Original articles

J. Perinat. Med.
8 (1980) 236

Comparative trial of extra-amniotic and vaginal prostaglandin E_2 in tylose gel for induction of labor

G. A. Clarke*, A. T. Letchworth**, A. D. Noble***

* Registrar, Dept. of Obstetrics and Gynaecology, Royal Hampshire County Hospital, Winchester
** Senior Lecturer, Dept. of Human Reproduction and Obstetrics, Southhampton University and Honorary Consultant, Dept. of Obstetrics and Gynaecology, Royal Hampshire County Hospital, Winchester
*** Consultant, Dept. of Obstetrics and Gynaecology, Royal Hampshire County Hospital, Winchester

1 Introduction

Oral, intravenous and local prostaglandins have now been widely studied for the induction of labor. Significant benefits have been demonstrated for the induction of abortion and the induction of labor when the cervix is unfavourable [12, 14].

When the cervix is favourable, prostaglandins alone have not been shown to have significant advantages over surgical induction and Syntocinon and are associated with a high incidence of gastrointestinal side effects [6, 15].

However, surgical induction is not without problems. When the cervix is unripe, artifical rupture of the membranes (ARM) may be difficult and labor may be long or fail to become established. It is also associated with the risk of umbilical cord prolapse and uterine infection. There is a growing reluctance by patients to undergo surgical induction with its discomfort, frequent requirement for intravenous infusion and subsequent confinement to bed. There is also an increased workload on nursing staff.

Local protaglandins (vaginal and extra-amniotic) have been used with success for pre-induction 'priming' when the cervix is unripe and have been found to produce less gastrointestinal side effects than other routes of administration [3,11, 13].

This trial sets out to compare the effectiveness of single doses of PGE_2 in tylose gel given either extraamniotically or vaginally prior to the surgical induction of labor in patients of varying parity and cervical 'ripeness'.

2 Method

Patients under two of the consultants at the Royal Hampshire County Hospital who required induction were included in the trial, unless there was clinical or biochemical evidence of placental insufficiency, suspected cephalo-pelvic disproportion, a scarred uterus, or a malpresentation.

Prostaglandin E_2 (PCE_2–Upjohn) in 10 ml of 6 per cent tylose gel (Hescht) was used. The vaginal dose given was 2.0 mgm and the extra-amniotic dose given was 0.3 mgm.

Patients for induction of labor were randomly assigned to either group according to whether their date of birth was in an odd or even year. **At midday on the day prior to planned surgical induction, the prostaglandins were inserted** via a WARNE disposable female urinary catheter after

0300-5577/80/0008-0236$02.00

assessment of the cervix for 'ripeness' using a modified BISHOP's score [1]. The catheter was then withdrawn. According to the route designated, **the PGE_2 was placed either into the posterior fornix of the vagina, or extra-amniotically posterior to the presenting part, just inside the internal os.** No cervical stretching or sweeping of fetal membranes was carried out. The patients were rested in bed for two hours and then allowed to ambulate. If labor became established, artificial rupture of the membranes was only performed when the cervix was at least 5 cm dilated. Fetal heart monitoring was performed when possible. The patients who were not delivered or in established labor within 20 hours were reassessed and artificial rupture of the membranes performed. Intravenous Syntocinon was then used in these patients when indicated.

3 Results

A total of 261 patients were studied, of whom 128 were given vaginal PGE_2, and 133 were given extra-amniotic PGE_2. There was no statistically significant difference in the two groups in respect of age, gestation, parity and cervical 'ripeness'. The indications for induction were varied but 'post-maturity' and pre-eclampsia were the most common indications. The induction of labor was considered successful if the patients were delivered vaginally within 24 hours of the application of the prostaglandins without further stimulation other than ARM in labor (Tab. I). The results were further subdivided according to parity and BISHOP's score (Tab. I).

Five patients became established in labor with PGE_2 with cervical dilatation greater than 5 cm, but then developed secondary inertia. They required intravenous Syntocinon and were not included in the successful induction group.

