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RESEARCH ARTICLE

An observational study comparing two regimens of PGE2 gel for pre-induction cervical ripening at term

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ABSTRACT

Objectives: The objective of this study was to compare the outcome in between two groups, one group receiving a 6 hourly repeat regimen (maximum 2 such) and another group receiving a 12 hourly repeat regimen of prostaglandin E 2 gel (maximum 2 such) for pre-induction cervical ripening. **Methods:** In this observational cross sectional analytical study, pregnant mothers with singleton pregnancy, viable foetus at 37-42 weeks gestational age receiving either repeated doses of prostaglandin E2 gel 0.5 mg every 6 hours or every 12 hours for maximum 2 times were selected matching their baseline characteristics. Mode of delivery and feto-maternal outcome were assessed. The sample size was 114 in each group. **Results:** More patients are delivering with a single dose of Prostaglandin E2 gel in the 12 hourly repeat group (24.56% in the 6 hourly group versus 30.7% in the 12 hourly group, p value = 0.2998). More patients are delivering vaginally in the 12 hourly repeat group (76.3% in the 6 hourly group versus 82.5% in the 12 hourly group, p = 0.2518). There is lesser number of neonatal and maternal complications with the 12 hourly repeat groups. But none of these results are statistically significant. **Conclusion**: Repeating prostaglandin E2 gel 12 hourly is as effective as repeating it 6 hourly, rather the 12 hourly regimen has lesser neonatal and maternal complications and is more cost effective although studies on greater population is needed to make these results statistically significant.

Keywords: Prostaglandin E2 gel, 6 hourly group, 12 hourly group.

Cervical ripening prior to oxytocin stimulation is highly desirable to ensure a successful induction. Prostaglandin E2 gel is a common method for pre-induction cervical ripening. The recommended regimens are: one cycle of vaginal PGE_2 tablets or gel, one dose, followed by a second dose after 6 - 24 hours if labour is not established (up to a maximum of two doses).[1] In this study, we want to compare a 6 hourly repeat regimen of PGE2 gel with a 12 hourly repeat regimen of PGE2 gel used intracervically for pre-induction cervical ripening at term.

Aims and objectives -

1. To compare the rates of vaginal delivery in 6 hr and 12 hr repeat group.
2. To compare the induction delivery interval in 6 hr and 12 hr repeat group.

To compare the rates of maternal complications like uterine hyperstimulation, fever, nausea, vomiting, retained placenta, post-partum haemorrhage, and foetal complications in 6 hr and 12 hr repeat group.

Materials and methods

It was an observational cross sectional analytical study done amongst patients admitted in dept of Obstetrics and Gynaecology in R. G. KAR Medical College from January 2017 to May 2018. There were two groups, group 1 where PGE2 gel was repeated 6 hourly, and group 2 where PGE2 gel was repeated 12 hourly. Sample size -114 in each group, calculated from a pilot study in the department of Obstetrics and Gynaecology in R. G. Kar Medical College with 15 patients in each group with similar baseline characteristics. PGE 2 gel was repeated only if the patient was not in active

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labour at the time of 2 nd gel application. Induction failure was considered if the patient had not gone into active labour, 24 hours after applying the first dose of PGE2 gel.

- Inclusion criteria -
  - Singleton pregnancy
  - Primigravida
  - Cephalic presentation
  - Term
  - With indications of induction
  - Postdated
  - Rh negative mother
  - GDM
  - PROM
  - PIH/ Pre-eclampsia
- Exclusion criteria -
  - Chorioamnionitis
  - APH
  - Congenital malformation
  - Foetal distress
  - Scarred uterus (post C/S, post myomectomy)
  - Heart disease
  - Multigravida
  - Multiple pregnancy
- Study variable : Independent – Age, S/E status, Religion, Rural/Urban, Gestational age; Dependent – Pre-induction BISHOP score, Mode of delivery whether vaginal or C/S, Induction delivery interval, No. of PGE2 gel repeated and APGAR score.

Outcome definition and parameters -

1. Primary outcome: vaginal delivery rate.
2. Secondary outcome: Induction delivery interval, rate of caesarean section, foetal complications, maternal complications like hyperstimulation, fever, nausea, vomiting, PPH, retained placenta.

Ethical clearance was obtained from Institutional Ethical Committee of R. G. Kar Medical College and Hospital, Kolkata. Statistical analysis was done using student t test, chi square test, fisher exact test. P value < 0.05 was considered statistically significant.

Result and observation

The two populations were comparable with respect to the baseline characteristics like age, socio-economic status, religion, residency, gestational age, pre-induction Bishop score (table 1).

