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CLINICAL ARTICLE

Obstetrics

Safety of the use of dinoprostone gel and vaginal insert for induction of labor: A multicenter retrospective cohort study

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Abstract

Objective: To assess adverse obstetric and neonatal outcomes associated with the use of dinoprostone for induction of labor, with particular attention on categories for which caution is recommended by the Italian Medicines Agency and the European Medicine Agency.

Methods: A retrospective multicenter observational study was conducted on a population of 1687 patients undergoing induction of labor with vaginal dinoprostone (gel or insert) between August 2019 and June 2022. Patients were subdivided based on maternal age, gestational age, and obstetric disorders. Data regarding the mode of delivery, the incidence of tachysystole, and the obstetric and perinatal outcomes were collected.

Results: The main adverse event associated with the use of dinoprostone was tachysystole. However, tachysystole was not associated with an increased risk of cesarean section (CS), neonatal intensive care (NICU) admission, low 1-min Apgar, or umbilical cord acidosis. Maternal age greater than 35 years, gestational age greater than 40 weeks, and obstetric disorders were not associated with an increased rate of tachysystole, NICU admission, low 1- and 5-min Apgar scores, and cord acidosis. The only associated adverse outcomes in those categories were postpartum hemorrhage with age greater than 35 years and tachysystole with gestational diabetes mellitus and hypertensive disorders. Not a single case of severe outcome (disseminated intravascular coagulation, uterine rupture, maternal and fetal death) was reported in the cohort.

Conclusion: Providing there is adequate maternal and fetal surveillance, in an inpatient setting, dinoprostone could be safely administered for the induction of labor and considered appropriate in high-risk pregnancies. Tachysystole can be self-identified by the patient and effectively managed.

KEYWORDS
adverse maternal and neonatal events, dinoprostone, induction of labor, tachysystole

1 | INTRODUCTION

Induction of labor (IOL) is a common obstetric intervention that stimulates the onset of labor using artificial methods.[1] It is recommended when the advantages of expeditious delivery outweigh the risks of continuing the pregnancy.[2] Since 1990, the rates of IOL have more than doubled.[3] Many methods are available for IOL, mainly including pharmacologic options or mechanical devices.[4,5]

Pharmacologic forms include synthetic prostaglandins (PG) and synthetic oxytocin. The PG commonly used in clinical practice due to their efficacy and safety are misoprostol (a synthetic analog of prostaglandin E1 [PGE1]) and dinoprostone (a synthetic analog of prostaglandin E2 [PGE2]). The use of exogenous PGE2 is one of the preferred agents for IOL because it is effective in achieving cervical ripening and carries lower risks.[6–8]

In July 2021, the Italian Medicines Agency (AIFA), in response to the European Medicine Agency (EMA), disclosed an information note recommending caution in the use of dinoprostone and imposing strong limitations on its clinical use. This action was taken in light of the potential risks to the mother and fetus that emerged during a pharmacovigilance review by the EMA.[9]

The main risk is uterine hyperstimulation, potentially leading to adverse obstetric outcomes such as uterine rupture, peripartum hemorrhage, and fetal distress, with variable neonatal outcomes, including perinatal death. The main limitation imposed by the new AIFA note is the requirement for continuous and frequent cardiotocography monitoring before and during the use of dinoprostone (based on the formulation). Furthermore, AIFA reports that dinoprostone should be used with caution in women older than 35 years, women with obstetric disorders, such as gestational diabetes mellitus (GDM), hypertensive disorders, and hypothyroidism, and pregnancies at gestational age greater than 40 weeks, due to higher risk for developing postpartum disseminated intravascular coagulation (DIC). Considering the progressive aging of European parturients, a majority of women fall into the above-mentioned limitation categories.[10]

These recommendations have great resonance at both national and European levels, severely restricting the use of this drug in clinical practice.[11] Although these indications aim to protect maternal and fetal health, none are supported by the unanimous position of various international societies,[2,12,13] allowing conflicting opinions in this regard.

This study aimed to assess the adverse events associated with the use of dinoprostone in IOL, specifically in those categories for which caution is recommended by the AIFA and EMA.

2 | MATERIALS AND METHODS

2.1 | Study population and design

A retrospective observational study was conducted on a population of patients undergoing IOL with exogenous PGE2 (dinoprostone) at two different Obstetrics Departments, Careggi University Hospital of Florence and the Polyclinic University Hospital of Modena, between August 2019 and June 2022.

