

## EDITORIAL

# Prostaglandins in Induction of Labour

**Harsh Shah**

Executive Editor, National Journal of Medical Research

## ABSTRACT

Prostaglandins are naturally occurring hormones that play a significant role in the commencement of labour. Prostaglandins have been utilised in clinical practise to ripen the cervix and elicit uterine contractions synthetically since the 1960s. When a woman's cervix is immature (when her Bishop score is less than six), they are more likely to utilise them. Cervical ripening and labour induction are aided by prostaglandins, which work on cervical collagen to relax and dilate the cervix in anticipation of giving birth. It's possible that prostaglandins have a role in inducing uterine contractions. The benefits of prostaglandins in inducing labour are discussed in this article.

**Keywords:** Prostaglandin, induction, labour, cervical ripening

Prostaglandin E2 acts on the cervix by dissolving the collagen structural network of the cervix. Prostaglandin E2, Dinoprostone, is available in 3 different preparations as a cervical ripening agent: controlled-release gel 10 mg (Cervidil), intravaginal 1 mg and 2 mg gel (Prostin), and intracervical 0.5 mg gel (Prepidil). Vaginal preparations (Prostin, Cervidil) are easier to administrate than intracervical (Prepidil) preparations. The controlled-release gel preparation (Cervidil) allows easier removal in case of uterine tachysystole with FHR changes and requires only a 30-minute delay before the initiation of oxytocin upon its removal compared with an interval of 6 hours for the gel.

Advantages of PGE2 include patient acceptance, a lower operative rate than oxytocin, and less need for oxytocin augmentation when used with an unfavourable cervix (Bishop < 7). Cost savings may be realized by a reduction in operative deliveries and/or lengths of stay. PGE2 is a bronchodilator and is not contraindicated in women who suffer from asthma. In a prospective study of 2513 women with known asthma and who received PG, none had evidence of an exacerbation of their condition.<sup>1</sup>

A 2009 Cochrane review including 63 studies (10 441 women) reported that compared with placebo vaginal PGE2 reduced both the likelihood of not achieving a vaginal delivery within 24 hours (18% vs. 99%, RR 0.19, 95% CI 0.14 to 0.25) and the use of oxytocin stimulation (21.6% vs. 40.3%). There was no difference in CS, but there was an increase with vaginal PGE2 in uterine tachysystole with FHR changes (4.6% versus 0.51%, RR 4.14, 95% CI 1.93 to 8.90). The tablet, pessary, and gel were equivalent, although the sustained released PGE2 insert was associated with a decrease in instrumental deliveries.<sup>2</sup>

A 2008 Cochrane review of intracervical gel versus placebo included 28 trials with 3764 women undergoing cervical ripening or induction regardless of membrane status. There were fewer women in the PG group who did not achieve vaginal delivery within 24 hours (RR 0.61 95% CI 0.47 to 0.79). There was a non-significant reduction in the overall risk of CS for all women (RR 0.88, CI 0.77 to 1.00), but there was a statistically significant reduction of CS (RR 0.82, 95% CI 0.68 to 0.98) in women with an unfavourable cervix and intact membranes, suggesting that oxytocin alone can and should be used for induction after term PROM. There was an increased risk of uterine tachysystole without

changes in FHR (RR 1.59 95% CI 1.09 to 2.33) but no increase tachysystole with FHR changes.<sup>3</sup>

The same review compared intracervical and intravaginal interventions in 3881 women in 29 trials. The risk of not achieving vaginal delivery at 24 hours was greater in the intracervical group (RR 1.26, 95% CI 1.12 to 1.41) but there were no differences in the risk of CS and tachysystole with or without fetal heart changes.

PGs have been used to induce labour with PROM at term. A 2006 Cochrane review included 12 trials (6814 women, PROM > 37 weeks) and compared planned management with either oxytocin or vaginal prostaglandin with expectant management. Overall, there was no difference for mode of birth; results were similar for CS and vaginal delivery. For women who underwent planned delivery, there was less chorioamnionitis or endometritis and fewer admissions to NICU, but no difference in neonatal infection rates. One trial found that women in the planned group were more likely to perceive the experience as being more positive.<sup>4</sup>

The timing of insertion may have an influence on interventions. One study of 620 women (nulliparous and parous) compared admission in the morning versus the evening and found that morning inductions were less likely to need oxytocin infusion (45% vs. 54%, RR 0.83, 95% CI 0.70 to 0.97). Nulliparous women admitted in the morning had fewer operative vaginal births (16.1% vs. 34.2%, RR 0.47, 95% CI 0.25 to 0.90). Adverse effects with the use of prostaglandin E2 include uterine tachysystole and maternal effects (i.e. fever, chills, vomiting, diarrhea). Care must be taken to avoid application of the higher dose vaginal preparations into the cervical canal. Rare, idiopathic adverse cardiovascular events may occur, but they almost always occur immediately after the administration of the agent.<sup>5</sup>

In the event of tachysystole, attempts should be made to remove the prostaglandin from the vagina. Intrauterine rescue may be required and use of a tocolytic agent may be considered (intravenous Nitroglycerin 50 mcg given over 2 to 3 minutes and repeated every 3 to 5 minutes to a maximum of 200 mcg). To date, the evidence for safety and efficacy remains inconclusive. Another option is the use of nitroglycerin spray (0.4 mg, 1 to 2 puffs sublingual), which has the advantage of a simple and rapid administration and

uptake, although there have been no clinical trials assessing dosing.<sup>6</sup>

Outpatient PG is an attractive option for reducing the use of health care resources. Large studies are lacking to determine their overall safety, in particular for rare but serious adverse effects. A 2003 RCT of 300 women evaluated outpatient versus in-patient induction with Cervidil. Three hundred eligible patients with uncomplicated, low-risk pregnancies and a Bishop score  $\leq 6$ , parity  $\leq 5$ , gestation  $> 37$  weeks, a reactive NST, and singleton cephalic pregnancy with intact membranes. Cervidil was inserted and the patient monitored for 1 hour before being allowed to go home. Use of oxytocin, epidural rate, operative delivery rate, CS rate, and median time to labour and delivery within 24 hours were the same for each group. The outpatient group spent a median of 8 hours at home and reported a higher satisfaction during the initial 12 hours (56% vs. 39%).<sup>7</sup>

Current recommendations for outpatient induction in low-risk pregnancies suggest continuous electronic fetal monitoring for 1 to 2 hours after administration of PG and the use of intermittent auscultation when labour is active.<sup>8</sup>

A 2010 Cochrane review including 28 RCTs with 2616 women who were induced with mechanical and pharmacological methods concluded that the outpatient setting was feasible, but that there was insufficient evidence to recommend which method was most effective and safe.<sup>9</sup>

Sweeping of the membranes during induction of labour increases success rates. Two randomized trials recruited women with term, cephalic, nulliparous and parous pregnancies and intact membranes scheduled for induction with PG vaginal gel if the cervix was unfavourable (Bishop  $\leq 4$ ) or with amniotomy if the cervix was favourable (Bishop  $> 4$  or cervix  $> 3$  cm). Both groups were treated according to institutional protocols for active management of labour. Both studies showed that membrane sweeping at the time of induction resulted in shorter induction to delivery time, lower use of oxytocin, and a higher rate of spontaneous vaginal deliveries. Tan et al.<sup>10</sup> benefit applied to both nulliparous and parous women, while Foong et al.<sup>11</sup> found that

the benefit of sweeping was limited to nulliparous women with an unfavourable cervix. Tan et al. also found both higher maternal satisfaction in the birth process and higher post-sweeping pain.

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