EFFICACY OF MISOPROSTOL AND PROSTAGLANDIN E2 GEL FOR INDUCTION OF LABOR IN TERM PREGNANCY

Qudsia Qazi[1], Syeda Sitwat Fatima[2], Samdana Wahab[3], Wajeeha Syed[4]

[1-4] Department of Obstetrics and Gynecology, Lady Reading Hospital, Peshawar - Pakistan.
Address for correspondence:
Dr. Samdana wahab
Assistant Professor, Department of Obstetrics and Gynecology, Lady Reading Hospital, Peshawar - Pakistan.
Email: qudsiakamran@gmail.com
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ABSTRACT

Objective: To compare the efficacy of Misoprostol with prostaglandin E2 in terms of induction to labor and delivery intervals in women with full term pregnancy.

Methodology: This randomized controlled trial was conducted in the Department of Obstetrics and Gynecology, Lady reading Hospital (LRH), Peshawar from July 2017 to June 2018 on 116 patients who were admitted for induction of labor. All the selected patients were randomly allocated into two groups i.e. group A who received 50 mcg tablet of Misoprostol and group B who received 2 mg of Prostaglandin E2 gel vaginally. The main outcome variables were interval from induction to labor, induction to delivery and mode of delivery. Student t test was applied for calculation of difference between the two groups to find out the efficacy of Misoprostol and Prostaglandin E2 Gel in induction and onset of significant uterine contractions and induction to delivery interval.

Results: The interval from insertion of drug to the onset of labor (7.26 ±4.77 hours versus 12.03 ±6.94 hours) and induction to delivery intervals (10.32 ±6.89 hours versus 15.04 ±8.16 hours) were shorter in group A than in group B. Cesarean section rate was higher in group A (24.1%) than in group B (12.1%).

Conclusion: Vaginal Misoprostol was more effective than prostaglandin E2 for elective induction of labor due to shorter induction to labor and delivery intervals.

Key Words: Efficacy, Induction of labor, Misoprostol, Prostaglandin E2

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INTRODUCTION

Induction of labor is a common practice in obstetrics. Induction of labor implies artificial initiation of regular uterine contractions before spontaneous onset of labor in order to generate progressive cervical dilatation and effacement for the purpose of delivery of feto-placental unit. Its need usually arises when the potential risks of pregnancy continuation are outweighed by the benefits of delivery to the fetus or mother[1]. Various obstetrical and medical conditions like prolonged pregnancy i.e. gestational age exceeding 41 weeks, preterm rupture of membranes, maternal diabetes and pregnancy related hypertension, demands induction of labor[2]. The rate of induction varies by location and in many centers it is more than 20% (range 9.5-33.7% annually)[3]. Cervical readiness for labor induction is assessed by calculating a bishop score before a regimen is selected. Cervical ripening agents e.g. prostaglandins are recommended for Bishop score of ≤6. Prostaglandins alter extracellular ground substance of cervix and thus ripen it. They also increase intracellular calcium levels and thus promote contraction of myometrium.

Although, currently available prostaglandins are prostaglandin E1 analogues i.e. Misoprostol and prostaglandin E2 analogues i.e. dinoprostone. Misoprostol was first synthetic analogue used initially for peptic ulcer prevention and treatment. However, its stimulant action on uterus led researchers to extend its use to various obstetrical conditions such as first trimester abortions, intrauterine fetal death and for cervical ripening[4,5]. Furthermore, extra-amniotic prostaglandin E2 is an established and widely used drug for cervical ripening but it is costly and needs refrigeration for preservation. In addition, intra vaginal Misoprostol, though not thoroughly studied, is gaining worldwide acceptance for induction of labor due to its advantages which are low cost, stability at room temperature[2,6], multiple routes of administration and potentially higher efficacy. Many studies demonstrate successful induction rate of Misoprostol to be 98.7% in comparison with 91.4% for pros-

taglandin E2[2,7,8]. On the other hand, Induction of labor with Misoprostol in women with full term pregnancy and live fetus remains a major challenge in modern obstetrics. Potential effects of induction with higher doses of Misoprostol are uterine hyper stimulation, meconium stained liquor, fetal heart rate changes, poor progress of labor and an increased risk of cesarean delivery. Misoprostol is suitable for environment and communities of developing and underdeveloped countries like Pakistan, which are cash strapped and resource less[9-11]. Our study was aimed to compare the effectiveness of misoprostol with prostaglandin E2 in terms of induction to labor and delivery intervals in women with full term pregnancy.