The primary objective was to assess the obstetric and neonatal outcomes associated with the use of dinoprostone in various formulations available in Italy. The secondary objective was to investigate, in the cohort treated with dinoprostone, the correlations between adverse obstetric and neonatal outcomes and maternal age, gestational age, and obstetric pathologies for which caution is advised before using dinoprostone.

Inclusion criteria were women with a singleton, full-term pregnancy who underwent IOL for various indications, as described below. Women with a history of previous CS or those undergoing IOL due to intrauterine fetal death were excluded. The need for IOL was discussed with the patients and determined following local hospital protocols, in accordance with national (Italian Society of Gynecology and Obstetrics) and international (American College of Obstetricans and Gynecologists, World Health Organization, National Institute for Health and Care Excellence) recommendations.

The decision to use dinoprostone or other pharmacologic and mechanical methods of IOL was based on the clinical evaluation of each patient and the Bishop score. Dinoprostone was chosen when clinically appropriate and when there were no contraindications for its use. The choice between rapid-release and controlled-relase preparations was left to the obstetrician's preferences.

Based on pharmacologic preparation, two groups were identified: the group using a rapid-release dinoprostone vaginal gel formulation (Prepidil 2 mg; RDD) and the group using a controlled-release dinoprostone vaginal insert (Propess 10 mg; CRD). Patients were further analyzed based on age (cut-off: 35 years) or gestational age (cut-off: 40 weeks) and obstetric disorders (GDM; hypertensive disorders).

The data pertaining to the recruited patients were collected by consulting computerized medical records. Information on the mode of delivery, the incidence of tachysystole, and maternal and perinatal outcomes was recorded.

The indications for IOL included premature rupture of the membranes, post-term pregnancies, pregestational or gestational maternal disorders (such as hypertensive disorders, GDM or pregestational diabetes, and intrahepatic cholestasis of pregnancy) or fetal disorders (such as suspected small for gestational age). In case of multiple indications for IOL, the one strictly determining anticipated delivery was taken into account.

Every woman underwent a 30-min cardiotocography before drug administration. Subsequently, patients receiving induction with RRD were instructed to maintain the supine position for at least 1 h after application while being monitored with cardiotocography. A further control lasting 30 min was conducted 2 h after administration. This protocol was repeated with each drug application.

Patients undergoing induction with CRD (positioned at the posterior vaginal fornix) underwent a cardiotocography surveillance lasting about 30 min, 1 and 6 h after the placement of the vaginal insert. In cases where induction with either formulation triggered tachysystole/hypertonicity and/or alterations of the cardiotocographic tracing, interventions aimed at preserving fetal well-being

were adopted, following local protocols. For both formulations, in cases of self-reported increased uterine contractions, vaginal bleeding of rupture of membrane, clinical examinations, and additional cardiotocography were performed.

2.2 | Ethics approval and consent to participate

The present study used retrospective data collection from clinical diaries. At admission, women signed to give permission to the use of their anonymized data for research purposes. Hence, institute review board approval was not required. In addition, a written informed consent before each and any induction of labor was obtained.

2.3 | Statistical analysis

Continuous variables were represented using mean, standard deviation, median, minimum and maximum values, whereas categorical variables were represented using absolute and relative frequencies. To evaluate the difference between groups, for continuous variables, we used the Student *t*-test or Mann–Whitney *U*-test, according to the Shapiro–Wilk test for normality; and the χ^2 test for categorical data. Kendall test, phi test, Good-Man+ Kruskal tau were also used for correlation analysis.

The statistical analyses were conducted using the SPSS version 23.0 software (IBM, Aronk, NY, USA) and the significance level was set at 5%.

3 | RESULTS

Among the 1687 patients included in the study, 1137 were induced with RRD and 550 received CRD. Maternal and obstetric characteristics are illustrated in Table 1.

The main indication for IOL was maternal disorders ($n = 683$, 40.5%; Table 1). In the CRD group, maternal age over 35 years and nulliparity were significantly higher compared with RRD ($P < 0.001$). In contrast, in the RRD group, the frequency of obesity and the median Bishop score were significantly increased ($P < 0.001$).

The obstetric and neonatal outcomes are detailed in Table 2.

The majority of women had a spontaneous vaginal delivery without significant differences according to the IOL method. Neither the rate (RRD 12.9%; CRD 13.1%), nor the indications for CS differed between the two IOL methods.

