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Journal:

J Matern Fetal Neonatal Med 2011

The Journal of Maternal-Fetal and Neonatal Medicine, May 2011; 24(5): 728–731

ISSN 1476-7058 print/ISSN 1476-4954 online
DOI: 10.3109/14767058.2011.557108

informa
healthcare

Induction of labor and pain: a randomized trial between two vaginal preparations of dinoprostone in nulliparous women with an unfavorable cervix

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Abstract

Objective. To compare pain associated with vaginal dinoprostone pessary vs. gel for induction of labor in women with an unfavorable cervix.

Study design. A randomized controlled trial in a large academic public general hospital. A total of 52 nulliparous women of gestational age $\geq$38 weeks, with Bishop score $\leq$4 and intact membranes were allocated either to a controlled-release vaginal dinoprostone pessary or repeat doses of vaginal dinoprostone gel. Pain was recorded hourly from early induction until the onset of labor.

Results. Mean pain experienced by women belonging to the two groups differed significantly ($p < 0.01$). Women in the controlled-release device group were also significantly more often severe pain-free than women receiving gel ($p < 0.05$). Both methods had similar rates of oxytocin infusion and vaginal deliveries.

Conclusions. The two induction procedures should be considered equivalent as far as ripening the cervix and initiating labor. In view of this finding, the low Bishop score should be considered an indication to prefer the controlled-release device, since it reduces pain thereby improving the physical and emotional wellbeing of the parturient.

Keywords: *Prostaglandins, cervical ripening, pain-score, vaginal pessary*

Introduction

Induction of labor has become a frequent clinical practice concerning approximately 20–30% of all pregnant women, half of them being induced in the presence of an unfavorable cervix [1,2]. Labor induction is known to cause worse pain than spontaneous labor, due to the pharmacological action of the drugs involved. Women may also feel uncomfortable about medicalization of labor, a fact that adds extra emotional stress [3,4]. Clinical experience has shown that pain associated with prostaglandin administration should be considered a relevant factor that adversely affects the outcome of induction. Accordingly, it is very important for the obstetrician to choose the induction method which offers a high degree of effectiveness and safety and the least possible discomfort. Topically administered dinoprostone is considered effective in achieving the first prelabor phase of cervical ripening and may be used in the form of repeated doses of vaginal gel or by means of a controlled-release vaginal insert [5]. The purpose of this study has been the evaluation of pain associated with the two induction procedures and their effectiveness to bring the woman into labor.

Materials and methods

Nulliparous women with medical and obstetric indications for induction of labor at the Obstetric Department of the University Hospital of Verona were included in the study. Other inclusion criteria were: gestational age $\geq$38 weeks, singleton gestation, cephalic presentation, unfavorable cervix (Bishop score $\leq$4), intact membranes. After obtaining the institutional Ethical Committee approval and the patient's informed consent, the subjects of the study were randomly assigned to either one of the induction methods described below. The controlled-release device (Propess®) is a 10 mg vaginal pessary, positioned in the posterior fornix during 24 h, releasing dinoprostone at a rate of approximately 0.5 mg/h [6]. Painful contractions, rupture of membranes, signs of uterine hyperstimulation or systemic side effects are indications to earlier removal. The gel containing 1–2 mg of dinoprostone (Prepidil®) is administered for a maximum of three doses at 6 h intervals. If the patient was not already in active labor, induction was continued by means of amniotomy and/or oxytocin infusion. Women were asked to hourly record the pain felt

(Received 1 December 2010; revised 20 December 2010; accepted 17 January 2011)

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during induction until the onset of labor by using an integrated scale which included visual analog, numeric rating (0–10) and verbal rating (no pain-worst pain) information. A graphic scale with facial icons was also used to avoid misunderstanding in case of foreign patients with language problems.

Statistical analysis

Significance of differences between patients using the vaginal gel and the controlled-release device were assessed by a *t*-test for continuous variables, Mann–Whitney for ordinal variables and by the Fisher exact test for 2 × 2 tables. Significance was set at $p < 0.05$. Box-plots were constructed according to the Tukey method [7]; for calculations the STATA ® software, version 10.1 was used. Survival curves were computed according to the Kaplan–Meier method and compared by the log-rank test. Severe pain was considered as event in survival analysis, whereas withdrawal because of beginning of labor was considered a censored observation at the time of occurrence.

