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Original Article

COMPARISON OF EFFICACY OF VAGINAL MISOPROSTOL AND PROSTAGLANDIN E2 FOR INDUCTION OF LABOUR IN PRIMIGRAVIDAE TITLE PAGE

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ABSTRACT

***Objective*:** To compare the efficacy of vaginal misoprostol and prostaglandin E2 in induction of labour in primigravidae.
Material Method: The study was conducted in the department of Obstetrics and gynaecology ward 8 from 1st January, 2006 to 31st December, 2006 at Jinnah Postgraduate medical center Karachi. It was a comparative clinical trial in which 100 primigravidae at term (37-42 weeks) were included in whom induction of labour was indicated and proforma was used for data collection.
Results: Hundred primigravidae were studied, 50 women were given misoprostol while the other 50 were given prostaglandin E2. The patients were induced with the Bishop score of 4 or less, the mean induction to delivery interval was 10.96± hours in misoprostol group and 13.06± hours in PGE2 group. 44% of patients required oxytocin for augmentation of labour in misoprostol group 70% required in PGE2 group. Vaginal deliveries were 94% in misoprostol group where as 74% in PGE2 group. The cesarean section rate was 6% in misoprostol group while 26% in PGE2 group. There was no significant difference in the Apgar score and neonatal deaths in both groups
Conclusion: Misoprostol is a cost effective, less expensive agent. It is significantly more effective for labour induction and cervical ripening than PGE2. There is a reduction in the induction to delivery interval and cesarean section rate. And there was no evidence of harm either to the mother or the new born in substantive outcome.

Keywords: Induction of labour, misoprostol, prostaglandin E2.

INTRODUCTION

Labour is said to be induced when an external agent is used to stimulate the uterus before the onset of spontaneous labour or it is defined as the stimulation of uterus with the aim of progressive cervical dilation and effacement to ensure delivery of the fetus at an appropriate time, when baby is thought to be safer outside the uterus than in it. Induction is preformed only upon indications when further prolongation of pregnancy might expose the mother or fetus or both to certain risk and when vaginal delivery is not contraindicated[1].

Induction of labour should be distinguished from augmentation of labour in which the patient has been in labour which is slow or has somehow slowed down and is accelerated[2]. During normal pregnancy a closed unripe cervix ensures integrity of pregnancy until term. At term, complex processes, this includes activation of prostaglandins causes cervix to become soft and compliant. This facilitates cervical dilation in response to myometrial contractions.

A successful labour is more likely when the cervix is ripe. Different methods have been

used for cervical ripening and induction of labour. Successful induction of labour ending up in smooth delivery reduces risk of cesarean section and the condition of neonate is also improved and when the cervix is unfavorable, there are more chances of failed induction and increase risk of cesarean section[3]. Vaginal prostaglandins proved to be beneficial in promoting both cervical ripening and myometrial contractility[4].

Misoprostol is a synthetic prostaglandin E1, analogue which is used as a cytoprotective agent in gastro duodenal ulcers[5], and it also acts as a myometrial stimulant of the pregnant uterus, it has a long shelf life and does not require any special storage conditions[6]. Although misoprostol can be administered orally or vaginally, the vaginal route has been shown to be more affective for termination of pregnancy and cervical priming in comparative studies[7, 8].

The systemic bioavailability of vaginally administered misoprostol is three times higher than that of orally administered misoprostol[9]. However, the oral route of administration is preferred to the vaginal route by patients as it is more convenient and discrete. Sublingual administration is now being evaluated and there is one report on its usage[10].

Prostaglandin E2 have also been used for induction of labour either as a intravaginal pessary or as a cervical vaginal jell.

Aims and Objective: To compare the efficacy of vaginal misoprostol and prostaglandin E2 for induction of labour in primigravidae.

MATERIAL AND METHOD

The study was conducted in the department of Obstetrics and gynaecology ward 8 from 1st January to 31st December 2006 at Jinnah Postgraduate medical center Karachi which is a tertiary care teaching hospital. It was a comparative clinical trial in which 100 primigravidae at term (37-42 weeks) were included in whom induction of labour to be indicated. Most of the patients were admitted in ward through antenatal OPD and few through the emergency, they were selected for induction according to departmental protocol.

A complete clinical examination followed the detailed history and general physical examination, abdominal examination and per vaginal examination was done to see the Bishop score. Induction was started in the morning if bishop score was less than 4 tablet misoprostol (Cytotec) or PGE2 (prostin) pessary were used. The dose of PGE2 3mg pessary or dose of misoprostol 100µg (200 µg tablet halved) placed digitally high in posterior vaginal fornix and repeated every six hours and four hours respectively.