Tachysystole was more frequent in women induced with CRD than with RRD. Overall, the rate of interrupted IOL due to the onset of tachysystole was 14.4%. Among them, the number of those requiring conservative maneuvers was similar between groups, while in the CRD group more women required pharmacologic tocolysis, in addition to those who removed the insert (Table 2).

Postpartum blood loss was significantly higher in the RRD group compared with the CRD group. However, the rate of severe postpartum hemorrhage (blood loss >1000 mL) did not differ between the two methods.

As for the neonatal outcomes, less than 1% of the neonates had a low 5-min Apgar score (<7) and/or umbilical cord acidosis (pH <7). These conditions were observed more frequently in women

TABLE 1 Comparison of the obstetric characteristics of women undergoing induction of labor with rapid-release vaginal dinoprostone gel or controlled-release vaginal insert.[a]

Characteristic	Total ($n = 1687$)	Rapid-release vaginal gel ($n = 1137$; 67.4%)	Controlled-release vaginal insert ($n = 550$; 32.6%)	*P* value
Maternal age, years	33.4 ± 5.5	33.4 ± 5.5	33.5 ± 5.4	0.354
Maternal age >35 years	574 (34%)	448 (39.4%)	126 (22.9%)	<0.001
Pregnancy BMI	24.7 ± 5.5	25.1 ± 5.6	23.9 ± 4.9	<0.001
Obesity (BMI >30)	261 (15.8%)	206 (18.5%)	55 (10.2%)	<0.001
Nulliparity	1126 (66.8%)	735 (64.8%)	390 (70.9%)	0.013
Gestational age, week	39.8 ± 1.2	39.8 ± 1.2	39.9 ± 1.2	0.079
Gestational age >40 weeks	848 (50.3%)	552 (48.6%)	295 (53.6%)	0.055
Bishop score	2 (2–3)	3 (2–4)	2 (2–3)	<0.001
Indication for IOL				
PROM	358 (21.2%)	263 (23.2%)	95 (17.3%)	<0.001
Post-term pregnancy	359 (21.3%)	260 (22.9%)	99 (18.0%)	
Maternal disorders	683 (40.5%)	424 (37.3%)	259 (47.1%)	
Fetal indications	286 (17.0%)	189 (16.6%)	97 (17.6%)	
Gestational diabetes mellitus	268 (15.9%)	181 (15.9%)	87 (15.8%)	0.988
Hypertensive disorders	168 (10.0%)	113 (9.9%)	54 (9.8%)	0.988

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); PROM, premature rupture of the membranes.

[a]Data are presented as median (interquartile range), mean ± standard deviation, or number (percentage).

TABLE 2 Obstetric and neonatal outcomes of women undergoing induction of labor with rapid-release vaginal dinoprostone gel or controlled-release vaginal insert.[a]

Outcome	Total ($n=1687$)	Rapid-release vaginal gel ($n=1137$; 67.4%)	Controlled-release vaginal insert ($n=550$; 32.6%)	*P* value
Mode of delivery				
Spontaneous vaginal delivery	1281 (75.9%)	861 (75.8%)	419 (76.2%)	0.540
Operative delivery	165 (9.7%)	106 (9.3%)	58 (10.5%)	
Cesarean section	242 (14.3%)	169 (14.9%)	73 (13.3%)	
Indication for cesarean section				
Failed induction	23 (1.4%)	14 (1.2%)	9 (1.7%)	0.100
Dystocia	99 (5.9%)	67 (5.9%)	32 (5.9%)	
Pathologic cardiotocographic tracing	95 (5.7%)	65 (5.8%)	30 (5.5%)	
Tachysystole	243 (14.4%)	42 (3.7%)	201 (36.5%)	<0.001
Conservative maneuvers	59 (3.4%)	37 (3.3%)	22 (4%)	0.260
Insert removal	–	–	62 (11.3%)	
Treated tachysytole	51 (3.0%)	24 (2.1%)	27 (4.9%)	0.002
Postpartum blood loss	425.8 ± 325.8	454.9 ± 335.2	387.3 ± 310.0	0.013
Severe postpartum hemorrhage (>1000 mL)	38 (6.6%)	24 (7.4%)	14 (5.6%)	0.248
1-min Apgar <7	73 (4.3%)	40 (3.5%)	33 (6%)	<0.001
5-min Apgar <7	13 (0.8%)	7 (0.6%)	6 (1.1%)	<0.001
Umbilical cord pH <7	6 (0.6%)	4 (0.5%)	2 (1.2%)	0.021
Birth weight, g	3337.08 ± 470.00	3346.65 ± 469.14	3316.99 ± 471.93	0.227
Neonatal intensive care unit admission	27 (1.3%)	15 (1.3%)	12 (2.2%)	0.126

[a]Data are presented as mean ± standard deviation or number (percentage).

