MULTIPLE-DOSE INTRACERVICAL PROSTAGLANDIN E2 FOR CERVICAL RIPENING

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SUMMARY

Eighty women planned for induction of labour at > 35 weeks of gestation with poor Bishop Score were included in this study. All had a single fetus with cephalic presentation with reactive NST. Common indications for induction were post-dated pregnancy, decreased fetal movements, PIH & IUGR. Prostaglandin E2 (PGE2) gel 2.5mg was instilled intracervically and, if required, repeated 12 hourly upto a maximum of 3 doses. In 68 patients (85%) cervical ripening was effected with one instillation, in 8 with two and in 1 patient with three instillations. Cumulative success rate was 96.25%. Thirty-seven patients (46.25%) went into labour and delivered with gel application alone. The mean instillation delivery interval was 13.48 hours in primigravidae and 10.04 hours in multigravidae (P=NS). There was no significant maternal or foetal morbidity or mortality with PGE2 gel. Multiple doses of PGE2 gel can improve the response rate in cervical ripening.

INTRODUCTION

The cervix, which was previously considered a passive structure in the process of human parturition, has come to be recognised as a dynamic organ in its own right (Ulmsten 1983). Spontaneous labour and vaginal delivery in an uncomplicated parturition follow a cascade of synchronous events that include soft-

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ening and effacement of cervix. An unripe cervix impedes attempts at induction and may predispose both mother and baby to increased morbidity in certain complicated pregnancies.

Various methods of cervical ripening have been tried. Of these, prostaglandin E2 administered intracervically has been reported to be most advantageous in terms of increased efficacy and diminished side effects (Rayburn et al 1989, Zanini et al 1990). A single dose of 0.5mg PGE2 gel is superior to placebo in maturing the uterine cervix. However if the maturing effect is insufficient, failure of induction and caesarean section rates are nearly as high as when the cervix has been ripened with placebo (Trofatter et al 1985, Yonekura et al 1985, Bernstein et al 1987).

This study aims to test the efficacy and safety of repeated application of PGE2 gel in ripening of cervix.

MATERIALS AND METHOD

Eighty women attending the Antenatal and High Risk Pregnancy Clinic at the All India Institute of Medical Sciences were included in this study. Inclusion criteria were as follows: gestational age >35 weeks, intact membranes, single fetus, cephalic presentation, Bishop score ≤5, patient not in labour, a reactive non-stress test (NST).

Patients were excluded from the study if any of the following were present: known hypersensitivity to prostaglandins, previous attempt at cervical ripening or induction of labour, previous uterine surgery, suspected or evident fetal compromise, history of vaginal bleeding, fever, glaucoma, asthma.

Detailed history was taken and general physical and obstetric examination done. Cervical assessment was done by Bishop's Score (Bishop 1964). Prostaglandin E2 gel (Cerviprime, Astra-IDL) 2.5 mg was instilled with all aseptic precautions in the cervical canal. The patient was kept in the recumbent position for one hour. Fetal heart rate and uterine contractions were monitored every 30 mins. Monitoring was continued if the patient went into labour during the 12 hour observation period and routine labour and delivery care provided.

If labour did not ensue, the Bishop Score was reassessed by the same examiner who had done the pre-instillation examination. Successful cervical priming was defined as a change in Bishop's Score of ≥3. If the cervix became favourable but the patient was not in labour, labour was induced. If the cervix did not become favourable, repeat instillation was done at an interval of 12 hours upto a maximum of 3 instillations.

RESULTS

Of the 80 patients recruited in this study, 32 (40%) were primigravidae and 48(60%) multigravidae. All had completed 36 weeks gestation. The mean gestation period was 39.25 weeks.

Bishop's Score was ≤2 in 35 (43.75%) patients and 3-5 in 45 (56.25%) patients. In both groups, 40% patients were primigravidae and the remaining multigravidae.

Indications for induction are shown in Table I.

