INDUCTION OF LABOUR USING PROSTAGLANDIN E_2 PESSARIES

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SUMMARY

199 patients were used in a double blind placebo controlled trial testing the efficacy of prostaglandin E_2 3 mg pessaries in the induction of labour. The trial showed that prostaglandin E_2 pessaries were effective in the induction of labour but that with only a 55% success rate the results were less than that quoted by others.

It was felt that the success rate could be increased by either reducing the time interval between insertion of the pessaries or by using a slow release vehicle for the prostaglandin. Surprisingly no significant shortening in the duration of labour was found between the prostaglandin group and the placebo group, despite a significant increase in the favourability of the cervix in the prostaglandin pessary group. Also no factors were found which definitely distinguished between the success or failure of induction of labour using prostaglandin pessaries.

It was felt that prostaglandin pessaries were a safe and reasonably effective method of induction of labour and that, with reduction in the time interval between insertion of pessaries or the use of a slow release vehicle for the prostaglandin, the efficacy would be greatly increased.

There have been a number of papers written on the use of prostaglandins, in different vehicles in the ripening of the unfavourable cervix ([1-5]) and from this has developed the concept of induction of labour, using prostaglandin pessaries ([6, 7]).

In using PGE_2 in both gel and pessary, for either the ripening of the cervix or the induction of labour, there always appeared to be a solid core of patients who remained unchanged. The clinical impression appeared to be at variance with Shepherd's results for PGE_2 pessaries ([7]).

This trial was instituted in order to assess the true efficacy of PGE_2 pessaries in the induction of labour and also in shortening the duration of labour. It was also hoped to elucidate any factors which may predispose to failure of induction, using PGE_2 pessaries.

MATERIAL AND METHODS

The patients, selected for the study, gave informed consent. They were randomly allocated into two groups on admission for induction of labour.

The trial was of the double blind, placebo-control variety, with random allocation of the active pessary between the two groups every 6 subjects.

All patients attending for induction irrespective of their cervical status as assessed by modified Bishop's score ([8]), were asked to enter the study with the exception of those not having a cephalic presentation and those in whom it was felt that inclusion in a placebo trial might involve delay and so increased risk to either mother or foetus.

Of the 201 patients entered into the trial, 2 were withdrawn, one from either group, because of the late diagnosis of breech presentation in primigravid patients, leaving 199 in the study.

Table 1 gives a comparability of the two groups, with ranges in parenthesis. Using the χ^2 test, no significant differences were found between the groups for age, parity, gestation and initial Bishop's score.

The induction rate in this hospital over the year prior to the trial was 19.1% and there was no significant change in policy during the period of the trial. The reasons for induction were as shown in table 2. The miscellaneous group included three in each group, induced

Table 1. — *Comparison of PGE_2 group and placebo group. (Results of χ^2 tests shown).*

	PGE_2 group (n = 95)		Placebo group (n = 104)		
Mean maternal age (years)	25.3	(16-39)	24.9	(17-35)	$p>0.50$
Mean gestation (days)	284	(259-296)	283	(261-293)	$p>0.50$
Mean pre-treatment Bishop's score	4.6	(1-10)	4.5	(0-9)	$p>0.50$
Number of primigravidae	52		57		
Number of multiparae	43	(1-6)	47	(1-5)	

because of weight loss, two in either group for poor obstetric history and one in each for rhesus disease.

The pessaries were prepared using a mixed macrogol base of polyethylene glycol 300 and polyethylene glycol 6000 to which was added ethanolic PGE_2 solution. 4.8 g pessaries were manufactured each containing 3 mg of PGE_2 (9). Macrogols were favoured to Witepsol because of their hydrophilic nature and the formulation used, namely polyethylene glycol 300: polyethylene glycol 6000: prostaglandin E, ethanolic solution = 62:28:10, had a low solidification point, allowing the PGE_2 solution to be added at a low temperature thus reducing the loss of potency. The shelf life of the pessaries was set at 28 days although, with the pessaries being prepared in batches of 6 pairs, the shelf storage was only a matter of days at the most.