TABLE 3 Relationship between of obstetric and neonatal outcomes and cesarean section of women undergoing induction of labor with rapid-release vaginal dinoprostone gel or controlled-release vaginal insert.[a]

	Tachysystole				Treated tachysytole				NICU admission			
Women with CS ($N=242$)	Total	Rapid-release gel	Controlled-release insert	*P* value[b]	Total	Rapid-release gel	Controlled-release insert	*P* value[b]	Total	Rapid-release gel	Controlled-release insert	*P* value[b]
	45 (18.6%)	30 (66.66%)	15 (33.33%)	0.365	28 (11.6%)	18 (64.28%)	10 (35.71%)	0.316	3 (1.3%)	1 (33.33%)	2 (66.66%)	0.630

Abbreviations: CS, cesarean section; NICU, neonatal intensive care unit.

[a]Data are presented as number (percentage).

[b]Chi-square test.

receiving CRD compared with RRD. The neonatal intensive care unit admission rate did not differ between the CRD and RRD groups.

One case of severe neonatal morbidity was recorded in the CRD group: the infant was treated with therapeutic hypothermia, without adverse neurodevelopmental outcomes at follow up.

Among the patients who underwent an urgent CS ($n=242$) three newborns (1.3%) required NICU admission (one in the RRD and two in the CRD group; Table 3).

Tachysystole was not associated with adverse maternal outcome and the only adverse neonatal outcome with respect to the general population treated with dinoprostone, was the 5-min Apgar <7 ($P<0.001$; Table 4).

No cases of DIC, uterine rupture, or maternal or fetal death were reported in any patient.

Table 5 illustrates the characteristics and the perinatal adverse outcomes in the prespecified subgroups.

Compared with younger women, those older than 35 years had higher body mass index ($P=0.006$) and obesity rate ($P=0.023$). Older women also showed a lower success rate of IOL (spontaneous vaginal delivery 70.7% versus 78.6%; $P=0.001$). However, after stratifying for the method of induction, the association between age older than 35 years and a lower success rate of IOL was maintained only in the RRD group ($P<0.01$). For CRD, no significant correlation with a lower success rate was noted in the category older than 35 years.

No differences were found between the two age groups in terms of the rate of tachysystole, low 5-min Apgar score, and cord acidosis. Only an increase of postpartum blood loss and severe postpartum hemorrhage was found in the group of older patients. Interestingly,

TABLE 4 Relationship between obstetric and neonatal outcomes with tachysystole of the women undergoing induction of labor with rapid-release vaginal dinoprostone gel and controlled-release vaginal insert.[a]

	CS	1-min Apgar <7	5-min Apgar <7	Umbilical cord pH <7	NICU admission
Dinoprostone	0.067	0.922	<0.001	0.157	0.952
Rapid release gel	0.060	0.731	0.537	0.321	0.567
Controlled-release insert	0.051	0.247	0.713	0.317	0.530

Abbreviations: CS, cesarean section; NICU, neonatal intensive care unit.

[a]Values are presented as *P* values; the correlation used tests: Kendal test and Good Man+ Kruskal tau test based on chi-square test.

TABLE 5 Comparison of obstetric and neonatal outcomes of women according to maternal age and gestational age undergoing induction of labor with rapid-release vaginal dinoprostone gel and controlled-release vaginal insert.[a]

