

COMPARATIVE STUDY BETWEEN PROSTAGLANDIN E2 VAGINAL TABLET AND INTRAVENOUS OXYTOCIN IN INDUCTION OF LABOUR

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SYNOPSIS

Induction of labour by a single vaginal prostaglandin (PG) E2 tablet was compared with standard induction with amniotomy and intravenous oxytocin in a controlled study of 80 patients of low parity and favourable induction features. Labour was successfully induced in 39 (97.5%) of the 40 patients given a single vaginal PGE2 tablet. 31 (80%) of these patients went on to delivery with prostaglandin alone while 8 (20.0%) of these patients who were in labour subsequently required additional intravenous oxytocin to augment labour in order to achieve delivery. Cervical score at amniotomy was more favourable for the PGE2 group. The induction-delivery interval is longer in the PGE2 group but the amniotomy-delivery time is shorter when compared with the oxytocin group. Pethidine requirement is less in the PGE2 group. The mode of delivery, blood loss and fetal outcome were not significantly different for both groups. No hyperstimulation was encountered and no significant side-effects attributable to the mode of induction was found.

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INTRODUCTION

Since time immemorial man had been trying various methods, many bizarre and some dangerous, to induce labour. The root of current method of induction of labour began in 1756 when Denman introduced artificial rupture of the forewaters for induction of pre-term labour in cases of contracted pelvis. A century and a half later, William Blair Bell (1909) introduced oxytocin to clinical practice and in 1948 Theobald successfully used posterior pituitary extract for induction of labour and thus set the path for modern method of induction of labour. Turnbull and Anderson in 1968 showed that intravenous oxytocin following amniotomy is both safe and efficacious and this had remained to this day as one of the most widely used method of induction of labour.

Man's quest for an alternative method began at around the same time. Karim in 1968 first demonstrated that intravenous prostaglandins (PG) could be used to induce labour. However as systemic prostaglandins has unacceptable side-effects, costs more, and is no more efficacious than intravenous oxytocin¹, attention was focused on local administration in the genital tract and favourable results were reported by various authors^{2,3,4,5}.

In Singapore amniotomy followed by intravenous oxytocin is the most common method of induction of labour. PGE2 vaginal tablets had been introduced in recent years and this study was undertaken to compare the 2 methods.

PATIENTS AND METHODS

A total of 80 patients were studied. All were of low parity 0, 1 or

2 and had a singleton pregnancy with a cephalic presentation at 38-42 weeks gestation. Only patients with a modified Bishop's cervical score (Table 1) of 4 or more were included. The patients profile and indications for induction were as shown in Table 2.

The patients were allocated to two equal groups. The mean age and parity of the two groups were not significantly different. The first group had induction of labour by the department's standard method of amniotomy and simultaneous intravenous infusion of a solution of 3 units of oxytocin (Orasthin, @ Hoechst) in 500mls of dextrose 5% beginning at 30 drops per minute and increasing at 10 drops per minute at 15 minutes interval till desired uterine contractions were achieved. The second group of patients was induced by a single tablet of 3 mg of PGE2 in lactic acid base (Upjohn) inserted in the posterior fornix, and had amniotomy when they were considered to be in labour as defined by the presence of intermittent regular uterine contractions more frequent than 1 in 10 minutes and lasting more than 25 seconds each, with cervical dilatation, and descent of the presenting part.

The second group was monitored with continuous cardiotocography (CTG) for 1-2 hours after insertion of the vaginal tablet and allowed feeds till rupture of their membranes. This is in contrast to the first group who were fasted from the onset.

Both groups were monitored with continuous CTG and not allowed oral intake after membrane rupture.

Vaginal examinations were carried out 4 hourly for both groups. For the PG group, after successful induction of labour, additional intravenous oxytocin was given to augment labour only if its progress was not satisfactory. If induction was not successful then no oxytocin would be given.

Intramuscular pethidine for pain relief was given as required for both groups.