METHODOLOGY

All patients admitted in Gynecology and Obstetrics Department, LRH Peshawar, from July 2017 to June 2018, for elective induction of labor, were evaluated for selection to this randomized controlled trial. Those meeting inclusion and exclusion criteria were approached for informed consent while hospital ethics committee approved the study. Sample size was calculated by PASS software and 116 patients were recruited in the study[12].

Inclusion criteria were all pregnant women of child bearing age, Parity ≤4, singleton pregnancy, cephalic presentation, gestational age of ≥37 weeks, Bishop score of ≤4 and intact membranes. Exclusion criteria were low lying placenta, malpresentations, previous uterine surgery, unsatisfactory cardiotocography (CTG) and contraindications to vaginal birth.

All selected patients were randomly allocated into two groups according to treatment regimen (group A or group B). Women randomized to group A (58 patients) received Misoprostol 50 mcg (Quarter part of 200ug breakable tablets available in the market) placed in posterior fornix of vagina and dose was repeated every 8 hours in case of failure to progress to active labor. Maximum three doses were given. Women randomized to Group B received Prostaglandin E2 (PG E2) 2mg gel placed in posterior fornix of vagina repeated every 12 hourly as per our unit's consultant led protocol for induction of labor. Cold chain was maintained. Maximum three doses were given.

Partogram was maintained by doing vaginal assessment with onset of active labor and keeping continuous record of fetal heart by intermittent auscultation. The time of onset of moderate to severe uterine contractions was recorded. Maternal vital signs were monitored every four hourly throughout labor. Induction was considered failed if patient did not enter into active phase of labor after maximum doses in both groups and cesarean section was offered. The other indications for cesarean section were fetal distress, secondary arrest of labor and prolonged second stage of labor. The primary outcome measures were induction to labor interval (starting from time of insertion of first dose until the start of active labor), induction to delivery interval and mode of delivery.

Data were analyzed using SPSS version 20. Mean ±SD was calculated for age of patients (in years), gestational age (in weeks), total doses and induction delivery interval (in hours). Frequencies and percentages were calculated for gravidity and mode of delivery. Chi-square test was applied for association and two sample independent t test was applied to test difference between Misoprostol and Prostaglandin E2 gel in induction and onset of significant uterine contractions and induction to delivery interval. A p value <0.05 was considered to be statistically significant.

RESULTS

The overall mean age was 27.19 years in Group A and 28.81 years in Group B. In group A mean gestational age was 41.1 ±2.8 weeks as compared to Group B 40.7 ±2.0 weeks. There was no significant difference between two groups with respect to maternal age and gestational age. Largest group of study consisted of para 1-3 i.e. 93.1% of group A and 79.3% of Group B (Table 1).

Indications for induction of labor were compared between the two study groups. Table 2 is showing most common indication i.e. postdates pregnancy in 43.9% cases of group A and 50% cases of group B followed by low biophysical profile with moderate oligohydramnios (in 12.3% vs 17.2%) and placental grade III maturity changes associated with moderate oligohydramnios in (13.7% vs 15.5%) cases. There was no significant difference between two groups with respect to indications for induction.

Our primary outcome measure is shown in Table 3 as induction to labor interval and induction to delivery interval. In group A interval between start of induction and onset of active labor is 7.2 ±4.7 hours. It is shorter as compared to 12.03 ± 6.94 hours for group B showing statistically significant difference (p =0.001). Table 3 also shows that Misoprostol had faster effect as compared to prostaglandin E2 as an inducing agent.