Per vaginal examination was done after every 3 hours to see the bishop score and tablet / pessary was repeated according to bishop score. No further dose was given if any abnormal uterine contractions or any irregular fetal heart rate are to be observed. When patients went into active labour they were shifted to labour room. Oxytocin was used for augmentation subsequent to artificial rupture of membranes according to departmental protocol and proforma has been used for data collection.

INCLUSION CRITERIA:

- Primigravidae
- 37 - 42 weeks of pregnancy
- Singleton fetus
- Cephalic presentation
- Bishop score less than 4

EXCLUSION CRITERIA:

- Malpresentation
- Abnormal weight of fetus more than 4 kg (ultrasound estimated) or other evidence of cephalo pelvic disproportion
- Absent membranes
- Any contraindication to receiving prostaglandins including h/o asthma, glaucoma, renal or hepatic dysfunction.
- History of previous surgery on uterus i.e. myomectomy.

MAIN OUTCOME MEASURES:

- Time from induction to delivery.
- Oxytocin requirement in labour
- Mode of delivery
- Fetal outcome.

DATA ANALYSIS:

Data was analyzed using SPSS version 10.0 by applying " t-test " to obtain the results.

RESULTS

Hundred primigravidae were studied and all of them were very cooperative and fulfilled the criteria. 50 women were given misoprostol while the other 50 were given prostaglandin E2. The characteristics of women in both groups were comparable. Regarding age distribution, the mean age was 22.51 ± 2.6 years in misoprostol group and 22.41 ± 2.6 years in PGE2 group.

The induced patients were divided into two groups, based on expected date delivery, group A from 37 to 40 weeks gestation and group B from 40 to 42 weeks. Out of 100 patients 37 (74%) belong to group A and 13 (26%) to group B, in misoprostol group while 35 (70%) and 15(30%) belonged to group A and B respectively in PGE2 group.

The mean gestational age was 38.96 ± 1.81 in misoprostol group and 39.18 ± 1.86 in PGE2 group. Out of 50 patients in misoprostol group 26% were induced in 37 weeks, 28% in 38 weeks, 12% in 39 weeks, 08% in 40 weeks, 10% 41 weeks and 16% in 42 weeks while in PGE2 group 32% patients were induced at for 38 weeks and 20% in 37 and 42 weeks each.

All the patients in the study at the time of admission had bishop's score of 4 or less in both group. The mean bishop score was 3.06 ± 1.07 in misoprostol group while 2.76 ± 1.07 in PGE2 group.

The induction delivery interval reflects the time interval between

MATERNAL DEMOGRAPHIC DETAILS OF INDUCTION OF LABOUR

	Misoprostol (n=50)	PGE2 (n=50)	P-value
Age (years)	22.51±2.6	22.41±2.6	p= 0.84 t= 0.04
Gestational Age (weeks)	38.96±1.84	39.81±1.86	P= 0.02 t= 5.35
Bishop score	3.06±1.07	2.76±1.07	P= 0.16 t= 1.97
Birth weight of fetus (kg)	2.815±0.49	2.878±0.51	P= 0.53 t= 0.40
Induction to delivery interva l (hours)	10.96±1.55	13.06±1.94	P= 0.001 t= 35.76
No. of Patients needing oxytocin augmentation P= 0.01	22 (44%)	35 (70%)	Chi-square = 6.9

first dose of drug to expulsion of fetus. The mean induction to delivery was 10.96 ± 1.55 hours, out of 50 patients 22 delivered within 12 hours in misoprostol group. In case of PGE2 group the mean induction delivery interval was 13.06 ± 1.94 hours. 44% (22) of patients required oxytocin for augmentation in misoprostol group and 70% (35) patients in PGE2 group.

The mean dose of misoprostol used was 216.0 ± 46.77µg and 5.22 ± 1.33 mg of PGE2, and it was adjusted according to the bishop's score. In misoprostol group 4% women delivered after single dose of 100µg, 76% women second dose of 100µg had to be used, and in the remaining 20% women, a third dose of 100µg was used. In PGE2 group one pessary of 3mg was used in 26% women, in 3 out of 13, a second pessary was not repeated because of meconium passage and fetal distress. Second pessary of PGE2 (3mg) was used in 74% women out of which induction failed in 6 women. Only one woman had uterine hyper stimulation with two tablets of 100µg of misoprostol. There was also meconium staining of liquor, after giving injection buscopan and oxygen inhalation patient was taken immediately for emergency caesarean section. Baby delivered with apgar score of less than 7 at 1 minute and 10 at 5 minutes and didn't need any resuscitation. While no such incidence occurred in PGE2 group.

