Original Article

# A comparison of intravaginal Misoprostol with Prostaglandin E2 (Dinoprostone) for induction of labour at term

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**Objective:** To compare the efficacy of Misoprostol and Dinoprostone used as labour inducing agents.

**Material & Methods:** The first 100 patients admitted in the labour ward of Shalamar Hospital Lahore for induction of labour between March 2003 & February 2004 and fulfilling the inclusion criteria were randomly allocated to the two drug trial groups and followed till outcome of the delivery. Parameters included induction to delivery interval, need for augmentation of labour, C-section rate, safety of drugs to mother and the neonate and the cost benefit rates.

**Results:** One case got dropped out on her personal choice and left the hospital. The remaining 99 were followed up. Among the vaginally induced Misoprostol group 56% women delivered vaginally within 12 hours, while in vaginally administered Dinoprostone group only 26% delivered within 12 hours. This difference was found statistically significant ($p<0.05$). The rate of C-Section in the two groups was not found statistically different ($p>0.05$). The most common side effect with Misoprostol was nausea while the patients in the other group experienced vomiting.

**Conclusion:** Vaginally prescribed Misoprostol reduced the induction to delivery interval but did not effect the rate of C-Section. No increase in maternal or neonatal complications was observed. It was highly cost effective.

**Keywords**: Induction of labour, Misoprostol, Dinoprostone, Caesarean section.

## Introduction

Induction of labour refers to iatrogenic stimulation of uterine contractions prior to the onset of spontaneous labour to accomplish an early delivery. It is the most commonly performed procedure in USA;[1] between 1990 and 1998 the rate of labour induction doubled from approximately 10 to 20%.[2] The reasons for the increase include desire to arrange more relaxed attitude towards marginal indications of induction, presence of favorable cervix at term and availability of cervical ripening agents, patient or provider concern about risks of expectant management e.g. still birth.[3] Induction of labour should be undertaken when the benefits to either mother or the fetus out weigh the risks of continuing the pregnancy.[4] The cervical dilatation and effacement are reasonable predictors of likelihood of successful induction followed by vaginal deliveries. Different methods are available for induction of labour e.g. membrane stripping amniotomy, insertion of balloon catheter with or without extra amniotic saline infusion, introduction of hygroscopic dilators, oxytocin and prostaglandins.

The commonest method of induction in current use is with prostaglandins. They can be used intravenously intramuscularly, orally or vaginally but the first three routes produce severe side effects.

In our unit Dinoprostone which is prostaglandin E2 was used for induction of labour at term in viable pregnancies. It is expensive, has a shorter shelf life and maintenance of the cold chain is essential for its efficacy. In search of an agent which is inexpensive, stable at room temperature and has longer shelf life, it was compared with a prostaglandin $E_1$ analogue named Misoprostol.

The FDA has restricted its use for clinical trial only for induction of labour at term in viable pregnancy. We wanted to know more about the drug and therefore designed this study to see the difference in efficacy and safety of the drugs, if any difference is there.

## Material & Methods

It was a quasi experimental study carried out from 1st March 2003 to 29th February 2004. The study was conducted in the department of Obstetrics and Gynaecology of the Shalamar Hospital Lahore, which is a tertiary care hospital. The sample size was 100 patients, 50 for each experimental group. The sample size was calculated by using Epi Info statistical software. The presumed relative risk for sample size was 3.0 at 95% confidence interval and 80% power.

All the patients having gestational age between 37 to

42 completed weeks with or without rupture of membranes with singleton pregnancy, cephalic presentation, bishop score 6 or less than six, reassuring fetal heart rate pattern, parity less than six and having fetus with estimated fetal weight between 2.5-4.0 kg were included in the study. The patients with any contraindication to vaginal delivery, previous uterine scar, placenta praevia, prior labour induction and known allergy to prostaglandins were excluded.

