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Comparative Observational Study of Low Doseintravaginal Misoprostol Tablet Versus Intracervical Dinoprostone Gel for Induction of Labor

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Abstract: ***Aim: To compare the efficacy and safety of low dose vaginal Misoprostol (25 mcg) and intracervical Dinoprostone gel for induction of labor. Method: An observational study was carried out wherein subjects in group 1 received intracervical Dinoprostone gel(0.5mg) and the subjects in group 2received tab Misoprostol 25 mcg per vaginally, 6 hourly for maximum 3 doses (n=48 in each group). Result: The primary outcome, i.e. number of vaginal deliveries within 12 hours of 1st dose of inducing agent was higher in Misoprostol group (31.8 % in group 1 vs 50 % in group 2, p=0.07) The mean IAL interval was shorter in Misoprostol group (9.88 hours in group 1 vs 6.8 in group 2, p=0.6). Statistically significant shorter duration of oxytocin use in Misoprostol group (7.85 hours in group 1 vs 5.16 hours in group 2, p=0.013). There was no significant difference between the mean IDI (14.53 hours in group 1 vs 17.01 hours in group 2, p=0.2) and the maternal and neonatal outcomes of the 2 groups. Conclusion: Low dose (25 mcg) intravaginal Misoprostol appears to be a safe, effective and an economical alternative drug to routinely used Dinoprostone gel for induction of labor, especially in developing countries with low resource settings.***

Keywords: low dose, Misoprostol, Dinoprostone, Induction of labor

1. Introduction

Induction of labor is the stimulation of uterine contractions before the spontaneous onset oflabor with or without ruptured membranes [1]. It is an intervention designed to initiate uterine contractions artificially to reduce the risk of maternal and neonatal morbidity and mortality [2].There are several methods of labor induction, including administration of oxytocin, prostaglandins, prostaglandin analogues and smooth muscle stimulants such as herbs, castoroil or mechanical methods such as digital stretching of the cervix and sweeping of the membranes [3].

Dinoprostone is a synthetic analogue of prostaglandin E2, which effects the uterine smooth muscles[4].It acts on the PGE2 receptor and regulates intracellular cyclic AMP levels and cellular membrane calcium ion transport [4]. It has been used for cervical ripening and labor induction and is a very efficacious drug with good safety profile.PGE2 vaginal gel contains 0.5 mg of Dinoprostone in thick clear gel in sterile translucent syringes stored at 2-8 degree Celsius.

Misoprostol is a prostaglandinE1 analogue which was widely used for the treatment of gastriculcer in patients taking NSAID's.It is used for the termination of pregnancy in the first, second and third trimesters, cervicalripening and induction of labor[5][6][7]. It is inexpensive and does not need to be stored in a refrigerator.It can be administered orally, intravaginally and intracervical for induction of labor. ACOG has recommended the use of vaginal misoprostol in doses of 25mcg every 3-6 hourly[8].

The present study is intended to compare the efficacy and safety of intravaginal Misoprostol (25mcg) and intracervical Dinoprostone gel (0.5mg) for induction and progress of labour and to assess the maternal and foetal outcome.

2. Literature Survey

The study was done in Department of Obstetrics and Gynaecology, Nazareth Hospital, Shillong. The hospital caters to both urban and rural patients belonging to the districts in proximity to Shillong. Nazareth Hospital is an entry level NABH accredited hospital which has more than 400 beds in total and 75 bedsin the Department of Obstetrics and Gynaecology. Each year approximately 2,500 deliveries take place in Nazareth hospital. This hospital offers tertiary and referral services to the nearby districts.

3. Aims and Objectives

Primary Objective
To compare the efficacy of low dose vaginal Misoprostol (25 mcg) and intracervicalDinoprostone for induction of labor.

Secondary Objective
To compare their safety by comparing
- Maternal outcome
- Fetal outcome

4. Materials and Methods

This was a prospective observational studyconducted in Nazareth hospital, a tertiary health carecentre in Shillong , Meghalaya, over a period of 1 year from1/9/2018 to 31/8/2019.

The inclusion criteria were primigravida and second gravida with single live fetus in cephalic presentation with gestational age of ≥ 37 weeks. The exclusion criteria were malpresentation, previous uterine surgery, abnormal placentation(placenta praevia or vasa praevia), contracted pelvis, contraindications or hypersensitivity to

prostaglandins (bronchial asthma ,glaucoma) and non-reassuring fetal status.

Detailed written informed consent was taken prior to induction. A CTG for fetal wellbeing & vaginal examination to assess the cervix was performed, prior to administration of either preparation. Women in Group 1 received intracervical Dinoprostone gel and women in Group2 received 25 mcg intravaginal Misoprostol tablets, n=48 in each group. Both the drugs were repeated 6 hourly for maximum 3 doses. FHS monitoring was done half hourly for the initial 2 hours after administration of each dose followed by 1 hourly until the next dose.