The success rate in the form of normal vaginal deliveries in induced patients of miso group was found 84% (42), 10% (5) instrumental vaginal deliveries and the failure rate in the form of cesarean deliveries were 06 %(3). While in PGE2 group 68 %(34) were normal vaginal deliveries, 06 %(3) instrumental and 26 %(13) cesarean sections.

Out of 3(6%) cesarean sections in misoprostol group 2 occurred due to fetal distress and one due to failure to progress while in PGE2 group 6 occured due to failed induction 4 due to failure to progress and 2 due to meconium stained liquor.

most common indication which presented about 34 %(17 patients) and the second was prolonged pregnancy which was 26 %(13 patient) in misoprostol group. While in PGE2 group P.I.H. and prolonged pregnancy presented about 36% and 30% respectively.

Regarding status and fetal outcome alive births were 76% and 24% were still born confirmed IUDs on ultrasound, in misoprostol group while in PGE2 group 96% were alive and 06% were still born confirmed IUDs on ultrasound, with no neonatal deaths in both groups.

In misoprostol group the mean weight of baby was 2.815 ± 0.49 kg and 2.878 ± 0.51 kg in PGE2 group. The apgar score of one and five minutes were >7 and 10 in both groups. In 02 cases of the misoprostol group and 01 in PGE2 group it was <7 at one minute and 10 at five minutes.

Regarding complications in live born neonates 2 babies from each misoprostol and PGE2 group were admitted in neonatal intensive care unit where they were diagnosed having respiratory distress syndrome and irritability in misoprostol group babies and jaundice in one baby of PGE2 group. All were recovered and shifted back to the ward within 24 – 48 hours.

DISCUSSION

As the frequency of induction of labour is increasing day by day and the rate of induction varies worldwide in different countries, units and between individual obstetricians within the same units, different methods have been introduced for induction.

All patients receiving misoprostol went into labour, whereas only 37 patients receiving PGE2 did so.The induction to delivery interval is an important aspect in induction of labour. Longer time interval is associated with more psychological

trauma. Prolong induction time also necessitates the use of intravenous hydration, increased analgesic requirement, and use of augmentation with oxytocin. In my study the induction to delivery interval was 10.96 ± 1.55 hours in misoprostol group and 13.06 ± 1,94 hours in PGE2 group, as compared to trial of Draycott et al[11]. Average induction to delivery interval was 10 hours, and 44% (22) of patients required oxytocin for augmentation of labour in misoprostol group and 70% in PGE2 group which supports the study of (Dandelion 1999 and Niger 2001) [12,13]. Successful inductions of labour ending up in smooth vaginal delivery and reduce risk of cesarean section. 94% of patients delivered vaginally in misoprostol group and 74% in PGE2 group, which is consistent with the study of Lee HY 1997[14] where maximum no. of patients delivered within 12 hours. The cesarean section rate was 6% in misoprostol group which was done due to fetal distress and failure to progress, where as 26% in PGE2 group which was mostly done due to failed induction. The mean amount of total dose requirement for delivery in misoprostol group was 216.00 ± 46.77 µgm and one patient delivered with single dose, while 5.22 ± 1.33 mg in PGE2 group. Fetal outcome was same in both groups with no neonatal deaths. Complications associated with prostaglandin administration were not statistically different between two groups and only one patient had uterine hyper stimulation in misoprostol group which is inconsistent with study of Charoenkul 2000[15]. Apart from it, common side effects which are noted with the use of drug include diarrhea, vomiting and rise in temperature. These effects are more pronounced with oral route of drug [16].

Misoprostol is well absorbed through all routes of administration. The unpleasant side effects like nausea, vomiting and diarrhea with vaginal route were not observed. Bulgaho et al also reported virtually no side effects with intra vaginal doses of 50 - 200 µg[17]. Vaginal administration also allows the body to be exposed to more of the drug's active metabolite. The peak plasma levels after vaginal route of administration is achieved within 60-80 minutes. Oral route may be desirable in set-ups with limited medical staff[18]

Misoprostol tablets are stable at room temperature and cost effectiveness of the drug is an added advantage for its use which is highly suitable for developing countries [19].

Misoprostol is significantly more effective for labour induction than PGE2. The maternal intrapartum and neonatal outcome were the same for both induction regimens. Thus, misoprostol is an acceptable choice for labour induction. Successful induction also allows shorter hospital stay which is also considered as an added advantage.

There is a need for further studies on larger scale to enable the safety of misoprostol to be firmly established, and to investigate other dosage regimens and the use of oral or sublingual misoprostol for the induction of labour. In the mean time, misoprostol should be used only within the context of appropriate clinical trials.