Outcome	Maternal age <35 years (*n* = 1113)	Maternal age ≥35 years (*n* = 574)	*P* value	Gestational age <40 weeks (*n* = 839)	Gestational age ≥40 weeks (*n* = 848)	*P* value
Pregnancy BMI	24.44 ± 5.56	25.22 ± 5.41	0.006	25.11 ± 5.91	24.31 ± 5.08	0.003
Obesity	156 (14.3%)	105 (18.7%)	0.023	156 (19%)	105 (12.6%)	<0.001
Mode of delivery						
Spontaneous vaginal delivery	875 (78.6%)	406 (70.7%)	0.001	669 (79.7%)	612 (72.2%)	0.001
Operative delivery	98 (8.8%)	66 (11.5%)	0.001	68 (8.1%)	96 (11.3%)	0.001
Cesarean section	140 (12.6%)	120 (17.8%)	0.001	102 (12.2%)	140 (16.9%)	0.001
Tacysystole	184 (29.3%)	62 (24.3%)	0.001	125 (29.4%)	121 (26.5%)	0.185
Treated tachysytole	37 (6.3%)	14 (6.8%)	0.197	20 (5.3%)	31 (7.4%)	0.136
Postpartum blood loss	396.77 ± 277.36	478.02 ± 393.68	0.004	403.75 ± 302.31	446.49 ± 345.55	0.057
Severe postpartum hemorrhage (>1000 mL)	17 (4.6%)	21 (10.2%)	0.009	15 (5.4%)	23 (7.7%)	0.170
1-min Apgar <7	61 (5.5%)	12 (2.1%)	0.034	34 (4.1%)	39 (4.6%)	0.377
5-min Apgar <7	9 (0.8%)	4 (0.7%)	0.258	5 (0.6%)	8 (0.9%)	0.508
Umbilical cord pH <7	4 (0.8%)	2 (0.5%)	0.653	3 (0.7%)	3 (0.6%)	0.379
Birth weight, g	3323.62 ± 469.62	3363.17 ± 470.04	0.051	3197.16 ± 487.51	3476.33 ± 470.10	<0.001
NICU admission	23 (5.1%)	5 (1%)	<0.001	14 (3%)	14 (3%)	0.480

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); NICU, neonatal intensive care unit.

[a]Data are presented as mean ± standard deviation or number (percentage).

the rates of low 1-min Apgar and NICU admission were significatively lower in the older group.

Women with a higher gestational age (over 40 weeks) had a lower success rate of IOL (vaginal delivery 72.2% versus 79.7%; $P = 0.001$) and a higher rate of CS (16.9% versus 12.2%; $P = 0.001$) compared with those with a lower gestational age. Neither tachysystole, nor other obstetric or neonatal outcomes changed with gestational age.

The correlation analysis showed that, in the group of women undergoing IOL with the RRD, the women with maternal age over 35 years had more incidence of CS ($P < 0.001$) compared with the CRD group. Similarly, the women with gestational age over 40 weeks in the RRD group had higher incidence of CS ($P = 0.001$) and 1-min Apgar <7 ($P = 0.048$; Table 6). On the other hand, a correlation was found between maternal disorders (GDM and hypertension) and the incidence of tachysystole ($P < 0.001$). Nevertheless, none of the other adverse obstetric and perinatal outcomes studied differed significantly in these high-risk categories.

4 | DISCUSSION

In this study we aimed to evaluate the adverse obstetric and neonatal outcomes associated with the use of dinoprostone in IOL, with particular attention paid to the categories for which caution has been advised by AIFA, that is, maternal age over 35 years, gestational age over 40 weeks, and maternal disorders (GDM and hypertension).

The main adverse event associated with the use of either RRD or CRD was tachysystole. This finding is in line with the literature[14–18] reporting a range of 4%–13%.[19,20] We confirmed here that a higher incidence of tachysystole could be expected in women with GDM or hypertensive disorders.[19,21] However, it is worth noting that tachysystole can be self-identified by the patient and effectively managed by professionals, thereby preventing severe adverse outcomes for both the mother and/or neonate, such as umbilical cord acidosis, low 1-min Apgar score, or NICU admission.

Caution has been recommended by AIFA for the use of dinoprostone in some patient subgroups because of the risk of DIC, uterine

TABLE 6 Relationship between maternal age and gestational age with the obstetric and neonatal outcomes of women undergoing induction of labor with rapid-release vaginal dinoprostone gel and controlled-release vaginal insert.[a]

	Rapid-release gel ($n = 1137$; 67.4%)		Controlled-release insert ($n = 550$; 32.6%)	
	Maternal age >35 years ($n = 448$; 39.4%)	Gestational age >40 weeks ($n = 552$; 48.6%)	Maternal age >35 years ($n = 126$; 22.9%)	Gestational age >40 weeks ($n = 295$; 53.6%)
Modalities of delivery				
Vaginal delivery	<0.01	0.001	0.242	0.031
Operative delivery	<0.01	0.001	0.242	0.031
Cesarean section	<0.01	0.001	0.242	0.031
Analgesic delivery	0.545	0.103	0.059	0.034
Tacysystole	0.348	0.318	0.829	0.333
Treated tachysytole	0.395	0.486	0.409	0.283
Postpartum blood loss	0.101	0.650	0.388	0.189
1-min Apgar <7	0.796	0.048	0.048	0.521
5-min Apgar <7	0.332	0.694	0.158	0.918
Umbilical cord pH <7	<0.001	0.306	0.318	0.343
Birth weight (g) mean ± SD	0.403	0.067	0.704	0.009
NICU admission	0.308	0.265	0.250	0.311

Abbreviation: NICU, neonatal intensive care unit.