Once the patients were enrolled to the trial all the background and obstetrical data was entered in a especially designed proforma. The patients were divided in 2 equal groups randomly i.e. A & B. Group A received tab. Misoprostol (200ug) which was dissolved in 4cc of xylocaine gel, out of which one cc i.e. 50ug was placed in post vaginal fornix which was repeated after every 4 hours to a max dose of 200ug. Group B received Dinoprostone 3mg ½ of which i.e. 1.5mg was repeated every 6 hourly to a max dose of 6.0mg. Contractions were assessed every 2 hours and administration of Misoprostol / Dinoprostone was stopped after regular uterine contractions. If contractions subsequently became inadequate then augmentation with injection syntocinon was done. Vaginal examination was performed before the administration of the 2nd dose. If labour had started or bishop score was 6 or greater then the second dose of the drug was not given. For women in both the groups FHR was recorded electronically during first hour after the first administration and at least every 4 hours for 20 minutes before the onset of labour and then ½ hourly when labour had started. The primary outcome was induction to delivery interval and the other outcome measures were need of oxytocin augmentation, rate of C-Section, safety in terms of maternal and neonatal complications and cost of the 2 drugs. The data was collected and then entered in SPSS version 10 and was analyzed statistically for outcomes. 't' test was applied to quantitative data and chi-square test was applied to qualitative data. The significance level was at 0.05 or less margin of error.

## Results

The total number of patients who were enrolled to the trial was 100 out of which one patient lost follow up. The difference between mean age, parity gestational age and bishop score was not statistically significant. The most common indication in both the groups was post date. Augmentation was required in 2% of the patients in group A compared to 14% in

**Table-1:** Distribution of cases in two groups according to need for augmentation with oxytocin infusion.

| Augmentation | Misoprostol | | Dinoprostone | | P-value |
|---|---|---|---|---|---|
| | No. | Percentage | No. | Percentage | |
| Required | 1 | 2.0 | 7 | 14.0 | p<0.05 |
| Not Required | 49 | 89.0 | 42 | 84.0 | |
| Missing Data | 0.0 | 0.0 | 1 | 2.0 | |
| Total | 50 | 100.0 | 50 | 08 | |

**Table-2:** Distribution of cases in two groups according to induction to delivery interval.

| Maximum time to delivery | ¡12 hrs | | 13-24 hrs | | 25-48 hrs | | P-value |
|---|---|---|---|---|---|---|---|
| | No. | Percentage | No. | Percentage | No. | Percentage | |
| Misoprostol | 28 | 56.0 | 16 | 32.0 | 6 | 12.0 | p<0.05 |
| Dinoprostone | 13 | 26.0 | 25 | 50.0 | 11 | 22.0 | |

**Table-3:** Distribution of cases in two groups according to mode of delivery.

| Mode of Delivery | Misoprostol | | Dinoprostone | | P-value |
|---|---|---|---|---|---|
| | No. | Percentage | No. | Percentage | |
| SVD (spontaneous vertex delivery) | 35 | 70.0 | 24 | 48.0 | p<0.05 |
| Forceps | 3 | 6.0 | 7 | 14.0 | p<0.05 |
| LSCS (lower segment c-section) | 12 | 24.0 | 18 | 36.0 | p>0.05 |
| Missing Data | 0 | 0.0 | 1 | 2.0 | |
| Total | 50 | 100.0 | 50 | 100.0 | |

delivery interval and 56% of the patients were delivered within 12 hours compared to 26% in group B (**Table 2).**

70% of the patients were delivered vaginally in group A with 24% rate of C-Section while only 48% of the patients in group B were delivered vaginally with 36% rate of C-section. This difference was however statistically not significant (**Table 3).**

Fever was experienced by majority of the patients in both the groups though more common in group B but the difference was not statistically significant Tachysystole was seen in 2% of the patients in group A. The commonest side effect was nausea experienced by 12% of patients in group A while it was vomiting in group B and was experienced by 24% of the patients.