A total of 96 instillations were done in 80 patients. In 68 patients (85%), cervical ripening was effected with one instillation and in 8 patients with 2 instillations. Four

Table I
INDICATIONS FOR INDUCTION OF LABOUR

Indication	No. of patients (n = 80)
Postdated pregnancy	29
Decreased foetal movement	18
PIH	16
IUGR	12
Previous stillbirth	3
Gestational diabetes mellitus	1
Bad Obstetric History	1

Table II
RELATION OF BISHOP SCORE TO INSTILLATION DELIVERY INTERVAL

Bishop Score	Instillation-Delivery interval (hours)	Primigravida (n=15)	Multigravida (n=22)	P Value
0-2	4-8	2	3	
	9-13	-	2	
	14-18	-	1	
	19-23	4	-	
	Mean	15.95 + 6.5	10.42 + 5.1	0.05 NS
3-5	4-8	2	5	
	9-13	4	6	
	14-18	1	4	
	19-23	2	1	
	Mean	11.83 + 6.3	10.8 + 5.5	0.05 NS

Table III
CHANGE IN BISHOP SCORE WITH PGE2 GEL

Gravidity	Bishop Score	
	Before	After
Primigravidae (n=15)		
Mean	2.3	6.1
Range	0-5	1-9
Multigravidae (n=22)		
Mean	2.6	6.4
Range	0-5	3-9

patients required 3 instillations. Of these, 3 failed to respond. Thus the cumulative success rate was 96.25%.

Forty (50%) patients went into labour and delivered with gel application alone. Thirty seven patients had vaginal delivery. Of these, 32 (86.5%) delivered after 1 instillation, 4 (10.8%) after 2 and one (2.7%) after 3 instillations. Three patients had caesarean section. The indications were fetal distress, non progress of labour and severe PIH.

Table III shows the relationship of Bishop Score to instillation-delivery interval in primi and multigravidae who delivered with PGE2 gel anone. The mean instillation-delivery interval was 13.48 hours in primigravidae and 10.04 hours in multigravidae.

There was no significant maternal or perinatal morbidity or mortality in the study cases. All the infants had an Apgar Score of more than 7 at birth.

Among the 40 patients who did not go into labour also, there was significant improvement in the Bishop Score. Table III shows the Bishop Score before and after PGE2 gel instillation vis-a-vis primi and multigravidae. These patients were then induced with oxytocin or oral PGE2.

DISCUSSION

Ripeness of cervix is one of the most important conditions which influences the success of induction. Intracervical application requires a much smaller dose of PGE2 gel than intravaginal administration and produces fewer side-effects (Zanini et al 1990). Post-dated pregnancy is the commonest indication for induction in most series followed by PIH & IUGR (Bernstein et al 1987, Norchi et al 1992, Miller et al 1991).

In our study, 85% patients responded to the first instillation of PGE2 gel. Similarly Norchi et al (1991/1992) found 75.6%

response to the first instillation.

Many workers have recognised the benefits of multiple instillations in patients who do not respond to the first instillation. In the present study the response improved to 95% with the second instillation and 96.25% with the third. This illustrates the value of multiple dose instillations for providing maximum benefit to the patient. Similarly, Mainprize et al (1987) and Norchi et al (1992) found 100% response rate with the third instillation. All patients went into labour or had significant Bishop Score Modification. As many as 9 instillations have been reported with 100% response at ≥ 9 instillations (Miller et al 1991) but the dose used in this study was only 0.25 mg. In our study, however, there was no significant improvement in the response rate from the second to the third instillation. Further management of non-responders needs to be judged on individual basis keeping in mind the indication of induction, the maternal and fetal condition and the urgency of delivering the baby, if any.

A large number of patients who receive PGE2 gel for the purpose of ripening ultimately go into labour and deliver, a fact which is gratifying for both patient and obstetrician. Various studies have reported 37-73% patients going into labour with one or more gel application (Norchi et al 1992, Sasikala 1994, Daftary et al 1994, Mainprize et al 1987, Handa et al 1994).

The safety and efficacy of intracervical PGE2 gel has been documented in a large number of studies (Rayburn et al 1989). Hyperstimulation and fetal heart deceleration were not seen in any of our patients, thereby confirming the very low incidence of problems with intracervical PGE2 gel.

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