More number of patients are delivering with a single CP gel in the 12 hourly group (30.70% in 12 hr group vs 24.56% in 6 hr group), p value being 0.2998, there being no statistically significant difference between this two groups (table 2).

Table 1: Showing distribution of baseline characteristics

Parameters	6 Hr Group	12 Hr Group	P Value
Age in years	24.24±2.96	23.8±2.93	0.2605
Low s/e status	84.2%	85.9%	0.7820
Hindu	59.6%	65.78%	0.3377
Urban residency	65.78%	60.52%	0.4627
Mean gestational age (in weeks)	39.43±1.37	39.37±0.97	0.611
% Having postdatism	35.08%	36.84%	0.9207
Pre-induction bishop score < 6	70.17%	67.54%	0.6678

Majority of patients delivering with one CP gel belong to Bishop score ≥6 (26.31% in the 12 hr group vs 19.29% in the 6 hr group), but the two groups have no statistically significant difference between them, p value by fisher exact test being 0.5174 (table 2).

Table 2: Showing number of patients delivered with only one gel in the 6 hourly group and 12 hourly group and relation of no of patients in the two groups who delivered with a single CP gel with bishop score

Pt delivering with single CP gel in 6 hr and 12 hr group	6 hr group	12 hr group
Yes	28(24.56%)	35(30.70%)
No	86(75.43%)	79(69.29%)
P value = 0.2998		
Bishop score	6 hr group delivering with 1 CP gel	12 hr group delivering with 1 CP gel
< 6	6(5.26%)	5(4.38%)
≥ 6	22(19.29%)	30(26.31%)
P value = 0.5174		

More number of patients are delivering vaginally in the 12 hr group (82.5% in the 12 hr group vs 76.3% in the 6 hr group), but there is no statistically significant difference between the two groups, P value being 0.2518 (table 3).

Table 3: Showing mode of delivery in the 6 hourly and 12 hourly group

Mode of delivery	6 hour group	12 hour group
Vaginal delivery	87(76.3%)	94(82.5%)
LSCS	27(23.6%)	20(17.54%)
	(17-fd, 10-np)	(14- fd, 6-np)
P value=0.2518		

Thus more number of patients are requiring oxytocin augmentation in the 6 hour group (9.64% in the 6 hr group vs 4.38% in the 12 hr group) , but there is no statistically significant difference between the two groups, P value being 0.119 (table 4).

Table 4: Showing no of patients requiring oxytocin augmentation and induction to delivery interval in the 6 hrly and 12 hrly gel groups

Oxytocin augmentation	6 hour group	12 hour group	P value
Yes	11(9.64%)	5(4.38%)	0.119
No	103(90.35%)	109(95.61%)	
Mean induction delivery interval in hrs	13.97± 5.03	14.7±3.52	0.2055

The mean induction delivery interval was more in the 12hourly group (14.7±3.52 hrs in the 12 hr group vs 13.97 ± 5.03 hrs in the 6 hr group), but the difference is not statistically significant, p value being 0.2055 (table 4).

Babies having APGAR ≤7 at 1 minute and NICU admission was more in the 6 hour group (4.38% in the 6 hr group vs 2.63% in the 12 hr group), but the difference is not statistically significant, p value being 0.4716 (table 5).

Table 5: Showing APGAR ≤ 7 at 1 minute and NICU admission in 6 hourly and 12 hourly group

NICU admission/APGAR ≤ 7 at 1 min	6 hr group	12 hr group
Yes	5 (4.38%)	3(2.63%)
No	109(95.61%)	111(97.36%)
P value= 0.4716		

Complication rates like uterine hyperstimulation, fever, vomiting, diarrhoea, PPH, manual removal of placenta (MRP) are slightly more in the 6 hour repeat group but there is no statistically significant difference in the two groups (table 6).

Table 6: Showing various maternal complications in the 6 hourly and 12 hourly group

Parameters	Uterine hyperstimulation	Fever	Vomiting, diarrhoea	PPH	MRP
6 hr group	3(2.63%)	3(2.63%)	3(2.63%)	4(3.5%)	2(1.75%)
12 hour group	1(0.87%)	2(1.75%)	2(1.75%)	29(1.75%)	1(0.87%)
P value	0.3130	0.6511	0.6511	0.4079	0.5611

