PRE-INDUCTION CERVICAL RIPENING WITH ENDOCERVICAL PGE_2 GEL AND A PLACEBO CONTROL STUDY

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SUMMARY

A randomised double blind study consisting of 100 cases was carried out. 50 cases received PGE_2 gel and 50 cases received placebo gel. The results revealed, that with PGE_2 gel, there was marked improvement in the Bishop score (8.25) in 42%, 44% of cases went into spontaneous labour; 68% of them delivered within 12 hours and rest of the 32% delivered within 24 hours. The induction delivery interval was very much reduced (11.5 hrs.) the success rate was 86%. With the placebo gel 2% of cases delivered within 12 hours and only 10% showed improvement in the Bishop score. The success rate was 12%. With PGE_2 gel, side effects were minimal, patient acceptability was high and caesarean section rate was less. Hence the drug can be recommended for routine use for induction of labour with poor cervical score.

INTRODUCTION

The state of the cervix greatly influences the outcome of induced labour. For a long time, the cervix has been regarded as only a passive inferior part of the uterus. Today, this concept is changed, because of an increased knowledge of the biochemistry and histology of the cervix, which indicates the cervix plays an active and prominent role in the delivery mechanisms than was thought previously. Ripening is a process, involving physically detectable softening, shortening and dilatation of the cervix. Various methods have been tried, without much success, prior to the introduction of prostaglandins. Many studies have demonstrated the

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ability of PGE_2 to soften the cervix and promote uterine contractions.

AIMS OF THE STUDY

To determine the effect of intracervical application of PGE_2 gel (Cervi prime) in comparison to placebo gel on cervical ripening, induction delivery interval, the need for oxytocin and maternal and fetal outcome.

MATERIAL AND METHODS

100 patients who had completed 37 weeks of gestation were selected from Government General Hospital, Guntur (A.P.) and assigned for pre-induction cervical ripening. It was a randomised double blind study in which 50 cases received intra-cervical PGE_2 gel and 50 cases placebo gel (Supplied by ASTRA-IDL).

The patients were evaluated clinically and the initial Bishop score was noted, prior to instillation and they were instructed to report labour pains, vaginal bleeding or draining. 12 hours later the Bishop score was reviewed, in patients who did not go into labour. Those who showed considerable improvement in the Bishop score, oxytocin infusion was started with 2½ units in 500 CC of 5% dextrose and monitored by regular uterine contractions, fetal heart sounds and cervical dilatation. ARM was done as and when necessary.

ASSESSMENT

The trial was considered successful if the modified, Bishop score at 12 hrs. or 24 hrs. after instillation of the gel was 6 more more, or the women had delivered spontaneously, before the cut off point. If there was no change in the Bishop score, even after 24 hours, the case was planned for other methods of induction or for the second application of the gel (Cerviprime). The mode of delivery, induction delivery interval, weight of the baby, Apgar score and complications if any were recorded.

RESULTS

The clinical profiles were comparable in the PGE_2 Gel and Placebo gel groups.

Table I shows the mean age, weight, gestational age and gravidity of the

Table I

Comparison of clinical profiles

Parameters	PGE_2 Gel	Placebogel
Total No. of cases	50	50
Mean age (yrs)	22.4	21.4
Weight (Kg)	57.13	55.69
Gestational age (Weeks)	39.46	39.5
Gravidity	1.74	1.64

women selected for the trial.

PIH and postdatism were the main indications for induction.

Out of 50 cases of PGE_2 gel group, in 43 cases (86%) gel stimulated the uterine activity, of which 22 cases (44%) delivered vaginally before the cut off point of 24 hrs. (30% within 12 hrs. and 14% within 24 hrs.) In 7 cases gel failed to ripen the cervix.

Table II

Indications for induction-singly or in combination

Indication	PGE_2 Gel No. of cases	Placebogel No. of cases
1. Postdatism (40 weeks + 7 days or more)	22	24
2. P.I.H.	31	26
3. IUGR	6	9
4. Cong anomalies	-	1
5. IUD	2	1
6. BOH	1	-
7. Oligohydramnios	-	1

Table III

Status at 12 hours and 24 hours

Status	PGE_2 Gel		Placebo Gel	
	Number	Percentage	Number	Percentage
1. Spontaneous labour	22	44	1	2
within 12-24 hrs.	15	30	1	2
More than 12-24 hrs	7	14	-	-
2. B.S. of 6 or more				
At 12 hrs.	20	40	2	4
At 24 hrs.	1	2	3	6
3. Trial success	43	86	6	12
4. Trial failure	7	14	44	88

In the placebo group, gel stimulated the uterine activity in 6 cases of which only one delivered vaginally before 12 hours. In the remaining 5 cases (10%) the Bishop score was improved to more than 6. One patient delivered between 12-24 hours. In 88% of cases gel failed to ripen the cervix. PGE_2 gel stimulated the uterine activity earlier when compared to the placebo.