Results

Between January 1st and June 30th 2010, 52 nulliparous patients were included in the study, 26 of them being induced with the controlled-release insert and 26 with the vaginal gel. Indications for labor induction in the two groups were: post-term pregnancy, fetal indications (reduced fetal movements, oligohydramnios, non-reassuring Fetal Heart Rate Monitoring (FHRM)), maternal indications (Pregnancy Induced Hypertension (PIH), diabetes). Reproductive characteristics of both treatment groups are presented in Table I.

Mean pain experienced by women belonging to the two groups was 2.45 and 4.73 for the vaginal pessary and the vaginal gel, respectively ($p < 0.01$, Figure 1).

Severe pain, i.e. pain of intensity > 5, was studied as another indicator of the tolerability of the two procedures and results are presented by means of survival curves (Figure 2): women in the controlled-release device group were significantly more often severe pain-free than women receiving gel ($p < 0.05$).

Table II shows primary outcome data of the two procedures: number of women who experienced initiation of labor; frequency of oxytocin use and mean infusion time during the dilating phase; mode of delivery. Indications for cesarean delivery included failed induction, abnormal FHR pattern, dystocia.

Discussion

According to labor ward experience, pain caused by vaginal prostaglandin administration for induction purposes may adversely affect the outcome of labor. This is particularly true when cervical ripening requires a longer stimulation as in the case of primigravidas with a firm and posterior cervix.

Aim of the present study has been the evaluation of pain associated with two different induction procedures in a group of pregnant women at term, all of them nulliparous and with a Bishop score ≤4.

Table I. Maternal reproductive characteristics.

	Vaginal insert ($N = 26$)	Vaginal gel ($N = 26$)
Maternal age, years (mean ± SD)	30.9 ± 4.1	30.6 ± 5.1
Baseline pre-induction (Bishop score), *N* (%)		
0–2	15 (57.7)	16 (61.5)
3–4	11 (42.3)	10 (38.5)
Nationality, *N* (%)		
Italian	19 (73.1)	19 (73.1)
Immigrant	7 (26.9)	7 (26.9)

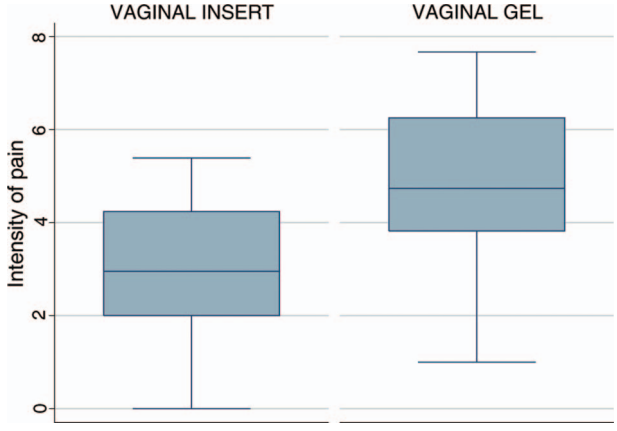

Figure 1. Box-and-whiskers plot of mean pain in the two treatment groups.

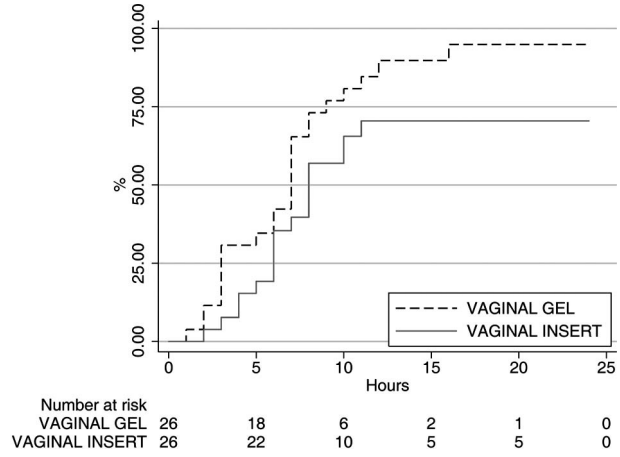

Figure 2. Cumulative rate of patients with severe pain during prostaglandin induction in the two treatment groups.

Table II. Primary outcomes in the two groups according to the induction procedure.