No further doses were given if any of the following were present

- Adequate contractions (≥ 3 contractions per 10 minutes lasting for 45-50 sec.)
- Bishop score ≥ 6
- ≥ 3 cm dilatation of cervix.
- Spontaneous rupture of membranes.
- Non-reactive NST/non reassuring fetal status.

Further augmentation if required was done by artificial rupture of membranes or oxytocininfusion. Progress of labor was charted on a partogram. Labor parameters, maternal and fetal outcomes were noted and compared in both the groups. All collected data were compiled and analyzed using IBM SPSS 22.0.

5. Results

Both the groups were matched for sociodemographic variables such as Age, BMI, Booking status of women, Gestational age and Gravidity.

No significant difference was found in both the groups w.r.t indications for induction of labor, except *PROM which was significantly more common in Misoprostol group(11.1% in group 1 vs 88.9 % in group 2, p<0.001).* The most common indication in Dinoprostone group was oligohydramnios whereas in Misoprostol group it was PROM and postdates.

Both the groups had equal mean Bishop score at induction (3±1). We did not find any significant association between the inducing agent and the number of doses required to achieve favourable Bishop score.

The mean IAL (induction to active labor) interval was comparatively shorter in Misoprostol group (9.88 ±4.75 hours in group 1 vs 6.8 ± 4.1hours in group 2, p=0.6), although statistically insignificant. No significant association was seen between the inducing agent and the number of women going into active labor in each group.

The use of oxytocin was also comparatively less for women in misoprostol group(77.6% in group 1 vs 76.6.% in group 2, p=0.9) *with statistically significant shorter duration of oxytocin use in misoprostol group (7.85 hours in group 1 vs 5.16 hours in group 2, p=0.013).*

Table 1: Duration of Oxytocin use in Hours

	Mean	Standard deviation	Minimum	Maximum
Dinoprostone gel	7.85	4.68	1.5	26.5
Misoprostol	5.16	3.25	1	15.5
p value- 0.013				

There was no significant difference between the mean IDI (induction delivery interval) of 2 groups (14.53 ± 4.85 hours in group 1 vs 17.01 ± 8.3 hours in group 2, p=0.2).

In the present study, no significant association was seen between the overall mode of delivery and the inducing agent (vaginal delivery- 44.9% in group 1 vs 29.8 % in group 2, p=0.12; LSCS- 55.1% in group 1 vs 68.1 % in group 2, p=0.9). Only 1 woman had instrumental delivery who belonged to Misoprostol group. A significantly higher number of vaginal deliveries were seen after 1st dose of inducing agent in Dinoprostone group (54.5% in group 1 vs 34.4% in group 2, p=0.04).

Our primary outcome parameter i.e. the number of vaginal deliveries within 12 hours of 1st dose of inducing agent was comparatively higher in Misoprostol group although it was statistically insignificant (31.8 % in group 1 vs 50 % in group 2, p=0.07).Vaginal deliveries within 12-24 hours was significantly higher in Dinoprostone group (63.6% in group 1 vs 35.7% in group 2, p=0.001).

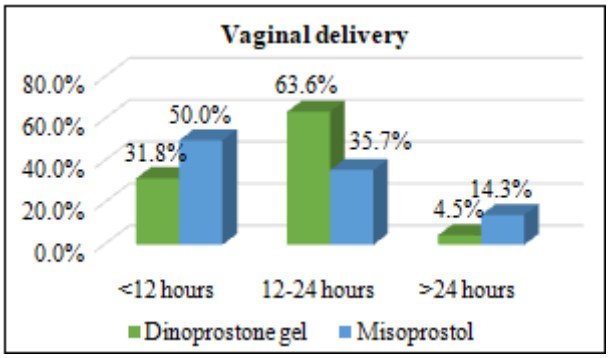

Figure 1: Vaginal delivery distribution.

In the present study, significant differences were noted in the indications of LSCS with fetal distress being a more common indication in Misoprostol group(out of 35 women who had fetal distress, 34.3% in group 1 vs 65.7% in group 2 , p=0.046) and failed induction of labor being more common in Dinoprostone group (out of 11, 72.7% in group 1 vs 27.3% in group 2, p=0.03).

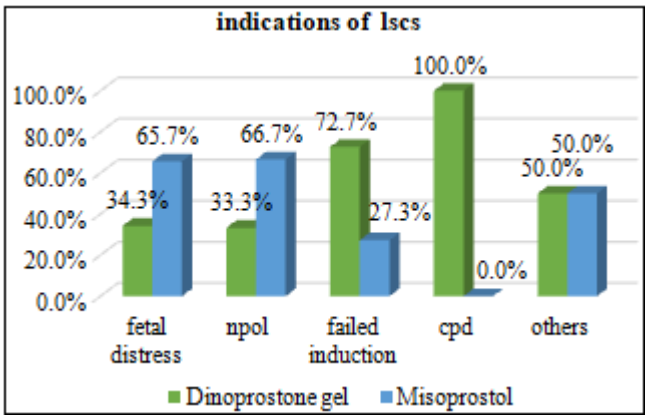

Figure 2: Indications of LSCS

In the present study, no significant differences were noted in the maternal and neonatal outcomes of the 2 groups.

