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ORIGINAL ARTICLE

The Risk Factors for Failure of Labor Induction: A Cohort Study

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Abstract
Purpose To assess how some factors may influence the failure of labor induction.
Methods We conducted a prospective observational study from January 2009 to December 2011 with 248 patients who were admitted to the Obstetrics Unit of Ferrara University for labor induction. We selected only patients with unfavorable characteristics such as nulliparity, maternal and gestational age, and Bishop score and specific obstetric conditions such as mild preeclampsia, isolated oligohydramnios, premature rupture membrane, gestational diabetes, and hypertension for the success of labor induction.
Results The induction was carried out by rapid-release gel dinoprostone. 200 patients (80.6 %) delivered vaginally (Group A), while 48 (19.4 %) underwent a cesarean section (Group B). Maternal age was one independent significant variable ($p = 0.01$, OR 1.08) determining the risk of cesarean delivery. Patients affected by mild preeclampsia had a three times higher risk for cesarean section. Despite the several unfavorable characteristics of the patients, the cesarean section rate was comparable to that of the normal population.
Conclusions Several factors and clinical conditions historically considered as negative predictors of induction result should be reassessed. The success of labor induction is determined by many maternal and fetal variables, which must all be taken into account to avoid unnecessary cesarean sections.

Keywords Cesarean section · Dinoprostone · Labor induction · Vaginal PGE

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Introduction

It is well established that labor has to be induced in approximately 20 % of pregnancies [1]. However, induction fails in 20 % of induced pregnancies [2]. Several factors are considered as predictors of induction failure such as Bishop's score < 6, nulliparity, gestational age < 41 weeks, maternal age > 30 years, pregnancy complicated by preeclampsia, premature rupture of membranes (PROM), isolated oligohydramnios, gestational diabetes, and hypertension [3–5]. There are several methods for labor induction; however, in these categories of patients, the preferred method is vaginal prostaglandin (PGE). It induces or accelerates the maturation of the cervix, also stimulating the myometrial activity [6]. Dinoprostone is an analog synthetic of PGE2 widely used in the form of a rapid-release vaginal gel and a controlled-release vaginal pessary. The latter formulation is particularly used for induction of labor in women with an unfavorable Bishop index (<4). Based on these considerations, we conducted a prospective observational analysis choosing a specific study population. In particular, we tested

the success rate of induction of labor in patients with risk factors for failure such as nulliparity, maternal age (>30 years), unfavorable Bishop score, method of induction, and obstetric conditions (gestational diabetes, mild pre-eclampsia, etc.).

Materials and Methods

A total of 248 patients, attending the Obstetrics Section of Ferrara University between January 2009 and December 2011 for labor induction, were included in the present prospective study. The inclusion criteria were as follows: singleton pregnancy, nulliparity, 37–40-week gestation, the absence of active labor, use of rapid-release gel dinoprostone, live fetus with cephalic presentation, and no contraindication to vaginal delivery. The induction of labor was decided for the following indications: PROM (spontaneous labor not started after 24 h), isolated oligohydramnios, mild preeclampsia, gestational diabetes (without maternal and fetal complications), and hypertension. The primary outcome measure was cesarean section (CS) rate. Secondary outcomes included CS rate with respect to the specific obstetric condition of the patient, neonatal safety outcome, and mean dose of dinoprostone. The dose of PGE, Bishop score pre-induction, maternal age, and birth weight were evaluated on success of labor induction. The dose of PGE was correlated to the clinical indication for induction. Apgar score was evaluated between the two groups as neonatal outcome. Bishop score was assessed by digital examination of the cervix. Labor induction was carried out according to the standard labor induction protocol used at the Obstetric Section of Ferrara University. The fetal well-being was evaluated using electronic monitoring during 1 h of observation and for the first 2 h after the administration of inducing agents. Intermittent auscultation was performed every hour before the onset of labor and every half hour during labor. If the fetal heart rate was abnormal during intermittent auscultation, continuous electronic monitoring was performed throughout the labor. Vaginal prostaglandin gel was inserted into the posterior fornix; its dosage (1–2 mg) was determined after assessing the cervical state. Patients were reassessed 6 h after the initial insertion of PGE, and if a patient did not exhibit regular uterine contraction ($\geq$5 in 20 min) and cervical change, a second dose of vaginal gel was inserted. Following day, another induction cycle by PGE was started if regular uterine contractions and cervical change had not developed yet. The induction cycle was repeated two additional times, up to a maximum of six administrations of PGE in total. Failure of induction was defined as no onset of labor 24 h following the initiation of induction of labor or onset of fetal distress detected by cardiotocography. According to the mode of delivery, patients were divided into two groups: Group A (vaginal delivery) and Group B (CS). The Ethic Committee approved the study. All data obtained from the cases were analyzed using the SPSS (17.0 for Windows) program. Results were expressed as mean ± SD or rate. Comparisons between groups and subgroups were performed with analysis of variance (one-way ANOVA). Student's test was used for continuous variables and Fisher's exact test was used for categorical variables. The association between CS and possible predictors was calculated by logistic regression analysis. Logistic regression multinomial analysis was performed to examine the risk of CS in the subgroups controlling for the related variables. A value of $p < 0.05$ was regarded as statistically significant. OR and 95 % CI were calculated where appropriate.