The mean Apgar score at 5 minutes was 4-7 in 82% of patients in group A and 94% of the patients in group B. The difference was statistically not significant. The admission to neonatal ICU was required in 20% of the patients in group A and 18% of the patients in group B. Cost effectiveness of both drugs was considered in terms of the cost of the drug and cost of the hospital stay. The preparation of misoprostol used in the study was a tablet of 200 ug which costs Rs. 65 only while Dinoprostone preparation was a 3 mg tablet which costed Rs. 689 in 80% of the patients in which only one tablet was used but the cost increased to Rs. 1378 in 18% of the patients. The difference was statistically significant.

74% of the patients were discharged within 3 days in group A compared to 68% in group B. Although the duration of hospital stay was not different in both groups but the over all cost of induction with Misoprostol was significantly lower as compared to Dinoprostone.

## Discussion

The common indications were post date PIH and prolonged ROM in both the groups. The results obtained are comparable to the study conducted in USA in 1999 in which also no difference was noted between 2 groups in demographic characteristics or indications for induction of labour.

The requirement of oxytocin was reduced with Misoprostol, induction to delivery interval was also reduced and insignificant reduction in rate of C-section was noted in our study. The mean apgar score & admission to NICU is also insignificantly different in our study. Similar results were found by Kolderup & colleagues[5] who did the study on 159 patients in Department of Obstetrics Gynaecology & Reproductive Sciences, University of California San Francisco, USA in 2001. Chang YK et al also found that misoprostol is more effective than prostaglandin E-2 & it didn't increase the risk of intrapartum & neonatal complications. They did the study on 86 patients in tri service General Hospital, National Defense Medical Center, Taipei, Taiwan in 2003. Agarwal et al [6] in 2003 did the study in All India Institute of Medical Sciences, New Delhi India, on 120 patients & found it safe, effective & with lesser need of augmentation & shorter induction to delivery interval. Lokugamage Au et al did the study on 191 patients in Royal free & University College London Medical School , University College London, London , UK & found that intravaginal misoprostol led to a shorter, more efficient labor. Although there was more anxiety related to CTG there was no increase in neonatal adverse effects & no difference in rates of oxytocin augmentation was found. Herabutya et al[9] did the study on 110 patients in Faculty of Medicine, Ramathibodi Hospital Mahidor University, Bangkok, Thailand & found that vaginal misoprostol is an effective agent for cervical ripening & induction of labor. Complications associated with prostaglandin administration were not statistically different between the 2 groups but hyperstimulation occurred more in misoprostol group.

Neiger et al did the comparative study on 61 patients in University of Tennessee Medical Center Knoxville USA & found that the vaginal misoprostol is more effective cervical ripening agent with significant reduction in oxytocin requirement.

Bolnick et al[19] did the study in University of New Mexico, USA on 151 patients & found no significant difference in induction to delivery interval.

We found misoprostol as a cost effective alternative to the current labor induction protocols & similar results were found by Sanchaz Ramos L et al who did the study on 223 patients.

Mundle WR & Young DC did the comparison in 221 patients & found vaginal misoprostol being less expensive & more effective & safe as no evidence of harm to mother or newborn was observed in substantive outcomes.

## Conclusion

The study showed that the Misoprostol reduces the induction to delivery interval and need of oxytocin augmentation of labour. However it does not affect the rate of C-section. No increase in maternal and neonatal complications was observed. The cost of

of the drug and cost of the hospital stay.

As the misoprostol was found very effective in reducing the induction to delivery interval when compared to Dinoprostone and no difference regarding maternal and neonatal safety was observed, therefore the author gives her preference to Misoprostol. However a multicentre trial is required to determine Misoprostol's efficacy, safety and cost effectiveness.