RESULTS

The results were summarized in Tables 3 and 4. Labour was successfully induced in 39 of the 40 patients (97.5%) with a single vaginal PGE2 tablet. For the patient who failed to go into labour, a second PGE2 pessary was inserted after 9 hours and she developed uterine contractions thereafter and delivered vaginally after 19 hours of labour. For the 39 patients who went into labour after a single PGE2 pessary, the mean time from in-

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Table 1.
MODIFIED BISHOP SCORE

Score	Length of cervix	Dilatation of cervix	Consistency of cervix	Position of cervix	Station
0	3 cm	Closed	Firm	Posterior	- 3 cm
1	2 cm	1-2 cm	Medium	Mid	- 2 cm
2	1 cm	3-4 cm	Soft	Anterior	- 1 cm
3	< 1 cm	5-6 cm			> 0 cm

Table 2.
DETAILS OF PATIENTS AT INDUCTION.

	Group 1 Amniotomy & Oxytocin	Group 2 PGE2 Pessary
No. of patients	40	40
Mean age in years (range)	26.4 (18-40)	28.7 (17-43)
Mean parity (range)	0.88 (0-2)	1.08 (0.2) ($p > 0.05$)
Indication		
Post date	13	10
Poor weight gain	13	16
Pre-eclampsia	6	4
Others	8	10

Table 3.
MATERNAL OUTCOME

	Group 1 Amniotomy & Oxytocin	Group 2 PGE2 Pessary
Mean cervical score at induction (range)	5.18 (3-7)	4.76 (3-8)
Mean cervical score at amniotomy (range)	— do —	7.00 (4-10)
Induction-amniotomy interval mean hr (+/- SD)	N.A.	7.31 (3.64)
Amniotomy-delivery interval mean hr (+/- SD)	8.51 (5.65)	4.94 (3.60)
Induction-delivery interval mean hr (+/- SD)	— do —	12.25 (5.66) ($p < 0.01$)
Mode of delivery		
Normal delivery	31	33
Forcep/Ventose	4	4
Caesarian section	5	3 ($p > 0.05$)
Mean blood loss ml (+/- SD) excluding Caesarian section	201 (122)	179 (102) ($p > 0.05$)
No. of patients requiring pethidine	20	10 ($p < 0.02$)

Table 4.
FETAL OUTCOME

	Group 1 Amniotomy & Oxytocin	Group 2 PGE2 Pessary
Mean Apgar score at 5 min (range)	< .95 (8-9)	8.95 (8-9)
Mean birthweight in kg (range)	3.26 (2.5-4.2)	3.18 (2.6-3.9)

section of tablet to membrane rupture was 7.31 hours (SD 3.64). The mean cervical score had then improved from 4.76 (range 3-8) to 7.00 (range 4-10).

Additional intravenous oxytocin was considered necessary for 8 patients (20%) in the prostaglandin group to achieve satisfactory progress in labour. All 8 delivered vaginally. However 3 of these patients delivered within an hour of oxytocin administration and it was questionable whether the addition of oxytocin was indeed necessary in these 3 patients. Thus over 80% of the patient would be expected to deliver with prostaglandin alone.

Five patients in the oxytocin group and 3 patients in the prostaglandin group had Caesarian sections for failure to make satisfactory progress. The difference was not statistically significant.

The mean blood loss at delivery, excluding Caesarian section, was not significantly different in the two groups.

No patients in the prostaglandin group required pain relief before membrane rupture. 10 required pethidine after membrane rupture which is significantly less when compared to 20 for the oxytocin group.

Apgar scores of the babies were similar for both groups. No case of uterine hyperstimulation occurred in either group and there were no significant side effects attributable to the mode of induction.

DISCUSSION

It had been almost two decades since Turnbull and Anderson⁶ introduced amniotomy and simultaneous intravenous oxytocin titration for induction of labour. Currently this is the most popular method used in Singapore. Albeit its efficacy and safety the method has its shortcomings.

Amniotomy before the onset of contraction may be painful and relatively more difficult. This is especially so if the cervix is unfavourable.

The need for an intravenous line is perhaps most objectionable to our patients and it limits their mobility and they have to be fasted from the very onset of induction. Sophisticated infusion apparatus are required as well as nursing attention to the infusion. It may also focus the attention of the patient on an apparatus which is causing her to have painful contractions and here experience of pain may be increased by the feeling that labour is artificial rather than being a natural process.

With amniotomy and intravenous oxytocin, once embarked upon, one is committed to deliver the patient within a set time lest infection should take place. Other minor problems include water intoxication⁷, neonatal jaundice^{8,9}, hemolysis⁹, and a tendency for post-partum haemorrhages^{10,11}.