Results

248 patients comprised the whole study population, of whom 200 (80.6 %) had vaginal delivery and 48 (19.4 %) underwent a CS. The characteristics of the study population were as follows:

- Mean maternal age: 32.81 (±5.66) years, median 34 years, maximum 44 years, minimum 16 years;
- Mean gestational age: 38.32 (±1.34) weeks, median 39, maximum 40, minimum 30;
- Mean Bishop score pre-induction: 2.56 (±1.69), median 2, maximum 6, minimum 0;
- Mean birth weight: 3,177.22 (±545.08) g, median 3,175 g, maximum 4,550 g, minimum 1,740 g.

The neonatal gender differed between Group A and B ($p = 0.01$):

- 114 male (57 %) and 86 female (43 %) in the Group A
- 18 male (37 %) and 30 female (63 %) in the Group B.

The mean maternal age differed between the two groups as did gestational age and Bishop's score. Apgar score was higher in infants born to mothers in the Group A (Table 1). After logistic regression analysis, maternal age proved to be one independent significant variable ($p = 0.01$, OR 1.08). Classifying patients according to medical indications for labor induction, five subgroups may be considered:

- 70 patients affected by *gestational diabetes* (CS: 5.7 %);
- 24 patients affected by *gestational hypertension* (CS: 8.3 %);
- 50 patients affected by *isolated oligohydramnios* (CS: 24 %);
- 16 patients affected by *mild preeclampsia* (CS: 50 %);
- 88 patients affected by *PROM* (CS: 25 %).

Table 1 Characteristics of patients for the analyzed variables

	Group A ($n = 200$) 80.6 %	Group B ($n = 48$) 19.4 %	CI 95 %	p value
Age	32.45 (±5.56)	34.33 (±5.91)	−3.66 to (−0.1)	0.03*
Weeks of gestation	38.41 (±1.31)	37.95 (±1.41)	0.02–0.87	0.03*
Bishop's score	2.68 (±1.68)	2.08 (±1.67)	0.06–1.12	0.02*
PGE dose (mg)	3.11 (±1.1)	3.37 (±0.95)	−0.6 to 0.07	0.1
Birth weight	3203.65 (±523.39)	3067.1 (±621.48)	−35.5 to 308.61	0.1
Apgar score				
1st min	8.50 (±0.92)	8.10 (±1.13)	0.40–0.15	0.01*
5th min	9.63 (±0.56)	9.35 (±0.69)	0.28–0.09	0.004*

*Statistical significant

Gestational diabetes was more present in the Group A, while mild preeclampsia was more significant in Group B (Table 2). After logistic regression multinomial analysis, patients affected by mild preeclampsia had a three times higher risk for CS (OR 3.02, $p = 0.04$). The mean dose of PGE was 3.16 (±1.08) mg (median 3 mg, minimum 1 mg, and maximum 7 mg) in the whole study population. Generally, a maximum of 4 mg of PGE was required for the onset of labor. Only six patients required a higher dose and nevertheless had a vaginal delivery. The mean total dose required of PGE was generally higher in the Group B, but the difference was not statistically significant (Table 1). The mean PGE dose was comparable in the subgroups. However, considering the mode of delivery, it was higher in the patients who underwent CS. Only in the "pre-eclampsia" subgroup, the PGE dose was higher for patients who gave birth vaginally (Table 3).

Discussion

The most common indication for medical induction of labor is prolonged pregnancy with heterogeneous frequency between 0.5 and 10 % [2]. However, for various medical indications, induction may be attempted at different gestational periods. For instance, several authors suggest induction by the 39th week of gestation in patients affected by gestational diabetes in order to reduce the risks correlated to fetal macrosomia [7]. In patients with PROM at term, it is generally accepted to induce labor to prevent fetal infections [8]. Pregnancies complicated by mild pre-eclampsia and gestational hypertension may be induced before the 40th week of gestation in order to reduce the unfavorable fetal and maternal outcomes [9]. On the contrary, there are discordant opinions about the need to induce labor in patients with isolated oligohydramnios. A meta-analysis found significantly higher rates of CS due to fetal heart rate abnormalities and lower Apgar scores in women with oligohydramnios, but no differences in fetal acidosis [10]. However, this analysis included high-risk and preterm pregnancies. None of the few retrospective studies of isolated oligohydramnios at term [11, 12] reported differences in Apgar score, neonatal intensive care unit admissions, neonatal acidosis, or perinatal death from normal pregnancies with induction of labor.