No Caesarean sections were required in the group who became established in labor following prostaglandin induction. The induction-delivery intervals in the successful groups were similar (Tab. II).

Hypertonus for the purposes of this trial was defined as failure of the uterus to relax between contractions, or contractions lasting longer than two minutes. There were no cases of hypertonus during this trial. There were eight patients in the vaginal group who had labors lasting less than four hours. All were multigravida with 'ripe' cer-

Tab. I. Relationship of cervical score and parity to incidence of labor after PGE_2 alone.

	Modified BISHOP Score < 5 (less than)		Modified BISHOP Score > 5 (greater than)		All patients
Vaginal	PG	MG	PG	MG	
Number of patients	32	27	29	40	128
Number who labored following PGE_2 alone	11	11	11	34	67
Percentage who labored following PGE_2 alone	34.4	40.7	37.9	85.0	52.3
Extra-amniotic					
Number of patients	34	33	35	31	133
Number who labored following PGE_2 alone	11	12	13	17	53
Percentage who labored following PGE_2 alone	32.4	36.4	37.1	54.8	39.8
Significance of difference (x^2)	NS	NS	NS	$p<.01$	NS

PG = Primigravid
MG = Multigravid
NS = Not significant

Tab. II. Results when labor followed administration of PGE_2 alone.

	Vaginal PGE_2	Extra-Amniotic PGE_2	Significance of difference
Mean induction delivery interval (hours ± SD)	9.9 ± 5.4	10.9 ± 5.4	NS (student)
Mean 1 minute APGAR score ± SD	8.2 ±1.1	8.4 ± 1.1	NS

vices. Two patients (one multigravida and one primigravida) in the extra-amniotic group also had labors of less than four hours. There were no apparent ill effects to mother or fetus from these labors.

Apart from one patient who had been suffering from diarrhoea and vomiting for two days prior induction, **no patients developed diarrhoea following the use of prostaglandins, and there were no cases of vomiting** prior to sedation being given in labor.

Of the patients who labored successfully following prostaglandin treatment, there was only one infant with an Apgar score of less than 5 at 1 minute and the APGAR scores in this case were 4 and 9 at 1 and 5 minutes respectively. The mean Apgar scores for the two groups of successful inductions showed no significant difference (Tab. II).

No significant fetal heart abnormalities were noted during the first stage of labor in either group when labor was successfully induced with prostaglandins. Four of the patients were delivered by forceps for suspected fetal distress in the second stage of labor, but all these infants had good APGAR scores at birth.

Only one patient out of the 261 studied developed an intra-partum pyrexia. This patient failed to establish in labor following vaginal prostaglandins and then required Caesarean section for failure to progress in labor 24 hours after surgical induction.

There was a moderate improvement in BISHOP's score for the two groups of patients requiring surgical induction (Tab. III). The mean induction delivery intervals for these patients (excluding Caesarean sections) were similar in both groups (Tab. III). Eight patients required Caesarean section for suspected cephalo-pelvic disproportion and failure to progress in labor after surgical induction.

Tab. III. Results when surgical induction was required.

	Vaginal PGE_2		Extra-Amniotic PGE_2	
Mean change in modified BISHOP score ± SD	2.1 ± 1.5		2.1 ± 1.5	
Mean induction delivery interval (hours ± SD)	PG	MG	PG	MG
	10.0 ± 5.4	7.1 ± 3.2	11.1 ± 5.6	6.7 ± 3.1

4 Discussion

Both routes of administration achieved significant reductions in the requirement for the surgical induction of labor. In the dosages used, the vaginal route established labor in a higher proportion of patients, but this was not statistically significant, except in the group of multigravida with 'ripe' cervices. In both schedules patients who were multiparous or had a high BISHOP's score were more likely to establish in labor with prostaglandins. This is in agreement with previous studies with local prostaglandins [2, 7].