Local prostaglandins offer some answers to these shortcomings. It is an effective alternative method of induction of labour. In this study single prostaglandin vaginal tablet was successful in inducing labour in 97.5% of the patients. While 20% required additional intravenous oxytocin to augment labour, almost half of these patients may not actually require the additional oxytocin augmentation as they delivered promptly thereafter. Thus over 80% of the patients would be expected to deliver with prostaglandin alone. This concurred with findings by other authors^{2,3,4,5,12}.

The PGE2 vaginal tablets used in this study produced a gradual onset of labour, over a mean period of 7.31 hours, which is more akin to spontaneous labour. The cervical score also improved from 4.76 to 7.00 and this facilitate easier and less painful amniotomy. This would also make induction of patients with unfavourable cervix feasible.

Although the mean induction to delivery interval is longer for patients induced by PGE2 vaginal tablet, the amniotomy-delivery interval was shorter than for patients induced by amniotomy and intravenous oxytocin.

In addition, no objectionable intravenous line is necessary and the method allow patients to have oral intake and to be ambulatory before the rupture of their membranes and hence

increase patient comfort.

Another advantage is that one is not committed to delivery should induction fail. A second attempt can be made at a convenient time.

Prostaglandins not only stimulate uterine contractions but also reduce the cervical resistance which in turn decrease the amount of uterine activity necessary to achieve cervical dilatation. Thus it is not surprising that the pethidine requirement in the prostaglandin group was less than the oxytocin group. Similar findings were reported by others¹².

Other advantages of induction by PGE2 pessaries, though not apparent in this study were reported by others. Kennedy et al¹² reported significantly less blood loss at delivery for patients induced by PGE2 pessaries when compared to those induced by amniotomy and intravenous oxytocin. This was not found to be significantly so in this study.

Caesarian section rate in this study was lower in the prostaglandin group but it was not statistically significant. Other authors such as Calder et al² and Hefni and Lewis⁴ reported reduced rate of Caesarian section in their patients induced with prostaglandin E2 pessaries.

Kennedy et al¹² also reported greater patient satisfaction with this method of induction of labour as compared to amniotomy and intravenous oxytocin.

A ready objection to induction of labour by PGE2 pessary is the cost of the vaginal tablet. A vaginal tablet of prostaglandin E2 cost S\$30 as compared to S\$10 for 2 vials of 3 units Orasthin and 1 litre of dextrose 5%. However when the cost of sophisticated infusion apparatus and trained staff required to monitor the pumps were considered, then PGE2 pessary induction would actually be more economical.

However induction by PGE2 vaginal tablets has its shortcomings as well. Caution has to be exercised in patients with glaucoma or raised intra-ocular pressure, and in asthmatics. Although there are no absolute contraindication to the use of PGE2, its use is not recommended in those who are sensitive to prostaglandins, those with history of pelvic inflammatory disease, and those in whom oxytocic drugs are generally contraindicated such as previous Caesarian sections or major uterine surgery, cephalopelvic disproportion, suspicion or presence of fetal compromise, and in grand multiparae. Oxytocin can be stopped easily and can be accurately titrated while PGE2 vaginal tablet on the other hand is dissolved in the vagina and its effect cannot be controlled. Hence hyperstimulation may occur in patients who are hypersensitive to prostaglandins. This is however very rare especially with low dose of prostaglandin being used. The use of oxytocin to augment labour that has been induced by PGE2 has to be practised cautiously too so as to avoid hyperstimulation. Uterine rupture has been reported in long labours induced with prostaglandins and maintained with intravenous oxytocin^{13,14}.

The need for a better delivery system is obvious. Time release pessary may be the answer to some of the above shortcomings. Embrey et al¹⁵ had shown good results with a slow release polymer pessary. Low dose tablets to be inserted in increments like oxytocin is another alternative and this had been tried by Liggins¹⁶. Further studies are still necessary to improve on the delivery system.

This study has demonstrated that the induction of labour with a single PGE2 vaginal tablet compared favourably with the standard method of amniotomy and intravenous oxytocin. It was found to be effective and safe. The minimal amount of patient interference makes the method more akin to natural labour and dispensed with the discomfort of the intravenous line.

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