[a]Values are presented as *P* values; the correlation used tests: Kendal test, phi test, Good Man+ Kruskal tau test based on chi-square test.

rupture, and maternal and fetal death. However, in our large cohort, not a single case of any of these severe events occurred, although the sample size was not powered to capture a very uncommon complication such as maternal mortality.

After assessing the maternal and neonatal outcomes in our large cohort, we found the use of both formulations of dinoprostone to be safe and medically appropriate for IOL, irrespective of maternal age, gestational age, and maternal disorders indicating IOL.

In women older than 35 years there was an increase of postpartum blood loss and severe postpartum hemorrhage, with no other associated adverse maternal complications. However, postpartum hemorrhage has been reported in older women also in spontaneous vaginal delivery, irrespective of labor induction.[22,23] Our results using dinoprostone formulations were in line with the current literature,[15,24–27] which shows a low incidence of both cesarean delivery and postpartum hemorrhage, without a significantly increased risk of the main adverse neonatal outcomes, also compared with other methods of IOL.

Surveillance of IOL has not been precisely defined in the available guidelines.[8,9,12,28,29] Almost all scientific societies agree on performing cardiotocography for about 30 min before IOL, but the recommendation after PG administration of whatever class has been much less defined. The maternal and fetal surveillance we adopted—namely, intermittent cardiotocography associated with midwife observation—seemed able to identify and allow appropriate management of the tachysystole episodes, which were expected mainly with the use of a CRD device.

The differences between the two formulations of dinoprostone may be helpful for obstetricians in the choice of the method of induction. CRD was found to have a higher success rate in the women older than 35 years, although associated with a higher incidence of tachysystole and some adverse neonatal events (low 1-min Apgar, low 5-min Apgar, umbilical cord acidosis).

This finding is similar to a previous systematic review and meta-analysis,[30] which assessed the effectiveness and safety of CRD for cervical ripening and IOL in women with a viable fetus. The review concluded that CRD is an effective cervical ripening agent compared with RRD, but may result in an increased incidence of excessive uterine activity. The present study provides higher-strength evidence, and direct comparison of the maternal and neonatal outcomes.

The main strength of the present study is the large cohort of women analyzed compared with other studies published to date, and this allowed us to explore many adverse events. Other strengths include the multicenter design, the generalizability, and the clinical relevance of the results.

There are some limitations. The absence of a control group limits our capacity to evaluate some of the adverse perinatal outcomes associated with the whole cohort of dinoprostone. However, as not a single case of the severe outcomes was reported in our cohort, a direct comparison was not deemed necessary. Additionally, our study was not powered to assess very rare adverse events, such as maternal mortality.

In conclusion, providing there is adequate maternal and fetal surveillance, in a controlled inpatient setting, dinoprostone can be safely administered for IOL in different categories of high-risk pregnancies, irrespective of maternal age and gestational age. Tachysystole is the main adverse event associated with the use of dinoprostone, which can be self-identified by the patient and effectively managed, in a hospital setting.

As it has been proven to be highly effective in achieving cervical ripening for IOL,[8,15,25,31] we believe that its use should not be restricted for low-risk categories in clinical practice.

AUTHOR CONTRIBUTIONS

MDT and FF contributed to conceptualization, resources, methodology, supervision, and writing—review & editing; RMP contributed to data collection, methodology, and writing—review & editing; OA contributed to formal and statistical analysis, writing the original draft, and writing—review & editing; SL contributed to formal analysis and writing—review & editing; MH contributed to data collection, formal analysis, investigation, and writing—review & editing; and FF contributed to conceptualization, resources, methodology, supervision, and writing—review & editing. All authors gave consent for publication.

CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to disclose.

DATA AVAILABILITY STATEMENT

All data generated or analyzed during this study are included in this published article.

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