The presence of ethanol in the dose has been proved not to have any irritant effect on the cervix (9).

Treatment commenced on the morning of admission with the insertion of the ascribed pessary into the posterior fornix after the assessment of the cervix, using the modified Bishop's score. The patient then remained in bed for 30 minutes after which time she was allowed to continue her normal activity. If, after a mean interval of 8 hours, labour had not ensued then a further pessary was inserted and the modified Bishop's score again estimated. If labour became established then the patient was transferred to the labour ward where, after further assessing the cervical status, low amniotomy was performed and full monitoring commenced. If labour did not occur then the Bishop's score was assessed after 24 hours from the first pessary insertion and the trial ended, reverting to other methods of induction of labour.

RESULTS

Of the 95 patients, given PGE_2 pessaries, 71 (74.77%) had contractions and 52 (54.74%) progressed into labour, 4 having a spontaneous rupture of membranes while the remaining 48 required only low amniotomy, without Syntocinon. In the placebo group 22 of 104 (21.15%) had contractions while only 14 (13.46%) went into labour. Analysis of the 14 placebo patients in whom labour commenced showed that all were past dates except one who was at term and all but 2 had initial Bishop's scores greater than 5.

The results showed a very significant difference ($p < 0.001$) for boch contractions and labour and therefore proved the initial premise that PGE_2 pessaries are effective in the induction of labour.

However, the efficacy of PGE_2 pessaries in the induction of labour was far from 100% in that 43 of the 95 (45.26%), in the active group, did not progress into labour although there were significant changes in the Bishop's scores between the active and placebo groups as seen in table 3, with 60 patients from the active group having increased the Bishop's score by 3 or more compared with only 27 from the placebo group. However, despite the

Table 2. — *Reasons for induction.*

Reasons for induction	Active group (n = 95)	Placebo group (n = 104)
Post dates	57	69
Hypertension/pre-eclampsia	31	26
Miscellaneous	7	9

Table 3. — *Changes in Bishop's score in active and placebo groups.*

Change in Bishop score	0	1	2	3	4	5	6	7	8	9	10	11
Active pessary group	10	14	11	14	17	9	6	6	2	5	—	1
Placebo pessary group	22	26	29	12	7	5	2	—	1	—	—	—

changes in the Bishop's scores between the various groups, once labour ensued there were no significant differences between the lengths of labour in the active "success" group (mean time = 6 hours 25 minutes with a range of 1 hour 0.2 minutes – 15 hours 00 minutes), the active "failure" group (mean time = 6 hours 51 minutes, range = 1 hour 21 minutes – 14 hours 41 minutes), and the placebo group (mean time = 6 hours 32 minutes, range = 1 hour 50 minutes – 16 hours 16 minutes) for those who progressed to vaginal delivery.

In the active group there were 89 vaginal deliveries, of which 14 were forceps deliveries, and 6 Caesarean Sections and this proved not to be significantly different from the placebo group, with 94 vaginal deliveries, including 13 forceps deliveries, and 10 Caesarean Sections ($p > 0.50$). Of the 6 Caesarean Sections, in the active group, all were performed in the "failure" subgroup, giving 100% vaginal delivery rate for the active "success" subgroup.

The indications for delivery by Caesarean Section in the active group were cephalopelvic disproportion of 3 cases and one each of intra-partum foetal distress, brow presentation and dysfunctional uterine action.

In the placebo group, 4 patients had Caesarean Sections because of cephalopelvic disproportion, 3 for foetal distress, 2 for abnormal presentation, brow and face, and 1 for failure to progress.