Discussion

There have been many studies comparing prostaglandin E2 gel with other methods of induction like Foley's catheter [2 - 4], prostaglandin F2α[5], misoprostol [6], different dosage regimens of prostaglandin E 2 gel [7, 8] and placebos. Demographic characteristics were similar in both the groups in our study, with respect to age, SE status, residency and religion. The mean gestational age was 39.43 ± 1.37 weeks in the group 1 and 39.37± 0.97 weeks in group 2 which is comparable. The mean gestational age was 39 weeks in the study by Garg et al [5], 38 weeks in the study by Laddad et al [4]. The mean pre-induction Bishop score was also comparable in both the groups. 70.17% had pre-induction Bishop score < 6 in the group 1 while 67.54% had pre-induction Bishop score < 6 in group 2. The rest had pre-induction Bishop score ≥ 6. Majority of patients delivering with one CP gel belong to Bishop score ≥6 (19.29% in 6 hr group, 26.31% in group 2). The mean Bishop score in the studies by Kanada et al[10] and Seeras et al[8] was 4, in the study by Garg et al [5] it was 1.8.

The most common indication for induction was post term pregnancies, although in the studies by Murmu et al[2], Kanada et al[10], and Laddad et[4] al had PIH was the most common indication. Both the groups had no statistically significant difference in the incidence of C/S. The percentage of C/S was 23.6% and 17.54% respectively in group 1 and group2 respectively, the most common indication being foetal distress. In a study by Seeras et al[8], there were similar results. In the studies by Kanada et al[10], Laddad et al[4], Zhang et al [6] there was no difference in mode of delivery between induction by Foley catheter, PGE 2 gel and misoprostol while in the study by Thomas et al [3], compared to placebo, the rate of C/S is decreased by PGE 2 gel. The most common indication of C/S was foetal distress in both the groups. The incidence of induction failure was in 37% of C/S cases in group 1 and 30% of the C/S in group 2. Incidence of failed induction was more using PGE2 as compared to intrauterine Foley catheter in the study by Garg et al[5]. In studies comparing a 2.5 mg dose with 5 mg dose of PGE 2 gel by Smith et al [7], the incidence was similar.

Group 1 had more need of oxytocin augmentation, though the difference is not statistically significant. The need for oxytocin augmentation was also more in group 1 as compared to group 2 in studies by Seeras et al [8]. The need for augmentation by ARM and oxytocin was similar between induction by Foley catheter and PGE 2 Gel, in studies by Kanada et al[10] and Murmu et al[2]. In studies comparing a 2.5 mg dose with 5 mg dose of PGE 2 gel by Smith et al[7], the need was also similar. The need of oxytocin was less when using PGE 2 gel as compared to placebo in studies by Trofatter [9].

Group 1 had lesser induction to delivery interval. The mean induction delivery interval in group 1 was 13.97 ± 5.03 hours and in group 2 was 14.70 ± 3.52 hours, the difference in the two groups is not statistically significant like studies by Seeras et al[8]. The induction delivery interval was similar when comparing a 2.5 mg dose of PGE2 gel and a 5 mg dose as per studies by Smith et al[7]. In the study by Laddad et al[4], the induction delivery difference with a single dose of PGE2 gel was 14 hrs, which was comparable with results using Foley catheter. The induction delivery interval is less using PGE2 gel when compared to placebo as per studies by Trofatter [9] et al 4.38% babies in the group 1 and 2.63% babies in the group 2 got admitted in the NICU with APGAR ≤7, the difference in the two groups is not statistically significant. Both the groups had similar incidence of side effects like uterine hyperstimulation, fever, vomiting and diarrhoea, PPH, manual removal of placenta. The neonatal outcome was similar, but incidence of uterine hyperstimulation more in the 6hour group compared to 12hour group as per studies by Seeras et al[8] The neonatal outcome was similar, but PGE 2 had more maternal side effects as compared to Foley induction in the study by Murmu et al[2]. The incidence of side effects was similar in studies comparing a 2.5 mg dose with 5 mg dose of PGE 2

gel by Smith et al[7]. Maternal and fetal outcomes were similar when compared to placebo as per studies by Trofatter[9] et al. Misoprostol had more incidence of uterine hyperstimulation as compared to PGE 2 gel as per studies by Zhang et al. The study by Thomas et al [3] also found similar efficacies between PGE2 gel, tablets, pessaries when compared to each other. Lower dose regimens were also as effective as higher dose regimens, although sustained release pessaries required less number of applications.

Conclusion

Thus, as per our study, repeating CP gel 12 hourly is as effective as repeating it 6 hourly. Infact, the 12 hourly regimen has lesser neonatal and maternal complications and is more cost effective. But studies on greater population are needed to make these results statistically significant.

Conflict of interest: None. **Disclaimer:** Nil.

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