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## References

1. Ventura SJ, Martun JA, Curtin SC. Birth final data for 1999. Natl Vital stat Rep 2001; 49:1-100.
2) Zhang J, Yancey MK, Hendersson CE. US national trends in labour induction 1989-1998. J Reprod Med 2002;47:120-4.
3) Rayburn WF, Zhang J. Rising rates of labour induction: present co- ncerns and future strategies. Obs tet Gynaecol 2002;100: 164-7.
4) American College of Obstetricians & Gynecologists. Introduction of labour ACOG practice bulletin # 10, Washington DC: ACOG 1999.
5) Kolderup L, Mc Lean L, Grullen V, Saffora K, Kilpatrick SJ. Misoprostol is more efficacious for labour induction than prostaglandin E2, but is it associated with more risk? Am J Obstet Gynaecol 1990; 180 6 (pt 1): 1543-50.
6) Agarwal N, Gupta A. Kriplani A, Bhootra N, Parul S. Six hourly vaginal misoprostol versus intra cervical dinoprostol for cervical ripening and labor induction. J Obstetr Gynaecol Res 2003; 29:147-51.
7) Chang YK, Chen WH, Yu MH, Liu HS. Intra cervical misoprostol and prostaglandin E2 for labor induction. Int J Gynaecol Obstetr 2003; 80 (1):23-8.
8) Wing DA, Jones MM, Rahall A, Goodwin TM, Paul RH. A comparison of misoprostol and prostaglandin E2 gel for pre induction cervical ripening and labor induction. Am J Obstet Gynaecol 1995; 172: 1804-10.
9) Herabutya Y, Prasertsawat P, Pokpirom J. A comparison of intra vaginal misoprostol & intrac- ervical prostaglandin E2 gel for ripening of unfavourable cervix and labor induction. J Obstet Gynaecol Res 1997;23:369-74.
10) Neiger R, Greaves PC. Comparison between vaginal misoprostol and cervical dinoprostone for cervical ripening and labour induction. Term Med 2001; 94(1):25-7.
11) Lokugamage Au, Forsyth SF, Sull ivan KR, Elrefacy H, Rodeck CH. Dinoprostone versus misoprostol randomized study of nulliparous women undergoing induction of labour. Acta Obstet Gynaecol Scand 2003;82:133-7.
12) Pandis GK, Papa Georghiou AT, Otigbah CM, Howard RJ, Nicolaides KH. Randomized study of vaginal misoprostol (PGE) and Dinoprostone gel (PGE2) for induction of labour at term.Ultrasound Obstet Gynaecol 2001;18:629-35.
13) Jouatte F, Subtil D, Marquis P, Plennevaux JL, Puech F. Medical indications of labour induction : a comparison between intravaginal misoprostol and intravenous prostaglandin E2. J Gynaecol Obstet Biol Reprod (Paris) 2001 ;29 :763-71.
14) Garry D, Figueroa R, Kalish RB, Catalano CJ, Maulik D. Randomised controlled trial of vaginal misoprostol versus dinoprostol vaginal interest for labour induction. J Matern Fetal Neonatal Med 2003; 13: 254-9.
15) Sanchez-Ramos L, Peterson DE, Delke I, Gavdier FL, Kaunitz AM. Labor induction with prostaglandin E, misoprostol compared with dinoprostone vaginal interest: a ranodomized trial. Obstet Gynaecol 1998;91:401-5.
16) Ramsey PS, Haris DY, Ogburn PL Jr, Heise RH, Magtibay PM, Ramin KD. Comparative efficacy and cost of the prostaglandin analogues, dinoprostone and misoprostol as labor pre induction agents. Am J Obstet Gynaecol 2003; 188: 560-5.
17) Nunes F, Rodrigues R, Meirinho M. Randomized comparison between intravaginal misoprostol and dinoprostne for cervical ripening and induction of labor. Am J Obstet Gynaecol 1999; 181: 626-9.
18) Moodlyey J, Venkatachalam S, Songca P. Misoprostol for cervical ripening at or near term: a comparative study S Afr Med J 2003; 93: 371-4.
19) Bolnick JM, Velazquez MS, Gonzalez JL, WF. Randomized trial between two active labor management protocols in the presence of an unfavourable cervix. Am J Obstet Gynaecol 2004; 190: 124-8.
20) Munale WR, young DC vaginal Misoprostol for induction, a