Table 4 shows mode of delivery in induced patients. The rate of spontaneous vaginal delivery was not significantly different between the two groups i.e. 63.8% of cases receiving Misoprostol delivered spontaneously compared to 69.0% of patients receiving prostaglandin E2 group. In Misoprostol group, 12.1% of patients underwent operative vaginal delivery compared to 19.0% of patients in prostaglandin E2 group. Delivery by cesarean section was observed in 24.1% of patients in Misoprostol group compared to 12.1% of prostaglandin E2 group which was not a statistically significant difference. Major indication for C/section was fetal dis-

Table 1: Demographic characteristics of study group

Variables		Type of Agent		P Value
		Misoprostol Mean (SD)	Prostaglandin E2 Mean (SD)	
Age		27.19 (7.06)	28.81 (6.80)	0.2107
Gestational Age (in Weeks)		41.1 (2.80)	40.70 (2.0)	0.3778
Parity	≤3 N (%)	54 (93.1%)	46 (79.3%)	0.0312
	=4 N (%)	04 (6.9%	12 (20.7%)	

Table 2: Indications for induction of labor (IOL)

Indication for IOL	Type of Agent		Total
	Misoprostol n (%)	Prostaglandin E2 n (%)	n (%)
Low Biophysical Profile	7 (12.3%)	10 (17.2%)	17 (14.8%)
Pregnancy Induced Hypertension	4 (7%)	2 (3.4%)	6 (5.2%)
Grade III Maternity Changes of Placenta with Oligohydramnios	08 (13.7%)	09 (15.5%)	17 (14.6%)
Postdates	25 (43.9%)	29 (50%)	54 (47%)
Diabetes	04 (7%)	02 (3.4%)	06 (5.2%)
Cardiac Disease	0 (0%)	01 (1.7%)	01 (9%)
Previous Intrauterine Death + Early Neonatal Death	02 (3.5%)	01 (1.7%)	03 (2.8%)
Decreased Fetal Movement	02 (3.5%)	01 (1.7%)	03 (2.6%)
Intrauterine Growth Restriction	01 (1.85)	0 (0%)	01 (9%)
Pre- Eclampsia	05 (8.8%)	02 (3.4%)	07 (6%)
Mild Fetal Hydrops	01 (1.8%)	01 (1.7%)	01 (0.9%)
Total	58 (100%)	58 (100%)	116 (100%)

Table 3: Mean time taken for onset of labor and delivery

Variables	Type of Agent	Mean (SD)	Std. Error	P Value
Doses of Agent Used	Misoprostol	1.55 (0.597)	.07845	0.6662
	Prostaglandian E2	1.6 (0.647)	.08499	
Induction Labor Interval (in hours)	Misoprostol	7.2 (4.780)	.62759	0.0001
	Prostaglandian E2	12.0 (6.947)	.91224	
Induction Delivery Interval (in hours)	Misoprostol	10.3 (6.892)	.90493	0.0011
	Prostaglandian E2	15.0 (8.160)	1.07152	

Table 4: Mode of delivery

Variables		Type of Agent		Total	P Value
		Misoprostol Mean (SD)	Prostaglandin E2 Mean (SD)	n (%)	
Mode of delivery	C-Section	14 (24.1%)	7 (12.1%)	21 (18.1%)	0.1883
	Instrumental	7 (12.1%)	11 (19%)	18 (15.5%)	
	NVD	37 (63.8%)	40 (69%)	77 (66.4%)	
Total		58 (100%)	58 (100%)	116 (100%)	

tress observed in 7 cases of Misoprostol and 5 cases of prostaglandin E2 group. Cesarean section was done for failed induction in 2 cases of Misoprostol group compared to 1 case of prostaglandin E2 group. Cesarean section for meconium stained liquor was done in one patient of Misoprostol group.

