at term. This combination was associated with significantly higher delivery <24h or vaginal delivery<24h rates and may reduce TID in nulliparous women. Observation of systematic antibiotic prophylaxis and exclusion of group B streptococcus patients, revealed no differences concerning maternal or fetal infection.

Studies generally report no impact of mechanical devices on infectious complications even in case of pre-labour rupture of membranes[11,17,24,25]. Mackeen et al highlighted an increased risk of clinical chorioamnionitis with the use of a Foley catheter and oxytocin versus oxytocin alone (8% vs 0%, $p<0.01$)[10]. In this study, 30% of patients presented vaginal portage of group B streptococcus which is an independent infectious risk factor in cases of PROM. Moreover, antibiotics were only administered in group B identified patients or to those with clinically suspected intraamniotic infection, and as expected, histological chorioamnionitis was more frequent than clinical chorioamnionitis. This is a current finding in a PROM context as membrane inflammation greatly contributes both to rupture and entry into labour[26,27].

Patients were interviewed about their childbirth experience focusing on pain management and satisfaction[28]. In our study, although catheter insertion was significantly more painful when compared to that of vaginal dinoprostone, pain levels at 6 and 12 hours after introduction of the ripening device were significantly lower in the double balloon (+oxytocin) group. This result may be explained by earlier epidural with concomitant administration of oxytocin (6 hours). Boyon *et al*. also observed a higher frequency of VASPI > 4 during prostaglandin use when compared with a double balloon catheter[29]. Concordant results have been described by Lim *et al*. who found that women were equally satisfied with both methods and would similarly recommend their IOL method[30].

Research Implications

Additional larger multicentric studies are required to support our results, notably concerning the role of parity. Furthermore mechanical device safety should be confirmed prior to extending use to group B streptococcus positive patients presenting with PROM.

Strengths and limitations

Our study is the first randomised controlled trial to compare the use of a double balloon catheter (+oxytocin) versus a vaginal dinoprostone insert for IOL in cases of PROM at term. The main limitations of this study concern the sample size and monocentric design. In addition, the nature of the intervention made it impossible to 'blind' physicians, midwives or patients. To compensate for this absence of blinding we chose to use an objective primary outcome (TID). We initially estimated the sample size using a clinical and relevant absolute difference of 9 hours, though our trial finally revealed an overall difference of 4 hours except for nulliparous women (more than 9 hours). A much larger study would be required to address questions concerning maternal or neonatal infections.

Summary

The RUBAPRO trial failed to demonstrate that combined double balloon catheter and oxytocin decreased TID, when compared to a vaginal dinoprostone insert, except in nulliparous women for whom a difference of 9 hours was observed. Delivery <24h and vaginal delivery <24h rates however increased in the double balloon catheter (+oxytocin) group for the entire population. Finally we observed no differences in caesarean delivery, maternal or neonatal infection rates, following the systematic administration of antibiotic prophylaxis.

FOOTNOTES:

Disclosure of Interests: The authors report no conflict of interest.

Contribution to Authorship:

ED, MR, DG developed the study concept, design and aims, designed data collection tools, analyzed the data and drafted and revised the paper.

ED, FP, MR monitored data collection throughout the study.

AD, MA, CH, LDB, PB provided substantial contributions to the conception and design of the work and co-investigated patient inclusion.

BP provided statistical expertise in clinical trial design, conducted analysis of the results and revised the paper.

ED, AD, FP, MR, BP, MA, CH, LDB, PB, DG contributed to refinement of the study protocol and approved the final manuscript.

Details of Ethics Approval

The protocol was in accordance with the Declaration of Helsinki and was approved by the Ethics Committee on August 22th, 2017 (Comité de Protection des Personnes Sud Méditerranée IV N°ID-RCB: 2017-A00811-52) and by the National Agency for Medicines and Health Products Safety on November 17th, 2017 (ANSM: 170440RS-22).

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TABLES

Table 1 - Demographic and Antenatal Characteristics

Variable	Double balloon + oxytocine (n=40)	Vaginal dinoprostone insert (n=40)
Maternal age in y Median [IQR]	27.5 [24.9-30.6]	27.7 [25.4-30.4]
Parity		
Nulliparous	29 (72.5%)	29 (72.5%)
Parous	11 (27.5%)	11 (27.5%)
Maternal prepregnancy BMI in kg/m² Median [IQR]	23.3 [20.6-28.4]	24.6 [22-27.3]
Associated pregnancy pathologies	7 (17.5%)	9 (22.5%)
Diabetes mellitus	5 (12.5%)	6 (15%)
HTN	0	0
Preeclampsia	0	0
IUGR	0	0
Other	2 (5%)	4 (10%)
Gestational age at PROM in w, Median [IQR]	39.4 [38.2-40.4]	39.3 [38.5-40.3]
Bishop score at randomization Mean ± SD	3.5 ± 1.1	3.5 ± 1.3

BMI: body mass index; HTN: hypertension; IUGR: intrauterine growth restriction; IQR: interquartile range; SD: standard deviation