Tachysystole was seen in 1 woman belonging to group 2. Meconium stained liquor was seen in 18 patients, 33.3% belonging to group1 and 66.7% belonging to group 2 but the difference was insignificant(p=0.1). FHR abnormality was seen in 22 foetuses, 40.9% belonging to group 1 and 59.1% belonging to group 2 but the difference was not found to be significant statistically(p=0.3).All the neonates had an APGAR score of >7 at both 1 and 5 minutes except for one baby belonging to Misoprostol group who had developed meconium aspiration syndrome (MAS) but it was insignificant statistically.The incidence of NICU admission of neonates was 6.1% in group 1 and 8.5 % in group 2.

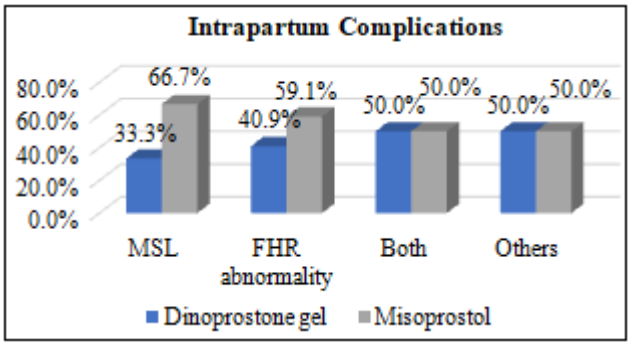

Figure 3: Intrapartum complications

6. Discussion

In our study, the mean Bishop Score at induction was equal in both the groups (p>0.05) which was consistent with the studies of Swati et al [9] and Jaya et al [12].

In the present study, the IAL interval was shorter in misoprostol group although it was statistically insignificant. Similar observation was made by Juveria et al [8] with statistically significant difference. However, in a study by Jaya et al [12] the result obtained was in contrast to our study.

In the present study, although statistically insignificant, oxytocin for augmentation of labor was used for fewer women in group 2 as compared to group 1. Similar results which were statistically significant were obtained by Swati et al [9], Sandhya et al [10] and Sunita et al [11].

In present study, no significant association was seen between IDI and the inducing agents (p=0.264). However, studies by Swati et al [9] and Sandhya et al [10] showed contrasting results where IDI was significantly lower in misoprostol group. In the present study, higher rate of vaginal delivery was achieved in Misoprostol group within 12 hours, although it was statistically insignificant (p=0.07). However, study by Sunita et al [11] showed a contrasting result. No significant association(p=0.3) was seen between APGAR score and the inducing drug which was in accordance with the studies of Swati et al [9] and Wanker et al [13]. However, in a study by Sandhya et al [10] significant differences were found between the 2 groups where neonates in group 2 (Misoprostol) fared better than neonates in group 1(Dinoprostone). In our study increased incidence of MSL and FHR abnormality in group 2 could be possibly because of more post-dated women in group 2. Similarly, in study by Swati et al [9] and Apurba et al [14], increased incidence of fetal distress could be because of more frequent (4 hourly) administration of Misoprostol.

7. Conclusion

In our study, we found that the mean IAL interval was shorter in Misoprostol group by 3 hours, the requirement of oxytocin use for augmentation was less with statistically significant shorter duration of oxytocin use in Misoprostol group. There were more number (approximately 18% higher) of vaginal deliveries within 12 hours of 1st dose in the Misoprostol group with less incidence of failed induction (approximately 45% less). The rate of MSL and FHR abnormality was higher in Misoprostol group but there were no adverse fetal outcomes. There were no statistically significant differences in the maternal and fetal outcomes in the 2 groups. The average cost of Misoprostol tablet was much lesser (25 Rs)as compared to Dinoprostone gel (300 Rs.). Misoprostol requires a less stringent condition for storage as it can be stored at room temperature as compared to Dinoprostone gel which requires refrigeration.

Hence, we conclude that low dose (25 mcg) intravaginal Misoprostol appears to be a simple, convenient, safe, effective and an economical alternative drug to routinely used Dinoprostone gel for induction of labor, especially in developing countries with low resource settings, thus allowing considerable cost-saving without compromising on maternal and neonatal outcomes.

8. Limitations

Our main limitation is the non-randomized study design. The study could not be blinded because of two different forms of drug (gel versus tablet) which enabled both the participant and administrator to know the drug administered. Our sample size was limited. Further analyses with large scale randomized controlled trials are required to draw solid conclusions.

9. Future Scope

Clinicians can choose among these inducing agents depending on cost, local logistics and patient preferences.

Their respective advantages and drawbacks should be assessed for better maternal and foetal outcome but with the present available data, Misoprostol promises to be more cost- effective alternative in low and middle income countries without fearing its efficacy, safety and acceptability.

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