

# Dinoprostone vaginal insert vs the Foley catheter in labor induction. Observational study

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**Background:** A common practice used prior to induction of labor (IOL) is cervical ripening. Currently, there is no consensus from world scientific societies on the method of first choice. One of the most popular method is prostaglandin PGE<sub>2</sub> (dinoprostone) usage. It is used in different doses and pharmaceutical forms. **Methods:** In our analysis we compared the obstetrical outcome of IOL using a dinoprostone vaginal insert (DVI) with 10 mg of dinoprostone, which released 0.3 mg/h of dinoprostone for 24 hours (Cervidil®, Ferring Pharmaceutical Poland) with an intracervical Foley catheter (20 F, 50–60 mL balloon). A total of 456 patients (100-DVI, 356-Foley catheter) were included in the study. All patients were in term, singleton pregnancy with intact fetal membranes. **Results:** In the DVI group, oxytocin was used less frequently during IOL (OR = 0.35, 95% CI 0.23–0.57) and meconium stained amniotic fluid was recorded less often (OR = 0.38, 95% CI = 0.15–0.99). Other obstetric outcomes such as percentage of cesarean deliveries, vaginal operative deliveries, incidence of postpartum haemorrhage, failed labour induction, unreassuring CTG trace did not differ between groups. Clinical condition of newborns and cord blood pH did not differ between groups. In the group of patients pre-induced with a Foley catheter, the need for labor augmentation with oxytocin is more common (62% vs 37%,  $P < 0.01$ ). **Conclusion:** Necessity of labor augmentation with oxytocin is more frequent in patients pre-induced with the intracervical Foley catheter compared to DVI usage. There is no difference between groups in obstetrical and neonatological outcomes.

## Keywords

Labour induction; Dinoprostone; Intracervical Foley catheter; Vaginal inserts

## 1. Introduction

Induction of labor (IOL) is one of the most common procedures performed in obstetrics. Currently, in developed countries, up to one in four deliveries is induced [1]. Due to the results of the ARRIVE trial [2] indicating the benefits of labor induction in healthy pregnant nulliparous woman after 39 weeks of gestation, the prevalence of IOLs may increase in the coming years. Cervical ripening is a naturally occurring process prior to the spontaneous onset of delivery. In case of unfavorable cervix we have to employ cervical ripening agents to minimize the risk of cesarean section (CS) and shorten the patient's length of stay in the delivery room. Choosing the best method for cervical ripening is difficult.

This is due to the wide variety of agents available as well as the many criteria for evaluating these methods used in clinical trials. In the evaluation of individual methods, the environment in which the study group is embedded must also be taken into account. Local conditions such as the prevalence of CS and obstetricians' attitudes towards this method of pregnancy completion vary considerably between countries. For this reason, observational studies play an important role in the evaluation of pre-induction methods by presenting real world data.

The Bishop score (BS) [3] has remained the gold standard for cervical assessment for almost 60 years. This scoring scale is used worldwide to assess the chance of successful IOL in a given patient. It has been shown that the individual axes of the scale as well as the total score have a negative predictive ability in relation to the delivery completion through CS [4]. At the same time, the need for pre-induction itself seems to reduce the odds of vaginal delivery [5].

In our study, we compared the obstetric outcomes of using two methods of pre-inducing labor in patients with unfavorable cervix (BS <7)—dinoprostone vaginal insert (DVI) with 10 mg of active substance released for 24 hours (Cervidil®, Ferring Pharmaceutical Poland) and intracervical Foley catheter.

## 2. Material and methods

Our study was single-center, retrospective and observational. We reviewed medical records of patients who delivered at the Department of Obstetrics and Gynecology, Provincial Combined Hospital in Kielce (tertiary referral ward). Approval for the study was granted by the bioethics committee at Jan Kochanowski University in Kielce. Informed consent was obtained from all subjects involved in the study.

In the study we included first 100 patients (since product was introduced in our Clinic practice) who underwent IOL with DVI (01.01.2018–1.10.2020) and have unfavorable cervix (BS <7). The decision on the type of product used was arbitrarily made by the IOL qualifying physician. The control group was a retrospective cohort of patients pre-induced

with an intracervical Foley catheter (size 20F, balloon filled with 50–60 mL of saline) who delivered in the clinic in year 2017–2018. In all cases, it were in-patient procedures.