CONCLUSION:

It is concluded that misoprostol is a cost effective, less expensive agent, alternative to current available labour induction protocols. It is significantly more effective for labour induction and cervical ripening than PGE2. There is a reduction in the induction to delivery interval with consequent less analgesic requirement and smooth vaginal deliveries with reduced rate of cesarean section. And there was no evidence of harm either to the mother or the new born in substantive outcome.

Thus, from a clinical and perinatal perspective, misoprostol is an acceptable choice for labour induction and because of the enormous economic and possible clinical advantages of misoprostol, there is the need for trials to establish its safety

REFERENCES

1. Biswas MK and Craigo SD. The course and conduct of normal labour and delivery. Induction of labour. In: *current Obstet 8th ed. Prinlice-Hall International,* 1994: 202 - 27.
2. Rana Saad. Termination of pregnancy: Induction/ Augmentation of labour. Obstetrics and Perinatal care for developing countries. 1st ed: *SAP Publications* 1998, 937-972.
3. Calder AA. Indication and augmentation of labour. In: *Dewhurst's textbook of Obstetrics and Gynaecology for postgraduate 6th ed. Oxford; Blackwell Science,* 1999: 252 258 .
4. Sultana A, Irfan Y, Jahan M. Comparison of the efficacy of vaginal misoprostol and PGE2 pessary for induction of labour. *Spectrum* 2002; Jan 22(1): 10-12.
5. Shearman DJC. Disease of the alimentary tract and pancreas. In: *Davidson's principles and practice of medicine* 17th ed. New York: Churchill livingstones, 1995:405-482.
6. Chien PFW. Third stage of labour and abnormalities. In: *Dewhurst's textbook of Obstetrics and Gynaecology for postgraduates 6th ed:* Oxford Blackwell Science, 1999:330 341.
7. el Refaey H, Rajasekar D, Abdalla M, Calder L, Templation A. Induction of abortion with mifepristone (Ru 486) and oralor vaginal misoprostol. *N Engl J Med* 1995; 332: 983 987.
8. Hopc, Ngai SW, Liu KL, Wang GC, Lee SW. Vaginal Misoprostol compared with oral misoprostol in termination of second-terimester pregnancy, *Obstet Gynecol* 1997; 90; 735-738.
9. Zieman M, Fong SK, Benowitz NL, Banskter D, Darney\ PD. Absorption kinetics of misoprostol with oral or vaginal administration. *Obstet Gynecol* 1997; 90: 88 – 92.
10. Prabhath T. Wagaarachchi, Premila W. Ashok, Norman C. Smith, Allan Templeton. Medical management of early fetal demise using sublingual misoprostol. B J *Obstet Gynaecol* April 2002; vol. 109, pp. 462 – 465.
11. Dracott T, Hawkes N, Read MD. Induction of labour with vaginal misoprostol after intra uterine death from *24* weeks

gestation. *J. Obstet Gynecol* 1996; 16:517-518.
12. Danielian P, Porter B, Ferri N. To compare the efficacy of vaginal misoprostol and dinoprostone vaginal gel for induction of labour at term. *Br. J. Obstet Gynecol* 1999; 106(8): 793-97.
13. Neiger R, Greaves PC. Comparison between vaginal misoprostol and cervical dinoprostone for cervical ripening and labour induction. *Tenn Med* 2001; Jan 94 (1):25-27.
14. Lee HY. A randomized double blind study of vaginal induction in prolonged pregnancy. Singapore *Med* J 1997; Jul38(7):292-94.
15. Charoenkul S, Sripramote M. A randomized comparison of one single dose of vaginal 50ug misoprostol with 3mg dinoprostone in pre-induction cervical ripening. *J Med Assoc:* Thai 200; 83 (9): 1026 - 34.
16. Shetty A, Danielian P, Templepon A. Sublingual misoprostol for the induction of labour at term. Am. J. *Obstet and Gynaecol* 2002; 186: 72-6.
17. Bugalho A, Bique C, Machungo F, Bergstrom S. Vaginal misoprostol as an alternative to oxytocin for induction of labour in women with late fetal death. Acta *Obstet Gynaecol Scand* 1995; 74:194-8.
18. Carlan SJ, Blust D, O'Brien WF. Buccal versus intra vaginal misoprostol administration for cervical ripening. *Am J. Obstet Gynecology* 2002; 186: 229-33.
19. Rozenburg P, Chevret S, Goffinet F, Zaleski ID, Ville y, Vayssiere C, et al. Induction of labour with a viable infant: a randomized clinical trial comparing intra vaginal misoprostol and intra vaginal dinoproston. *Br. J. Obstet Gynecol* 2001; 108: