|| ISSN(online): 2589-8698 || ISSN(print): 2589-868X ||
International Journal of Medical and Biomedical Studies
Available Online at www.ijmbs.info
PubMed (National Library of Medicine ID: 101738825)
Index Copernicus Value 2018: 75.71
Original Research Article Volume 3, Issue 9; September: 2019; Page No. 255-258

A CLINICAL COMPARATIVE STUDY BETWEEN MISOPROSTOL (PGE_1) AND DINOPROSTONE (PGE_2) FOR INDUCTION OF LABOUR AT TERM - A PROSPECTIVE RANDOMISED CONTROLLED TRIAL

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Article Info: Received 11 August 2019; Accepted 28 September. 2019
DOI: https://doi.org/10.32553/ijmbs.v3i11.684
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Conflict of interest: No conflict of interest.

Abstract

Background: *Comparative study beween misoprostol and dinoprostone for induction of labour at term has been done at various centres which showed misoprostol to be more effective. This study was done, 18 years back in 2001, when the most common method of induction was dinoprostone. Since then both the drugs has been used equally for induction of labour at term. But in recent past, PGE_1 is not being used widely because of fear of untoward effect. Hence, the importance this article which shows misoprostol to be more effective with less side effects, easy for storage and low cost. This study is to compare the effectiveness between the two molecules of prostaglandins PGE_1 and PGE_2 for induction of labour in term. The complication can be reduced by proper selection, 1 to 1 and continuous fetal monitoring.*

Methods: *It was a prospective RCT. 200 Women at term in whom induction of labour was indicated with no contraindications for the use of prostaglandin attending labor room in a tertiary care centre (SAT Hospital Government Medical College Trivandrum) for a period of five months, from September 1^{St} 2000 to January 31^{st} 2001 was chosen to compare the effectiveness of Misoprostol and Dinoprostone for induction of labour at term. Both the groups were comparable in age, parity and bishop score.*

Results: *Among 200, 123(61%) were primigravida and 146 (73%) were in the age group of 21 – 30 yrs. Median induction delivery interval was about 9 hrs shorter in PGE_1 group. Only14.14% required oxytocin augmentation in PGE_1 Group compared to 50.54% in PGE_2 group. There was 8 failures in PGE_2 and there was one case of hyper stimulation in PGEI group for which LSCS was done. PGE_2 costs 10 times more than PGE_1.*

Conclusion: *Misoprostol is faster acting with low induction delivery interval and requirement for oxytoccin augmentation. Misoprostol is low cost drug, affordable to most of our patient from low socio economic status.*

Keywords: *Term pregnancy, Tab Misoprostol, PGE_1, Dinoprostone gel, PGE_2, Induction of labour.*

Introduction

Induction of Labour- Defined as deliberate termination of pregnancy beyond 28 weeks by any method which aims at non spontaneous initiation of uterine contractions, with progressive cervical effacement, dilatation and descent of presenting part. The aim of successful induction is to achieve vaginal delivery with both mother and baby in good condition.

Term Pregnancy: Includes all pregnancies after 37 completed weeks from the last day of menstrual period.

Methods of Cervical priming can either be Pharmacological or Non- pharmacological. The human cervix is a complex and heterogeneous organ that undergoes extensive changes throughout gestation and parturition. The cervix is dominated by fibrous connective tissue composed of an extracellular matrix consisting of predominantly of collagen with elastin and proteoglycans & a cellular portion consisting of smooth muscle, fibroblast, epithelium and blood vessel.

Misoprostol is a synthetic PGE_1 acts on myometrium. It can be given through oral, sublingual, intravaginal and rectal route. It is cheaper than PGE_2 and requires no refrigeration. Dinoprostone gel contains PGE_2. It acts by softening of cervix. It can be used intracervically. The gel is costly and requires refrigeration for storage purpose. The aim of this

study is to compare the effectiveness of two methods of induction of labour, Tab Misoprostol and Dinoprostone gel.

Methodology

This study was conducted from September 1st 2000 to January 31st 2001 at labour room SAT Hospital Medical College Trivandrum. Ethical committee clearance was obtained for the study.

The Inclusion Criteria included full term patients with ultrasound confirmed dates, with singleton fetus of cephalic presentation, with intact membrances and Bishop score < =6.

Exclusion Criteria included any type of Previous scar on uterus, Patients in active labour, with ruptured membranes and hypersensitivity to prostaglandins and patients with any serious maternal disease or fetal condition

Patients attending labour room for induction of labour were given lots from 1 to 200for randomization. Patients who took odd numbers were assigned for PGE_1 and those who took even numbers were assigned for PGE_2.