Patients with singleton, term pregnancy, cephalic presentation of fetus, intact fetal membranes and unfavorable cervix (BS <7) were included in the study. Patients with more than one method of pre-induction (e.g., Foley catheter + DVI in a sequential way) and patients after previous cesarean section were excluded from the study. Indications for labor induction were in accordance with the recommendations of the Polish Society of Gynecologists and Obstetricians for labor induction [6]. According to the cited recommendations, women in postdate pregnancy should undergo IOL after 41 weeks of pregnancy, gestational diabetes after 39 weeks, pre-gestational diabetes and uncomplicated gestational or pre-pregnancy hypertension—38 weeks of gestation, mild preeclamptic woman should undergo IOL after 37 gestational weeks. For less frequently used indications, we refer to the original source [6].

The DVI and Foley catheter were maintained for a maximum of 24 hours. DVI and Foley catheter were removed in case of initiation of active phase of labor (dilation  $\geq 4$  cm, regular contraction activity) or rupture of fetal membranes. In case of no spontaneous onset of labor after 20–24 hours of pre-induction, oxytocin was infused intravenously - low-dose regimen, also in case of necessity to augment labor, the same infusion regimen was used. Amniotomy was performed at 4–6 cm cervical dilation. All patients after transfer to delivery room had continuous CTG record. We compared the groups with respect to the percentage of CS and vacuum extraction (VE) and the most frequent indications for operative deliveries, as well as meconium stained amniotic fluid (MSAF) and postnatal neonatal status - clinical (Apgar score) and biochemical (cord blood pH). We assessed the percentage of neonates born with pH <7.2, the cut-off point was determined based on literature data indicating a higher risk of neurological complications in such children in the future [7, 8].

Statistical analysis was performed using Statistica 13.1 software (Tibco Software Inc., Palo Alto, CA, USA). For qualitative variables, we presented data as percentage of events per group and odds ratio (OR) (DVI vs Foley group) with 95% confidence interval (CI). We compared the qualitative variables using Pearson's  $\chi^2$  test. We used Yates correction in case of small expected numbers. For variables with distribution not significantly differ than normal, we represented the central tendency as the arithmetic mean and the scatter of the variable as the standard deviation, and we compared groups using the Student's *t* test. When assumptions about normal distribution were not met, we used the median and interquartile range (IQR) as measures of scatter to represent central tendency, and we compared groups using the Mann-Whitney U test. The differences were considered statistically significant in case of *P*-value < 0.05.

**Table 1. Baseline characteristics of groups.**

	Foley (n = 356)	DVI (n = 100)	<i>P</i>
age (years, SD)	28.39 (4.72)	29.02 (3.6)	<i>P</i> = 0.84
pluripara	21.63%	25.00%	<i>P</i> = 0.47478
gestational age (weeks, IQR)	40 (0.8)	40 (0.7)	<i>P</i> = 0.92
epidural analgesia	21.07%	10.00%	<i>P</i> = 0.01204

SD, standard deviation; IQR, interquartile range.

### 3. Results

A total of 456 patients (100 - DVI, 356 Foley catheter) were included in the analysis. In both groups, the most common indication for IOL was postdate pregnancy (63% in DVI and 68% in Foley group respectively, *P* = 0.34), gestational diabetes (14% and 16%, *P* = 0.61) and hypertensive disorders in pregnancy (13% and 9%, *P* = 0.45) the other indications were, accordingly 10% and 7% (*P* = 0.55).

All patients were Caucasian. Baseline characteristics of the patients are shown in Table 1. The groups did not differ in the percentage of multiparous women or median gestational age at IOL time. Epidural anesthesia was more common in the group of patients induced with the Foley catheter. Obstetrical outcomes are presented in Table 2. In the group of patients pre-induced with DVI, labor augmentation with oxytocin was used less frequently (OR = 0.35, 95% CI 0.23–0.57), MSAF was observed less often (OR = 0.38, 95% CI = 0.15–0.99), but the difference was on the borderline of statistical significance. Other observed outcomes including percentage of CS and VE, incidence of postpartum haemorrhage, failed induction (18 hours of oxytocin infusion without achieving active stage of labor), unreassuring CTG trace were not significantly different between groups. Neonatal birth status as measured clinically by the Apgar scale also did not differ between groups. The groups did not differ in the percentage of newborns born with pH <7.2 and <7.1.