Despite the wide variation in parity and cervical score, both schedules were found to be without significant risk to the mother of the fetus. Although not all patients could be monitored throughout labor, patients were monitored when indicated. The absence of any detected significant fetal heart abnormalities and the good APGAR scores of all infants at 5 minutes is reassuring.

Gastro-intestinal side effects have been frequent with many prostaglandin regimes [4, 8, 10], but in the dosages used in this trial these did not occur.

Recent work has demonstrated the value of ambulant labor [5]. The use of local prostaglandins extends the advantages of this type of labor to a greater proportion of induced labors.

In the group of patients who were not successfully established in labor with the use of prostaglandins, there was a moderate improvement in the BISHOP's score, which was comparable for both routes of administration. The mean induction-delivery intervals for these self-selected labor resistant groups were acceptable although no direct comparison could be made with non-primed labors. Previous trials have shown the benefits of cervical priming with extra-amniotic and vaginal prostaglandins followed by surgical induction, with respect to length of labor, success or surgical induction, and maternal and fetal well-being [2,

7, 9]. A relatively small percentage of primiparous patients and those with unripe cervices became established in labor. As more experience is gained, a variable dose of prostaglandins could be given, being calculated according to parity and BISHOP's score.

Patient response is difficult to assess objectively but it has been felt that the simplicity of the induction procedure and the ability to ambulate in early labor has led to an improved acceptance by patients of induction of labor.

Although both routes of administration achieved similar results, **vaginal prostaglandins have the advantage of simplified applications**, ease of removal if required and the avoidance of the potential risks of trans-cervical invasion of the uterus [8]. The availability of vaginal pessaries would further simplify the administration of the prostaglandins.

Summary

Two hundred and sixty-one patients of varying parity and cervical 'ripeness" were given Prostaglandin E_2 (PCE_2) in tylose gel either vaginally (2.0 mgm) or extraamniotically (0.3 mgm) prior to planned surgical induction.

Surgical inductions was avoided in 52 per cent of the vaginal group and 40 per cent of the extra-amniotic group. When subdivided according to parity and cervical ripeness, **both groups were comparable except in the multigravid patients with high cervical 'scores', when the vaginal route was significantly more likely to establish labor.**

Both groups were without significant ill-effects to the mother or fetus.

Keywords: Parity, prostaglandines, ripeness.

Zusammenfassung

Vergleichende Untersuchung über extraamniale und vaginale Prostaglandin E_2-Applikation zur Weheninduktion

261 Patientinnen unterschiedlicher Parität und mit verschiedenen zervikalen Reifebefunden erhielten einen Prostaglandin E_2-Tylose-Gel (PGE_2), der kurz vor einer geplanten „operativen" Einleitung entweder vaginal (2.0 mg) oder extraamnial (0.3 mg) appliziert wurde.

Die „operative" Einleitung konnte in der vaginalen Gruppe bei 52%, in der extraamnialen Gruppe bei 40% umgangen werden. Unterteilt man die Gruppen nach Parität und zervikalem Reifestatus, so haben beide Applikationsformen bis auf die Gruppe der Mehrgebärenden vergleichbare Erfolgsquoten. **Bei Mehrgebärenden mit einem reifen Zervixbefund scheint die vaginale Anwendung die Wehentätigkeit besser zu stimulieren.**

Es wurden in beiden Gruppen weder bei der Mutter noch beim Kind Nebenwirkungen beobachtet.

Schlüsselwörter: Parität, Prostaglandine, Reifestatus.

Résumé

Essai comparatif d'application extraamniotique et vaginale de prostaglandine E_2 sous forme de gel de tylose pour induction du travail.

De la prostaglandine E_2 (PGE_2) a été appliquée à deux cent soixante et une patientes ayant des parités et maturités cervicales diverses, soit par voie vaginale (2,0 mgm), soit par voie extraamniotique, avant d'entreprendre l'induction instrumentale.

L'induction instrumentale a été nécéssaire dans 52% des cas du groupe «vaginal» et dans 40% des cas du groupe «extra-amniotique». En tenant compte des parités et maturités cervicales, les deux groupes étaient comparables, à l'exception des multipares à haut score cervical, où la voie vaginale était significativement plus apte à induire le travail.