In Misoprostol group100 women were induced with Tab misoprostol 50µg applied to posterior vaginal fornix under aseptic precaution and every 6 hours for a maximum of 4 doses.

In Dinoprostone group 100 women were induced with 0.5 mg dinoprostone gel intracervically under aseptic precaution, every 6 hours for a maximum of 2 doses.

After induction, women were monitored for fetal and maternal wellbeing and progress of labour. The results observed were subjected to statistical analysis by 't' test and a 'p' value of <0.05 was considered statistically significant.

Results:

Total number of patients in the study was 200, among them, 73% belongs to age group 21 -30 yrs (Table -1) and 61% were primigravida and 39% were multigravida (table -II) There were 2 groups misoprostol and dinoprostone induced, each contained 100 patients. 78% of patients in PGE_1 group delivered after I st dose where as in PGE_2 58% delivered. Only for subjects in PGE_1 required 3rd application. (Table –III). Out of 92 cases who entered active phase of labour in PGE_2, 47 cases required oxytoccin augmentation (50.54%) where as in PGE_1 of the 99 cases only 14 (14.14%) required oxytoccin augmentation. (Table IV). PGE_1 had a highly significant reduction in median induction delivery interval compared to PGE_2 (10 hrs vs 19 hrs 55 minutes, P= <0.00011) (Table V) Even though there is an absolute difference of 7 cases of LSCS between the 2 groups (P=0.0648) not statistically significant (Table VI) There was no significant difference in maternal complications in both groups. (Table VII a and b). The apparent increase in PPH in PGE_1 may be to sample variation but it is no statistically significant. There was a case of uterine inversion may be due to mismanagement of 3rd stage of labour (Table VIII). There was no significant difference in neonatal outcome (Table IX).

Table I

Age	Total	PGE_1	PGE_2
<=20	41 (20.5%)	22 (22%)	19(19%)
21-30	146 (73%)	72 (72%)	74(74%)
31-40	13 (6.5%)	6 (6%)	7(7%)

Table -II Obstetrical score

Parity	Total	PGE1	PGE2
Zero	123(61%)	58(58%)	65(65%)
One or more	77(38.5%)	42(42%)	35(35%)

Table -III

No. of times applied	PGE1	PGE2
Once	78	58
Twice	18	42
Thrice	4	0

Table –IV Oxytoccin augmentation

Oxytoccin	Total	PGE1	PGE2
Necessitated	61 (31.93)	14(14.14)	47(50.5)
Not necessitated	130 (68.7)	85 (85.86)	45 (49.5)

Table - V Induction Delivery interval in minutes

	PGE_1	PGE_2
Minimum	240	300
Maximum	1492	1920
Mean	627.44	1184.9
Median	600	1195
SD	303.993	331.82

Table – VI Mode of Delivery

	Total	PGE_1	PGE_2
Vaginal delivery(VD)	179	91	85
Vaccum Extraction (VE)	15	8	7
LSCS	9	1	8

Table VII (a) Maternal complication

	Total	PGE_1	PGE_2
Maternal fever	5	3	2
Nausea & Vomiting	10	6	4

Table VII (b)

	Total	PGE1	PGE2
Hyper systole	4	3	1
Hyper stimulation	1	1	0

Table VIII Postpartom hemorrhage

No.of pads	PGE_1	PGE_2
One	32	38
Two	64	60
Three or more	4	2

Table IX Neonatal outcome

	Total	PGE_1	PGE_2
Meconium staining mild Of liquor	5	2	3
moderate	3	2	1
Apgar at 5'		9 at 5'	9 at 5'
Admission to NICU		NIL	NIL

Discussion

In this study a sample size of 200 was selected with 100 in PGEI & & 100 in PGE_2 group study period was 5 months (from September I^{st} 2000 – January 31^{st} 2001). Local ethical committee clearance was obtained for the study. Candidate are selected keeping in not inclusion & exclusion criteria and registered into the trials after getting written informed consent.

Data collected on a structured proforma & entered in a master chart. Statistical analysis done using descriptive statistics and inferential statistics. Statistical significance using Mann whitney utest, chil square test, OR & confidence interval are calculated.