### 4. Discussion

Intracervical Foley catheter is one of the most common methods used for cervical ripening. Its popularity is due primarily to its low cost, but also to its low rate of complications, efficacy and the limited number of patients in whom it is contraindicated. However, taking into account the induction to delivery time (IDT) its effectiveness compared to most biochemical methods is lower [9, 10]. The chance of vaginal delivery within 24 hours after induction is lower than with prostaglandins PGE1 (misoprostol) and PGE2 (dinoprostone) regardless of the route or method of prostaglandin administration. The absolute probability of VD not achieving in 24 hours for the Foley catheter is estimated at 0.65 (95% Credible interval (CrI) 0.48–0.79) [9] with dinoprostone the probability of VD not achieving in 24 hours ranges from 0.52 to 0.62 depending on the form of administration (vaginal insert, gel or vaginal tablet) [9]. The chance of completing labor via CS is not different with the Foley catheter and prostaglandin PGE2 [9].

**Table 2. Results of analysis.**

	Foley group (n = 356)	DVI group (n = 100)	P	OR (95% CI)
cesarean section	27.53%	22.00%	<i>P</i> = 0.26733	0.74 (0.44–1.26)
vacuum extraction	1.69%	4.00%	<i>P</i> = 0.16259	2.43 (0.67–8.79)
oxytocin augmentation	62.08%	37.00%	<i>P</i> = 0.00001	0.35 (0.23–0.57)
meconium stained amniotic fluid	12.08%	5.00%	<i>P</i> = 0.04155	0.38 (0.15–0.99)
placental abruption	0.28%	0.00%	<i>P</i> = 0.59571	N/A
postpartum hemorrhage	2.25%	3.00%	<i>P</i> = 0.66463	1.35 (0.35–5.17)
failed induction or arrested labor (as CS indication)	13.48%	11.00%	<i>P</i> = 0.51330	0.79 (0.4–1.59)
unreassuring CTG trace (as operative delivery indication)	11.24%	7.00%	<i>P</i> = 0.21833	0.59 (0.26–1.37)
1st minute Apgar <8	3.66%	7.00%	<i>P</i> = 0.15035	1.98 (0.77–5.1)
5th minute Apgar <8	1.69%	2.00%	<i>P</i> = 0.83503	1.18 (0.24–5.97)
pH <7.2	2.25%	4.00%	<i>P</i> = 0.33328	1.81 (0.53–6.14)
pH <7.1	0.00%	1.00%	<i>P</i> = 0.05891	N/A
pH (median, IQR)	7.351 (0.086)	7.3745 (0.0675)	<i>P</i> = 0.001	N/A

The above mentioned indicators (absolute probability of VD not achieving in 24 hours and ITD) are particularly important in the context of cost-effectiveness analysis of the studied product. Longer IOL time translates directly into involvement of maternal ward staff. Reducing IOL time especially in the nulliparous female group on a population scale may translate into a reduction in the number of medical staff positions needed. Thus, current research directions focus on the one hand on selecting pre-induction for its potency of action and on the other hand on its applicability in outpatient's settings, while maintaining the highest possible level of safety for both mother and child. Randomized trials available in the literature comparing the form of dinoprostone analyzed in our study—DVI with Foley catheter in terms of IDT are not conclusive, but a meta-analysis of six randomized trials published in 2016 shows a shorter IDT in patients induced with DVI (mean difference [MD] = 5.73 h, *P* = 0.01 in favor of DVI) while showing no advantage in the percentage of patients who delivered vaginally within 24 h (38.4% in the Foley group and 45.3% in DVI group, *P* = 0.31) and no difference in CS rates. Oxytocin was used more frequently during IOL in the Foley group (RR = 1.86 95% CI 1.25–2.77) [10]. In most centers, oxytocin administration requires adequate and continuous fetal monitoring and takes place in the delivery room. Less frequent oxytocin administration may translate into shorter stay of patients in the delivery room and possibility of greater mobility due to lack of connection of the patient to the infusion pump.

Only a low rate of adverse effects will allow the transfer of labor pre-induction from hospital to outpatient settings. Studies show that among two most commonly used prostaglandins, i.e., dinoprostone and misoprostol, prostaglandin PGE<sub>2</sub> is the safer substance in terms of adverse maternal and neonatal outcome. Use of misoprostol in comparison to dinoprostone is associated with higher risk of postpartum haemorrhage (aOR = 4.62 95% CI 3.27–6.54), postpartum maternal blood transfusion (aOR = 1.31 95% CI 1.01–1.71), neonatal intensive care unit admission of new-