Table 2 - Labour and delivery characteristics

Variable	Double balloon + oxytocine (n=40)	Vaginal dinoprostone (n=40)	P value
Time PROM to IOL in h Median [IQR]	25.9 [22.8-29.4]	26.8 [24-29.4]	0.46
Time IOL – loss ou removal of device in h, Median [IQR]	8.6 [5.0-12.0]	13.0 [6.6-18.4]	**0.02**
Time IOL – active labour phase in h, Median [IQR]	10 [6.8-12.5]	13.4 [8-19.8]	**0.03**
Nulliparous	10 [7.5-12.5]	14.7 [9.7-23.6]	**0.03**
Parous	9.4 [5.5-12.5]	9.9 [4.3-15.3]	0.60
Time IOL – full dilatation in h Median [IQR]	13.9 [11.8-18.3]	16.6 [9.3-24]	0.45
Nulliparous	14.5 [11.9-19]	19.9 [13-29.5]	0.06
Parous	12.3 [10.2-15.8]	8.7 [4.9-16.6]	0.22
Time IOL – delivery, h Median [IQR]	16.2 [14-19.4]	20.2 [12-30.4]	0.12
Nulliparous	17 [15.3-22]	26.5 [15.5-33.6]	**0.006**
Parous	12.6 [10.6-16.2]	9.0 [4.9-16.8]	0.19
Time IOL – vaginal delivery, h Median [IQR]	15.8 [13.8-18.9]	17.8 [9.7-27.9]	0.48
Nulliparous	16.3 [14.4-21]	23.1 [14.4-33.6]	0.06
Parous	12.6 [10.6-16.2]	9.0 [4.9-16.8]	0.19
Rate of IOL – delivery <24h	36 (90%)	23 (57.5%)	**0.001**
Nulliparous	26 (89.6%)	12 (41.4%)	**0.001**
Parous	10 (90.9%)	11 (100%)	1.00
Rate of IOL – vaginal delivery <24h	31 (88.5%)	22 (66.6%)	**0.03**
Nulliparous	21 (87.5%)	11 (50%)	**0.01**
Parous	10 (90.9%)	11 (100%)	1.00

IOL: Induction of labour; IQR: interquartile range

Table 3 – Maternal outcomes

Variable	Double balloon + oxytocine (n=40)	Vaginal dinoprostone (n=40)	P value
Oxytocin use during labour in UI, Mean (± SD)	2.74 ± 3.22	1.33 ± 1.73	**0.002**
Abnormal FHR rate leading to:			
Ripening device removal			
Oxytocin discontinuation	0	0	1.00
	6 (15%)	3 (7.5%)	0.48
Uterine hyperstimulation	2 (5%)	1 (2.5%)	1.00
Fever during labour	1 (2.5%)	1 (2.5%)	1.00
Epidural use	40 (100%)	38 (95%)	0.49
Delivery mode			0.78
Vaginal delivery	35	33	
Spontaneous	30 (75%)	27 (67.5%)	
Extraction	5 (12.5%)	6 (15%)	
Caesarean section	5 (12.5%)	7 (17.5%)	
Caesarean indications	5	7	
Failure of induction	1 (20%)	1 (14.5%)	
Failure of dilatation progress	4 (80%)	5 (71%)	
Nonreassuring FHR	0	1 (14.5%)	
Postpartum hemorrhage	5 (12.5%)	6 (15%)	0.75

SD: Standard Deviation

Table 4 - Neonatal outcomes

Variable	Double balloon + oxytocine (n=40)	Vaginal dinoprostone (n=40)	P value
Birth weight, g Median [IQR]	3152.5 [2922-3542]	3275 [3047-3505]	0.36
5-minute Apgar score <7	2 (5%)	1 (2.5%)	1.00
Umbilical artery pH Mean (± SD)	7.23 ± 0.07	7.24 ± 0.08	0.44
Umbilical artery BE Mean (±SD)	-4.10 ± 2.11	-4.89 ± 2.95	0.19
Lactates, mmol/L Mean (±SD)	4.15 ± 1.84	4.22 ± 1.59	0.87
NCIU Admission	1 (2.5%)	2 (5%)	1.00

BE: Base Excess; NCIU: Neonatal Intensive Care Unit; IQR: interquartile range

Table 5 – Materno-fetal infectious outcomes

Variable	Double balloon + oxytocine (n=40)	Vaginal dinoprostone (n=40)	P value
Clinical chorio-amnionitis	0	1 (2.5%)	1.00
Bacteriological chorioamnionitis	0	3 (7.5%)	0.24
Histological chorio-amnionitis	6 (15%)	5 (12.5%)	0.56
Postpartum endometritis	0	0	
Materno-fetal infection **No** **Probably** **Confirmed**	 38 (95%) 1 (2.5%) 1 (2.5%)	 39 (97.5%) 1 (2.5%) 0	1.00

Table 6 – Ripening device tolerance

Variable	Double balloon + oxytocine (n=40)	Vaginal dinoprostone (n=40)	P value
VASPI at insertion device, Mean (± SD)	4.6 ± 2.8	2.9 ± 2.5	**0.02**
Nulliparous	4.7 ± 2.9	3.3 ± 2.6	0.07
Parous	3.6 ± 2.5	1.4 ± 1.5	0.13
VASPI at H6, Mean (± SD)	3.8 ± 2.9	5.8 ±2.9	**0.04**
Nulliparous	3.7 ± 2.9	5.6 ± 3.0	0.08
Parous	4.4 ± 2.7	7.0 ± 0.0	0.10
VASPI at H12, Mean (± SD)	2.5 ± 3.1	5.7 ± 2.9	**0.008**
VASPI at H18, Mean (± SD)		6.2 ± 1.3	
VASPI at H24, Mean (± SD)		5.1 ± 4.1	
Acceptability			
Yes	37 (92.5%)	36 (87.5%)	0.84
No	3 (7.5%)	3 (7.5%)	
No data	0	1 (2.5%)(il manque 1)	

VASPI: Visual Analog Scale of Pain Intensity; SD: Standard Deviation

FIGURE LEGENDS

Figure 1: Flowchart describing the main stages of the study.

Figure 2: Flowchart of randomization into treatment groups.

Figure 3: Kaplan-Meier survival curves illustrating induction to delivery time