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Comparison of two preparations of dinoprostone for pre-induction of labour in nulliparous women with very unfavourable cervical condition: a randomised clinical trial

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Abstract

The aim of this study was to compare the clinical effects of preinduction cervical ripening by using two ways of dinoprostone administration. In a prospective, open-label trial, 144 consecutive nulliparous women with a Bishop score <4 who required induction of labour at term were randomised to receive dinoprostone via either a vaginal insert (10 mg over 12 h) or a cervical gel (0.5 mg, twice in 12 h). If labour did not start by 24 h after this preinduction, patients received 2 mg vaginal dinoprostone gel followed 6 h later by oxytocin infusion.

The main outcome measure was the rate of caesarean sections (CS). Secondary measures were: changes in Bishop score at 6 h and 12 h, delivery within 12 h and 24 h, need for oxytocin for induction, failure of induction (delivery after >48 h), need for pharmacological interventions to manage tachysystole/hyperstimulation, length of stay in hospital. The CS rate was lower in the vaginal insert group (22.9%) than in the cervical gel group (34.3%), though the difference did not reach statistical significant difference ($P = 0.13$). The indications for CS overlapped between the groups. The rate of vaginal delivery within 12 h and 24 h was similar, as was the rate of failure of induction. More women in the gel group (41.4% versus 24.3%) required the use of oxytocin (OR = 2.21; 95% CI = 1.07–4.55). Tachysystole or hyperstimulation in the vaginal insert group (7) was twice that with cervical gel (4). Four women in the vaginal insert group and three in the cervical gel group reported infectious complications. A long stay in hospital (>4 days) was less frequent with vaginal inserts (21.4 versus 38.6%; OR = 0.43, 95% CI = 0.19–0.97).

The more challenging preinductions of labour at term are associated with increased obstetric interventions such as a high CS rate and a more frequent requirement for oxytocin inductions. In terms of success and failure, vaginal inserts releasing dinoprostone do not differ from dinoprostone given by the traditional cervical route. However, the use of vaginal inserts reduces the need for obstetric interventions and allows shorter periods in hospital.

Keywords: Cervical maturation; Caesarean section; Fetal heart rate; Dinoprostone; Labour induction

1. Introduction

The advantages of preinduction cervical maturation by topical application of prostaglandins have been known for several years [1]. However, selected groups of patients, such as nulliparous women and those with a very unfavourable condition of the cervix, are still a challenge to clinicians, both these groups being associated with more failures and an elevated caesarean section (CS) rate [2]. A slow-release dinoprostone vaginal insert is now available worldwide. Two meta-analyses of the efficacy of this formulation reached contrasting conclusions. Sanchez-Ramos et al. [3] concluded that the ''vaginal insert was less effective than other prostaglandins'', whereas Hughes et al. [4] found ''no clinically significant differences'' between the effects of this preparation and of other standard prostaglandin preparations.

However, the clinical trials so far published involved nonhomogeneous populations with both nulliparous and multiparous women in most cases. In addition, the baseline

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cervical conditions were often so diverse that the Bishop score ranged from 0 to 8 in the same patient sample. This heterogeneity of inclusion/exclusion criteria in the available trials seems to be the main reason why no conclusions have been reached that can be applied to specific clinical situations.

For these reasons, we decided to compare the efficacy and safety of the slow-release vaginal dinoprostone insert with dinoprostone administered intracervically in a challenging clinical population of a kind frequently encountered; we selected that of nulliparous women with very unfavourable cervical conditions requiring labour induction at term.

2. Materials and methods

2.1. Subjects

This prospective, randomised, controlled study was carried out between May 2001 and June 2003 in consecutive patients requiring labour induction. Inclusion criteria were: singleton pregnancy, nulliparity, Bishop score < 4, gestational age $>$ 37.0 according to a first trimester ultrasound evaluation. Exclusion criteria were: previous uterine surgery, known hypersensitivity to prostaglandins, fetal malpresentation, suspected cephalopelvic disproportion, placenta praevia, rupture of membranes, any other condition contraindicating vaginal delivery.

One hundred and forty-four consecutive women requiring induction of labour and fulfilling the above criteria were randomised. The study was approved by the IRB. Written informed consent was signed before treatment, as in every case of labour induction at our institution.

The patients were allocated to treatment with either the 10 mg vaginal dinoprostone insert (Propess, Ferring, Germany) or 0.5 mg intracervical dinoprostone (Prepidil gel, Upjohn, Kalamazoo, MC, USA) in the morning in blocks of eight, with the aid of a computer-generated random list. The resident in charge of labour induction was informed of the next treatment allocation by the senior midwife (who kept the list). Treatment groups were designated the ''vaginal insert'' and ''cervical gel'' groups. Data were collected and analysed by one of us (P.V.), and the random assignments were not revealed until after the analysis was complete. Then results were presented to the other co-authors for discussion.

2.2. Protocol

The treatment protocol was as follows:

1. In the outpatient clinic, the women underwent a gynaecological examination and an ultrasound scan, and were then scheduled for labour induction on the next day.
2. Patients were admitted in the morning, signed their informed consent forms, underwent Bishop scoring and were randomised.
3. Fetal heart rate (FHR) and uterine activity were monitored for 30 min.
4. Either a vaginal insert or intracervical gel was then administered.
5. FHR and uterine activity were monitored for at least 30 min every 2 h.
6. After 6 h a gynaecological examination was performed to assess the Bishop score: in the cervical gel group women with a Bishop score < 4 received another dose of intracervical gel, while those with Bishop scores between 4 and 6 received 2 mg dinoprostone gel by the vaginal route (Prepidil gel).
7. Twelve hours after the start of treatment the Bishop score was re-evaluated and the vaginal insert was removed.
8. On the next morning, 24 h after the start of treatment 2 mg dinoprostone was administered to women in both groups who were not yet experiencing regular uterine contractions.
9. Six hours later every woman who was not yet in labour had her labour induced with an oxytocin infusion given according to a standard protocol. Amniotomy was performed only in women in labour with at least 5 cm of cervical dilatation. Oxytocin augmentation was done in the second stage of labour if necessary.

2.3. Statistical analysis

The main outcome measure was the rate of caesarean sections (CS). When intracervical gel was used for labour induction in nulliparous women with immature cervix we observed a CS rate of 38% (unpublished data). Data in the literature data indicate a lower rate of CS with the vaginal insert than with other prostaglandin preparations, and on the basis of this we had set up the hypothesis that this vaginal insert would allow a reduction of 50% in the CS rate in our population. Therefore, we estimated that 138 cases were enough to allow evaluation of the difference between treatments with 80% power.

Secondary measures were: changes in Bishop score at 6 h and 12 h, delivery within 12 h and 24 h, need for oxytocin to attain induction, failure of induction (delivery $>$48 h after administration), requirement of pharmacological intervention to manage tachysystole/hyperstimulation, length of admission stay.

3. Results

One hundred and forty subjects completed the study. In four other cases (two in each group) the protocol was violated because the mothers developed intolerance to their contractions in the absence of tachysystole or hyperstimulation. These patients refused to continue induction and then required and underwent CS a few hours after the start of preinduction cervical ripening. According to the intention-to-treat analysis, demographic and clinical data in the 144