In only one case in the trial was antepartum foetal distress found. This occurred in a 23 year old primigravida, at 39 weeks gestation with pre-eclampsia, who, after being in the placebo group, was given 4 live pessaries over a period of 2 days and showed a deceleratory pattern on cardiotocography. At delivery by Caesarean Section, the infant was small for date and the placenta badly infarcted.

The apgar scores at 1 minute showed no significant differences between the active "success" group (mean = 7.90 ± SD 1.52), the active "failure" group (mean = 8.02 ± SD 1.61) and the placebo group (mean = 7.47 ± SD 1.89).

Analysis of the "success" and "failure" subgroups was performed to determine any factors which might predispose to failure of PGE_2 pessaries to the induction of labour but as table 4 illustrates no dif-

Table 4. — *Comparison of the success and failure subgroups in the active pessary group.*

	Success group (n = 52)	Failure group (n = 43)	
Mean maternal age (years)	25.5 (16-36)	25.1 (18-39)	$0.50 > p > 0.10$
Mean gestation (days)	287 (262-296)	284 (259-292)	$0.50 > p > 0.10$
Pre-treatment Bishop's score < 5	25	23	$p > 0.50$
Pre-treatment Bishop's score $\geqslant 5$	27	20	
Number of primigravidae	24	28	$0.10 > p > 0.05$
Number of multiparae	28	15	

ferences were found in analysing maternal age, gestation, parity or initial Bishop's score of the two groups.

DISCUSSION

This paper shows that there is a place for PGE_2 pessaries in the induction of labour, as claimed in other papers on the use of prostaglandins ([3, 4, 5, 6, 7]), in the induction of labour. There are several advantages to their use. It is a non invasive procedure with a very high patient acceptability. It produces a "normal" labour with no requirement for oxytocin augmentation having been found in the 52 patients, in whom labour was successfully induced. Low amniotomy was not performed until labour was established and as such there was a reduction in the amniotomy-delivery interval and this has been shown to reduce the maternal and foetal complications ([10]).

They do not, however, as used here, produce a shorter labour when compared with the other groups, despite improvement in Bishop's score.

There were no cases of prostaglandin induced uterine hypertonus in this study and this concurs with MacKenzie who found it to be an infrequent occurrence in the literature and of a similar incidence to that observed in either spontaneous or oxytocin induced labours ([2]).

There was only one case of Caesarean Section for dysfunctional uterine action. This occurred in the active "failure" group in a patient with a Bishop's score of 3, unchanged by PGE_2 pessaries.

The results given here, namely about 55% success rate in inducing labour, using PGE_2 pessaries (3 mg), fall short of the results of Shepherd *et al.* ([7]) and Pearce *et al.* ([6]) but are compatible with others in the literature. The difference is not explained by dosage differences as 3 mg PGE_2 were used.

There does appear to be a dose relationship to the efficacy of PGE_2 in the induction of labour, as evidenced by the literature ([1, 4, 5]). This relationship is complexly altered by the cervical state ([11]) and also by parity, with particular reference to the primigravid patient ([4]).

In this trial 2 pessaries were administered, with a mean interval of 8 hours, and it was obvious that some of the patients in the active group contracted but did not reach the threshold of labour. This may have been achieved in a greater number by either reducing the interval between insertions or by utilising a slow continuous release vehicle for the PGE_2 as suggested by Embrey ([12]) and so achieving a more uniform effect.

This method of induction of labour has been shown to be effective and safe but it is not yet possible to achieve 100% success rate. Increasing the dose or more frequent administration, depending on the parity and Bishop's score, may be more effective but this study has not shown any factor which distinguishes the failure group. The only difference, demonstrated by MacKenzie *et al.* ([3]), as a possible prediction of outcome, was that the levels of Oestradiol 17 β were higher in those progressing to labour.

Further research, along the lines of Oestradiol 17 β levels collated with parity and Bishop's score in order to tailor the dose of PGE_2 to be incorporated into a slow release vehicle, must surely produce a more effective and efficient method for the induction of labour.

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