As there was no difference in baseline characters, the 2 groups were comparable statistically. Misoprostol appears to be more effective induction agent than dinoprostone vaginal gel in the regimens compared in this trial. There is reduction in induction delivery interval of over 9 hours. 78% of cases delivered after a single dose where as in PGE 2 group 58%. The requirement for oxytocin augmentation in labour was reduced from 50% to 14%, and the amount of oxytocin required in augmented cases also reduced. There was no statistically significant difference of uterine tachysystole. There was only case of hyperstimulation requiring tocolysis in PGEI Group, for which LSCS was done and the baby had an apgar of 9at5'. There was no statistically significant difference in the mode of delivery There was no clinically relevant adverse effect on the fetus or on the mother.

The 50µg dose regimen was selected with regard to the published trials, as compromise between efficacy and unacceptable side effects. It may be possible that efficacy can be retained and side effects reduced even further with a 25µg dose. This drug has the benefit of being very inexpensive in comparison with other available prostaglandins. A more recent meta analysis has recommended that all future trials involving misoprostol should not use doses of more than 25µg dose of more than 25µg given 4-6 horly.

In the reference study by Peter Danielian et al (BJOG august 1999 Vol 106 PP793- 797) a sample size of 211 women at term was selected, out of this 105 received misoprostol & 106 received dinoprostone gel. Dose of misoprostol was 50µg 4hrly intervals to a maximum of four doses and dinoprostone gel 1 mg 6hrly to a maximum of 3 dose.

In our study the duration of application of misoprostol was increased from 4 hours to 6 hours to reduce the side effect and the dose of dinoprostone has reduced from 1 mg to 0.5mg and for a maximum of 2 doses rather than 3. Here misoprostol group had a highly significant reduction in induction delivery interval compared with dinoprostone group (14.4 hrs us 22.9 hrs $p<0.00001$). In addition more women delivered after only one dose 77% VS 49% $p<0.0001$). there was a reduced need for oxytocin augmentation in labour & no difference in mode of delivery there was no adverse materanal or fetal outcome associated with misoprostol. Hence results of these 2 studies are almost comparable.

Rolwonds S et al in their randomized controlled trial (Aust NZJ ohst &gynaecology 2001 may 41(2)145-152 included 126 women at term, of this 63 received misoprostol & 63 received dinoprostone. The mean induction to delivery interval was significantly shorter in misoprostol group (925.8 VS 1577.6 minutes) & more women in PGEI Group delivered in less than 12 hours (92% vs 76.5%) women in the misoprostol group were less likely to require a repeated dose of prostaglandin for cervical priming & less likely to require oxytocin for augmentation of labour there was no difference in the number of women who were delivered vaginally or by caesarean section. More women developed hyperstimulation during labour in PGEI group, however there was no difference

between the groups in neonatal out come in respect to low cord PH or apgar score at delivery or admission to the neonatal special care nursery. Results of our study is also comparable with this study.

Summary and Conclusion

Base line characteristics

In this study it was statistically proven that both PGE_1 & PGE_2 Group were comparable for age, socioeconomic status, educational status occupation & parity.

Induction delivery interval

The median induction delivery intervals in PGE_1 group 10 hrs, where as in PGE_2 Group 19 hrs 55'. This reveals strong correlation between IDI & type of drug used, & it is inferred that PGE_1 is superior to PGE_2 for term labour induction.

About 78% of cases of PGE_1 group delivered after the I^{st} dose, where in PGE_2 group only 58% delivered after I^{st} dose.
Success rate was 99% in PGE_1 group & 92% in PGE_2 group.

Oxytoccin augmentation

In PHE_2 50.54% required oxytoccin augmentation compared to only 14% in PGE 1 group. This was statistically highly significant therefore inferred that PGE_1 is more effective than PGE_2 in induction of labour at term.

Neonatal & Maternal complication

There was no statistically significant difference in the incidence of hypertonic contraction, apgar at 5', admission to NICU, postpartum haemorrhage, maternal fever.

Mode of Delivery

There was no statistically significant difference between the two group in the mode if delivery.

Conclusion

Comparative study between misoprostol and dinoprostone was done at various centers Worldwide, which showed misoprostol to be more effective.
Median induction delivery interval was about 9 hrs shorter in PGE_1 group. Only 14.14% required oxytocin augmentation in PGE_1 Group compare to 50.54% in PGE_2 group.
There was 8 failures in PGE_2 and one case of hyper stimulation in PGE_1 group for which LSCS was done.
PGE 2 costs 10 times more than PHE_1
This study has got clearance from the local ethical committee. This drug could be viable alternate to Dinoprostone

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