	Vaginal insert ($N = 26$), *N* (%)	Vaginal gel ($N = 26$), *N* (%)	*p* value
Women initiating labor after vaginal prostaglandin	17 (65.4)	19 (73.1)	0.764
Oxytocin in dilating phase	11 (42.3)	16 (61.5)	0.267
Infusion time, minutes (mean ± SD)	143.6 ± 98.0	157.5 ± 103.8	0.726
Cesarean deliveries	9 (34.6)	10 (38.5)	0.99

Other authors have estimated that approximately 50% of labor inductions are carried out under unfavorable conditions, when softening and shortening of the cervix has not yet taken place. Therefore, the real challenge for the obstetrician is to choose the proper procedure which will ripen the cervix and achieve labor while causing the least discomfort and pain in this group of patients.

The obstetrician and the midwife share the task of alleviating the painful experience of labor induction. Optimization of pain control in the management of labor should be a priority especially in those units that cannot provide 24-h anesthetic cover.

To our knowledge there are no studies that have looked into the relation between pain and the method of induction. There are data, however, showing that, with respect to spontaneous labor, prostaglandin-induced labor requires higher doses of anesthetic for lumbar epidural analgesia [8].

Our study has focused the attention on pain caused by vaginal prostaglandins before the diagnosis of established labor, therefore pain recording after this early phase was discontinued.

According to our data, the controlled-release vaginal insert was less painful than the repeated doses of vaginal gel with regard to both mean and severe pain: the difference is likely due to the gradual release of minimal prostaglandin concentrations, which is specific of the insert. Conversely, the acute pharmacological impact of each dose contained in the vaginal gel may have caused early painful uterine contractions before the softening of the cervix; pain associated with the vaginal gel reached its peak soon after each administration, which in the majority of cases consisted of 2 mg dinoprostone gel. Repeat gel administration with concurrent vaginal examinations also caused discomfort to the woman.

After studying the early inductive phase, we deemed necessary to quantify the use of i.v. oxytocin during labor, since it is a pain-inducing drug as much as vaginal prostaglandins. Our data showed that similar amounts were infused in both treatment groups to support uterine activity after established labor and during the 2nd stage of labor.

Since the method of choice should combine least discomfort with unaffected effectiveness, maternal outcome of induction was also analyzed. Previous studies comparing the controlled-release pessary with other methods have produced conflicting results. Lack of consensus likely depends on the heterogeneous characteristics of the control group in terms of parity, gestational age, pre-induction Bishop score, substance and dosage used. In earlier studies, the pessary has been indifferently compared with vaginal or intracervical gel containing prostaglandin E_2, and with misoprostol, a strong analog which has multiple indications [9–17]; more recently equal effectiveness has been reported for both procedures [18,19].

In order to assess the effectiveness of the induction protocol in our study population, we chose first to evaluate how often the method successfully induced adequate cervical effacement and dilatation, initiating labor: as previously found in other authors' series [17,20,21], successful priming was obtained equally often with both procedures. Secondly, we quantified prevalence and duration of oxytocin infusion during the dilating phase: we observed lower rates with the vaginal insert (42.3 vs. 61.5%) although the difference did not reach statistical significance. Other studies [17,22] report a slightly lower frequency of oxytocin infusion (25–32%) after induction with the vaginal pessary: this difference is likely due partly to the highly unfavorable cervical conditions of our nulliparous patients and also to our induction protocol which did not include any dose of vaginal gel, after removal of the pessary and prior to oxytocin, to complete the priming phase as most other authors do [17,19,22].

The cesarean delivery rate has been found similar in the two groups, 34.6 and 38.5% respectively for pessary and gel. Within our institution, these rates are somewhat higher than the figure of 25.5% which is the cesarean rate among total inductions (unpublished data), but it obviously depends on the very unfavorable characteristics of our study population. Moreover we do not consider this specific outcome a trustworthy indicator of the appropriateness of the induction protocol. After all, mode of delivery often depends on other events that intervene later in labor, such as cephalopelvic disproportion or fetal distress, thus confounding any possible causative association between choice of induction procedure and mode of delivery.

In conclusion, in view of our findings, a Bishop score ≤ 4 in a nulliparous woman at term should be viewed as an indication to prefer the dinoprostone controlled-release vaginal device which, by limiting pain, appears to be an appropriate instrument to initiate labor while preserving the quality of birth.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the article.

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