DISCUSSION

In this study, Misoprostol was found more effective than prostaglandin E2 for IOL. It has shorter induction to labor and delivery interval as shown in many studies[13,14]. Misoprostol use has gained worldwide acceptance for cervical ripening. Its use for induction of labor has been endorsed by American College of Obstetricians and Gynecologists[15].The current study was planned to establish comparative efficacy of Misoprostol versus prostaglandin E2 for induction of labor in our settings where prostaglandin E2 is expensive and its storage at low temperature is an issue. Prolonged pregnancy was common indication for induction of labor in present study i.e. in 43.9 % cases of Misoprostol group while 50% cases of Prostaglandin E2 group. NICE guidelines recommend induction of labor from 41 weeks and onwards to reduce the risk of perinatal death and meconium aspiration syndrome. A study by Raval et al[16] also showed post date pregnancy to be commonest cause of IOL i.e. in 36% cases of Prostaglandin E2 and 24% in Misoprostol group.

The average age of our study population was 27.1 years which was comparable with the results of a systematic review by Wing et al[17] showing an average age of 29.5 years. This difference could be due to early marriages of women in our part of the world than developed countries. Induction of labor with prostaglandins has dramatically improved outcomes in women with low bishop score. Our study showed that vaginal Misoprostol (Prostaglandin E1 analogue) is more effective and faster in improving bishop score and thus its induction to labor and delivery time is shorter than prostaglandin E2. In our study, induction to labor interval was shorter i.e.7.2 ±4.7 hours with Misoprostol as compared to 12.03 ±6.9 hours with prostaglandin E2 group. This

finding was not given significance in previous studies and is a useful observation of our study. Thus low dose Misoprostol is as effective as prostaglandin E2 in improving bishop score and uterine contractions.

Induction to delivery interval was also significantly shorter i.e. 10.32 ±6.89 hours with Misoprostol compared to 15.04 ±8.16 hours with Prostaglandin E2. Our results were comparable with those of Saima et al[14] showing shorter Induction delivery interval with Misoprostol i.e. 9.0 hours compared to 10.8 hours with Prostaglandin E2. Similar findings were observed by Hofmeyr[13] and Beigi et al[18]. They showed that mean induction to delivery interval with the use of oral Misoprostol was 8.7 hours16. Thus vaginal prostaglandin E2 gel is slower in action with longer labor duration than Misoprostol. We found a significantly higher incidence of spontaneous labor with 50ug of Misoprostol compared to 2mg of prostaglandin E2 pessary.

The potential risk of induction of labor with prostaglandins is an increased risk of cesarean section (c/section) particularly in nulliparous women at term with an unfavorable cervix due to failed induction. In our study, successful vaginal delivery and c/section rates were not significantly different between the two groups as 75.9% cases of Misoprostol group delivered vaginally compared to 88.0% cases of prostaglandin E2 group. 14 cases in Misoprostol group delivered by c/section compared to 7 cases in prostaglandin E2 group. Indications for c/section in each group were fetal distress, failed induction of labor, secondary arrest of labor and grade III meconium stained liquor. Our results are comparable with those of Crane et al[19] showing no difference in rates of c/section between Misoprostol and prostaglandin E2 group (19.5% versus 19.4%, RR =0.99, 99% CI 0.83-1.17). In earlier studies, higher doses of Misoprostol were associated with higher rates of hyper stimulation and fetal heart changes needing emergency c/sections. Thus low doses are safe and effective with no excess of adverse events.

CONCLUSION

Misoprostol vaginal tablet significantly reduces the induction to labor and delivery interval and has a similar vaginal delivery and cesarean section rate when compared with vaginal prostaglandin E2 gel.