Therefore, the choice of proceeding with induction should be weighted in order to avoid unnecessary CS. Thus, we conducted a prospective observational analysis to verify the rate of vaginal delivery in patients with unfavorable characteristics for a good response to induction. Indeed, by analyzing the characteristics of the study population, it should be underlined that the mean age was 32.81 years. This is important because the factor age is determinant in favoring vaginal delivery. In particular, several studies showed that maternal age >30 years is correlated with a higher rate of CS [3]. Another parameter to highlight is the mean gestational age, which was 38.32 weeks, about 3 weeks less than the gestational age at which labor is commonly induced (>41 weeks). Moreover, the mean Bishop score pre-induction (2.59 points) was highly unfavorable, considering 4 as the threshold value [13, 14]. Another unfavorable factor was the use of rapid-release gel dinoprostone for induction as several authors showed that a 24-h controlled-release vaginal dinoprostone pessary was more effective for labor induction in women with an unfavorable cervix [6]. Despite these unfavorable factors for successful induction, the CS rate was only 19.4 % against 80.6 % of vaginal delivery. Therefore, although we selected a group of patients at risk for induction failure, we had a CS rate comparable to that of the normal population [15]. The Neonatal Apgar score was different between the two groups (Table 1). This is reasonable because the fetuses of Group B underwent a different stress (CS); nevertheless, the Apgar score average was within the normal range (≥7) in both groups. Then, the

high rate of vaginal deliveries did not correlate with a poor neonatal outcome. Analyzing the characteristics of the two groups, significant differences were visible for Bishop score, maternal age, and gestational age. However, one significant independent variable was maternal age which was higher in Group B ($p = 0.01$, OR 1.08). Given the influence of the maternal age on the success of spontaneous delivery [3], this finding leads us to state that the CS rate would probably have been lower if age had not been different between the two groups. Neonatal gender was different between the two groups; in particular, female fetuses were numerically higher than male fetuses ($p = 0.01$). This information has no specific confirmation as the male gender is generally associated with adverse pregnancy outcomes [16]. Analyzing subgroups, a higher CS rate in the patients affected by PROM, mild preeclampsia, and isolated oligohydramnios (24, 50, and 25 %, respectively) is visible. However, only patients affected by mild preeclampsia had a statistically higher risk for CS (about three times). However, this finding is particularly influenced by the fetal condition; in fact, preeclampsia could determine fetal hypoxia resulting in reduced stress tolerance of labor [17]. Also, it is interesting to note that gestational diabetes not complicated by fetal macrosomia did not represent a risk for CS (Table 2).

The mean PGE dose in the whole study population was in accord with the results reported in the literature [15] and it was not significantly different between Group A and B ($p = 0.1$). Analyzing subgroups, PGE dose was generally higher in patients who underwent CS. One exception was represented by the "preeclampsia" subgroup in which it was higher in patients who had vaginal delivery. This was due to the fact that early CS was necessary for acute fetal distress in Group B. These results confirm that the different obstetric conditions of patients do not influence the dose of PGE; in particular, obstetric conditions such as gestational diabetes and isolated oligohydramnios do not require a higher dose of PGE. Instead, the unstable fetal conditions may mostly influence CS risk. Our results are extremely interesting because although we selected a group of patients at risk for labor induction failure, the success rate was still high. Therefore, factors such as "nulliparity," "gestational age," "unfavorable Bishop score," and "kind of used dinoprostone" and clinical conditions such as gestational diabetes, hypertension, isolated oligohydramnios, and PROM do not separately alter the induction result. Then, the success of labor induction is determined by many maternal and fetal variables which must all be taken into account to avoid unnecessary CS. Therefore, labor induction is a medical act of great responsibility which requires an overall assessment of maternal–fetal status.

Table 2 Comparison of different maternal clinical conditions between the two groups

	Group A (%)	Group B (%)	*p* value
Gestational diabetes	66 (33 %)	4 (8.33 %)	0.001*
Gestational hypertension	22 (11 %)	2 (4 %)	0.1
Isolated oligohydramnios	38 (19 %)	12 (25 %)	0.4
Mild preeclampsia	8 (4 %)	8 (16 %)	0.004*
PROM	66 (33 %)	22 (45 %)	0.1

*Statistical significant

Table 3 Mean total PGE dose between the two groups with regard to maternal clinical conditions

Subgroups	Mode of delivery	Mean PGE dose	*p* value
Gestational diabetes	Vaginal delivery	3.18	0.2
	CS	4	
	Total	3.22	
Gestational hypertension	Vaginal delivery	2.9	0.1
	CS	4	
	Total	3	
Isolated oligohydramnios	Vaginal delivery	3.31	0.4
	CS	3.5	
	Total	3.36	
Mild preeclampsia	Vaginal delivery	3.75	0.3
	CS	3	
	Total	3.37	
Prom	Vaginal delivery	2.9	0.1
	CS	3.27	
	Total	3	

Conflict of interest The authors have no conflict of interest to declare.

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