With the PGE_2 gel, out of 21 cases, 20 showed improvement in the Bishop score within 12 hours and more so it was in multis but only one multi took 24 hours, where as, with the placebo gel only 5 cases showed improvement in the Bishop score.

Details of cases who went into spontaneous labour

There was only one patient who went into spontaneous labour in the placebo groups and 22 patients in the PGE_2 group within 12 hours. The time taken for the onset of labour (5.2 hr), duration of labour (6.7 hrs.), instillation delivery intervals (11.5 hrs), were less in the PGE_2 gel group.

In the cerviprime group 96% of cases had vaginal delivery and only 2 cases required C. Section. The need for ARM was in 12% of cases. In the placebo group 16% of cases required forceps delivery and 8% required caesarean section. The need for ARM was also increased (28%).

There were 7 failures in the PGE_2 gel group : 2 cases delivered spontaneously within 12 hours after the 2nd application of the gel. The remaining 5 cases received oxytocin, out of which, 3 were delivered vaginally and 2 cases required C. Section, the indication being PROM and failure to progress with the oxytocin. In the placebo group 44 cases did not show any improvement in the Bishop score. In 10 patients Cerviprime was instilled and all of them delivered spontaneously; rest of the 34 patients received oxytocin infusion, of whom 30 patients delivered vaginally and 4 patients required C. Section, the

Table IV

Comparison of Bishop score in relation to parity and time

Parity	PGE_2 Gel B.S. before	Total No. of cases	B.S. 12 hrs.	No. of cases	B.S. 24 hrs.	No. of cases
Primi	1.2	9	9.6	9	-	-
Multi	1.75	12	10.5	11	8	1
	Placebo gel		B.S.			
Primi	1.5	2	8	1	8	1
Multi	1.7	3	6	1	8.5	2

Table V

Outcome of Labour

Course and outcome of labour	Number of cases	
	PGE_2 Gel	Placebo
Spontaneous onset of labour	22	1
Oxytocin required in those with improved B.S.	20	5
Primiprost tablets	2	-
ARM + Oxytocin	6 (12%)	14 (28%)
Induction delivery-Interval (in vaginal deliveries)	11.5 hrs.	20.6 hrs.
Duration of III stage	5 mts.	7.6 mts.
Normal delivery	47	38
Forceps	1 (2%)	8 (16%)
C. Section	2 (4%)	4 (8%)

Table VI

Management of Trial failures and the outcome

Methods of Management	PGE_2 Gel	Placebogel
Oxytocin	3	30
C. Section	2	4
2nd application of PGE_2 gel	2	10
Total	7	44

indication being failure to progress in 2 and fetal distress in the other 2 cases.

DISCUSSION

The use of PGE_2 gel facilitates cervical ripening and even initiates labour (Calder & Embrey, 1973); (Verma and Norman, 1984). Larger doses of Prostraglandins when used as abortifacients produced side effects. The recent reports show that lower doses of PGE_2 (0.5 - 2 mg) applied locally can minimise maternal side effects without decreasing its efficacy as a cervical ripening agent.

According to Trofftter et al (1985) single dose of PGe_2, showed increased Bishop score and shortened induction delivery intervals Baveja et al (1988) showed that PGE_2gel (0.5 mg) stimulated uterine activity in 69.7% of which, 37.6% delivered vaginally before the cut off point of 12 hours. Williams & Wilkerson (1985) reported that 87.5% showed successful cervical ripening and 37.5% went into labour.

Bhide and Daftary (1993) in their study with PGE_2 gel have reported that the Bishop scores improved from 1.4 & 2.8 to 7.2 ± 2.4 and 8.5 ± 3.4 in primis and multis respectively. The induction delivery interval in the PGE_2 gel group was 16.4 hours and the C. Section was required in 5.8% (2 in 34) of cases. In the placebo group the induction delivery interval was 28.3 hrs. and C. Section rate was 14.7%.

Out study showed success rate of 86% with the cerviprime gel out of which 44% went into spontaneous labour and 42% showed improvement in the Bishop score correlating with the results of Williams Wilkerson (1985).

The induction delivery interval was remarkably reduced (11.5 hrs.) with PGE_2 gel compared to placebo (20.6 hrs) C. Section rate was 4% in the trial failures whereas it was 8% in the placebo group. Similar findings were reported by Floberg et al (1983), Nimrod et al (1984), Wilquist et al (1986) and Noah et al (1987).

There were no maternal or fetal complications in our study : Patient acceptability is high as they are ambulatory. PGE_2 gel (cervi prime) can be recommended in cases of heart disease, PIH and eclampsia where fluid overload is a problem with oxytocin. The drug can be used for induction of labour, in cases with poor Bishop score.

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