RECOMMENDATIONS

Misoprostol deserves consideration and further evaluation in a larger study to establish its important role in the practice of obstetrics and gynecology in resource depleted countries like ours where expensive prostaglandins have other problems as well like storage

REFERENCES

1. Memon A, Sikandar R. Misoprostol for induction of labour: the Hyderabad experience. J Liaqat Uni Med Health Sci 2007; 6:56-9.
2. Papanokolaou EG, Plachouras N, Droughia A, Andronikou S, Vlachou C, Stefos T et al. Comparison of Misoprostol and dinoprostone for elective induction of labour in nulliparous women at full term: A randomized prospective study. Reprod Biol Endocr 2004; 2:70.
3. Tenore JL. Methods for cervical ripening and induction of labour. Am Fam Physician 2003; 67:2123-8.
4. Abbasi RM, Sirichand P, Rizvi S. Safety and efficacy of oral versus vaginal Misoprostol use for induction of labor at term. J Coll Physicians Surg Pak 2008; 18:625-9.
5. Ayad IA. Vaginal Misoprostol in managing premature rupture of membranes. East Mediterr Health J 2002; 8:515-20.
6. Rozenberg P, Chevret S, Senat MV, Bretelle F, Paule Bonnal A, Ville Y. A randomized trial that compared intravaginal Misoprostol and dinoprostone vaginal insert in pregnancies at high risk of fetal distress. Am J Obstet Gynaecol 2004; 191:247-53.
7. O'Brian WF. Cervical ripening and labor induction: progress and challenges. Clin Obstet Gynaecol 1995; 38:89-100.
8. Le Roux PA, Olarogun JO, Penny J, Anthony J. Oral and vaginal Misoprostol compared with dinoprostone for induction of labor: A randomized controlled trial. Obstet Gynecol 2002; 99:201-5.
9. Crowely P. Interventions for preventing or improving the outcome of delivery at or beyond term. Cochrane Database Syst Rev 2000; (2):CD000170.
10. Rand L, Robinson JN, Economy KE, Norwitz ER. Post term induction of labor revisited. Obstet Gynecol 2000; 96:779-83.
11. MacKenzie IZ. The therapeutic roles of prostaglandins in obstetrics. In: Studd J, ed. Progress in obstetrics and gynaecology.Vol,8. Edinburgh: Churchill Livingstone, 1990; 149-73.
12. Jain S, Pasrija S, Sakure S, Sarda N. A randomized study of low-dose oral Misoprostol and intracervical prostaglandin E2 gel for cervical ripening and labour induction in term pregnancy. J Evol Med Dent Sci 2018; 7:2023-8.
13. Hofmeyr JG. Induction of labor with an unfavorable cervix. Best Pract Res Clin Obstet Gynaecol 2003; 17:777-94.
14. Ali S, Mubasher S, Haq AN. A comparison of vaginal Misoprostol and prostaglandin E2 for induction of labor at term. J Gynaecol Obstet 2014; 2:81-5.

15. ACOG Committee on Practice Bulletins-Obstetrics. ACOG Practice Bulletin No.107: Induction of labor. Obstet Gynaecol 2009; 114:386-97.

16. Raval BM, Zalavadiya NS, Yadava PA, Mehta ST. Comparative study of intra vaginal Misoprostol (PGE1) with intracervical dinoprostone (PGE2) gel for induction of labour. Int J Reprod Contracept Obstet Gynaecol 2018; 7:3769-73.

17. Wing D. Induction of labor: indications, technique, and complications. Up To Date Online 14.2 (www.UpToDate.com). Accessed 31 July 2006.Google Scholar]}

18. Beigi A, Kabiri M, Zarrinkoub F. Cervical ripening with oral Misoprostol at term. Int J Gynaecol Obstet 2003; 83:251-55.

19. Crane JM, Butler B, Young DC, Hannah ME. Misoprostol compared with prostaglandin E2 for labor induction in women at term with intact membranes and unfavourable cervix; a systematic review. Br J Obstet Gynaecol 2006; 113:1366-76.

CONTRIBUTORS

QQ conceived the idea, designed the study, drafted the initial manuscript and supervised the whole project. SSF, SW and WS helped collection of data, analyzed and compiled results, carried out bibliography, critically appraised the draft and did corrections after reviewers' suggestions. All authors contributed significantly to the submitted manuscript.