Les deux groupes étaient sans différences significatives pour ce qui est de la morbidité maternelle ou foetale.

Mots-clés: Maturité, parité, prostaglandine.

Acknowledgements: We thank the medical and nursing staff of the Obstetric Unit of the Royal Hampshire County Hospital for their co-operation, Mr. GRAYSON for his help with preparation of the gel, and Mrs. C. ALLISON for her preparation of the typescript.

Bibliography

[1] CALDER, A. A., M. P. EMBREY, K. HILLIER: Extra-amniotic prostaglandin E_2 for the induction of labour at term. J. Obstet. Gynaec. Brit. Cwlth. 81 (1974) 39

[2] CALDER, A. A., M. P. EMBREY, T. TAIT: Ripening of the cervix with extra-amniotic prostaglandin E_2 in viscous gel before induction of labour. Brit. J. Obstet. Gynaec. 84 (1977) 264

[3] EMBREY, M. P., A. A. CALDER, K. HILLIER: Extra-amniotic prostaglandins in the management of intra-uterine foetal death, anencephaly and hydatidiform mole. J. Obstet. Gynaec. Brit. Cwlth. 81 (1974) 47

[4] EMBREY, M. P., K. HILLIER: Therapeutic abortion by intra-uterine instillation of prostaglandins. Brit. Med. J. 1 (1971) 588

[5] FLYNN, A. M., J. KELLY, G. HOLLINS, P. F. LYNCH: Ambulation in labour. Brit. Med. J. 2 (1978) 591

[6] KELLY, J., A. M. FLYNN, P. V. BERTRAN: A comparison of oral prostaglandin E_2 and intravenous syntocinon in the induction of labour. J. Obstet. Gynaec. Brit. Cwlth.

[7] MACKENZIE, I. Z., M. P. EMBREY: The influence of pre-induction vaginal prostaglandin E_2 gel upon subsequent labour. Brit. J. Obstet. Gynaec. 85 (1978) 657

[8] MACKENZIE, I. Z., M. P. EMBREY: Single extra-amniotic injection of prostaglandins in viscous gel to induce abortion. Brit. J. Obstet. Gynaec. 83 (1976) 505

[9] MACLENNAN, A. H., R. C. GREEN: Cervical ripening and induction of labour with intravaginal prostaglandine E_2. Lancet I (1979) 117

[10] MURNAGHAN, G. A., H. LAMKI, S. RASHID, J. PINKERTON: Induction of labour with oral prostaglandin E_2. J. Obstet. Gynaec. Brit. Cwlth. 81 (1974) 141

[11] SHEPHERD, I., C. SIMS, I. CRAFT: Extra-amniotic prostaglandin E_2 and the unfavourable cervix. Lancet II (1976) 709

[12] SOUTHERN, E. M., G. D. GUTKNECHT, N. R. MOHBERG, D. A. EDELMAN: Vaginal prostaglandin E_2 in the management of foetal intrauterine death. Brit. J. Obstet. Gynaec. 85 (1978) 437

[13] STEINER, H., H. P. ZAHRADNIK, M. BRECKWOLDT, D. ROBRECHT, H. G. HILLEMANNS: Cervical ripening prior to induction of labour. Prostaglandins. 17 (1979) 125

[14] VALENTINE, B. H.: Intravenous Oxytocin and Oral Prostaglandin E_2 for ripening of the unfavourable cervix. Brit. J. Obstet. Gynaec. 84 (1977) 846

[15] WEEKES, A. R. L., H. H. MAKANJI, C. R. WEST: Comparison of intravenous oxytocin and prostaglandin E_2 for accelerating labour. Brit. Med. J. 1 (1976) 987

Received December 5, 1979. Revised January 28, 1980. Accepted March 14, 1980.

A. T. Letchworth, M.D.
Dept. Obstet. & Gynecol.
Royal Hampshire County Hosp.
Winchester
England