born born after 37 weeks of gestation (aOR = 1.37 95% CI 1.07–1.75), Apgar <7 at 5 min of life (aOR = 2.91 95% CI 1.70–5.00) as well as the need for mechanical ventilation of a newborn (aOR = 2.37 95% CI 1.20–4.68) [11]. The most commonly raised complication of prostaglandin use in labor pre-induction in the literature is uterine muscle hyperstimulation. In the case of DVI, the percentage of patients who develop tachysystole during the use is relatively low and estimated from 0 to 4% [12–14], and hyperstimulation with FHR involvement 0–2.8% [12, 14]. When using the Foley catheter, the prospect of hyperstimulation is not significantly higher than when using placebo (0.92 95% CrI 0.37–1.93) [9]. The main advantage of the use of prostaglandins in the form of vaginal inserts, apart from the controlled release of the substance, is its ease of removal from the vagina, even by the patient herself, what with the short half-life of dinoprostone (T<sub>1/2</sub> = 1–3 minutes) [15], results in short resolution of tachysystole—median time to resolution in post-hoc analysis of EXPADITE data = 8.5 minutes [16]. There are also reports in the literature of a beneficial additive effect of simultaneous use of DVI with Foley catheter for nulliparous woman. In a randomized pilot study published in 2020, a 48% reduction in median to delivery time was observed in the study group compared to the Foley catheter-only group (21.2 h vs 31.3 h), but the difference was on the borderline of statistical significance (*P* = 0.05). The borderline statistical significance may have been due to the small group size and insufficient power to demonstrate a true difference. The study showed no difference in complication rates between groups [17]. The question raised about the synergistic effect of the two methods therefore needs further study.

In our study, we did not show differences in the birth status of newborns. The advantage of our analysis is the assessment of cord blood pH in all newborns (percentage of missing data—0.3%). The acid-base analysis of cord blood is a test with greater predictive ability in relation to the neurological development of the child in the future compared to the clinical assessment on the Apgar scale [7, 8]. In our opinion,

the fact that the median pH values differ between the groups is of little clinical significance. Despite the difference in medians between the groups, both values are within the range of normal pH. One should also keep in mind the sensitivity of the median to extreme values and outliers. From a clinical point of view, the percentage of newborns with pH <7.2 seems to be more important, because at this cut-off point the risk of neurological complications in the child increases [7]. The groups did not differ in terms of newborns born with low pH values. In our study, no infants were born with pH <7, and no infants underwent therapeutic hypothermia. The lack of differences in neonatal clinical status is supported by the literature. Metanalyses results indicate that clinical and biochemical status of neonates and chance of NICU admission did not differ regardless of whether dinoprostone or Foley catheter was used for pre-induction of labor [9]. This also referred to the DVI form [10].

An important aspect to consider when evaluating a pre-induction method is patient satisfaction with the method used. In our opinion, patient satisfaction is an underreported outcome in the literature. We found no studies in directly comparing the satisfaction of patients pre-induced with DVI and Foley catheter. Given the discomfort experienced by the patient during mechanical cervical dilation, and the more complicated insertion process compared to inserts or vaginal tablets, the intracervical Foley may be a less satisfying and more concerning method compared to biochemical methods. We found one 2003 study compared intracervical misoprostol (50 µg) in vaginal tablet form with a Foley catheter according to patient's satisfaction. Satisfaction differed significantly between groups (method acceptance was 85% in the misoprostol pre-induced group versus 35% in the Foley catheter pre-induced group,  $P < 0.05$ ) [18]. In our opinion, the result of the study can be extrapolated to the situation presented in our analysis because of the same process of insertion of the tablet and vaginal insert. The study also shows that the potency of DVI 10 mg corresponds to 100 µg of misoprostol released over 24 hours [19].

A limitation of our study was the lack of adjustment of OR for potential confounding factors (such as BMI or epidural analgesia [EA]). However, the groups by including all patients eligible for IOL over a given time period using the selected method reflect the general population and do not differ in demographic characteristics (except for the proportion of patients who received EA). However, the 2018 Cochrane meta-analysis did not indicate that intrapartum use of EA was associated with an increased risk of CS and worse neonatal birth outcomes [20].

## 5. Conclusions

Obstetric outcomes and neonatal clinical status do not differ regardless of whether DVI or the Foley catheter was used to pre-induce labor in patients in term pregnancy with intact fetal membranes.

In the group of patients pre-induced with the use of the

Foley catheter the necessity to augment labor with oxytocin is more frequent.

## Author contributions

These should be presented as follows: JM, MM designed the research study. JM, MM performed the research. JA collected dataset. JM analyzed the data. JM, MM wrote the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

## Ethics approval and consent to participate

Informed consent was obtained from all subjects involved in the study. Protocol of study was approved by the Ethics Committee of Jan Kochanowski University in Kielce (approval number: 03/21).

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## Conflict of interest

Authors declare no conflict of interests.

## Data availability

The data that support the findings of this study are available in OSF Storage at DOI: 10.17605/OSF.IO/JS2V4.

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