Labour Induction at Term; Oral versus Intravaginal Misoprostol

S RIZVI F UMBER A W YUSUF
Department of Obstetrics & Gynaecology, Lady Willingdon Hospital, Lahore
Correspondence to Dr. Sarwat Rizvi, Senior Registrar, E-mail: ramss_1@yahoo.com

Objective: To compare oral misoprostol (100 µg) to vaginal misoprostol (25 µg) for cervical ripening and labor induction.
Study design: Interventional study. **Place & duration of study**: The study was carried out at Lady Willingdon Hospital, Lahore, during August 2006 to January 2007. **Patients & methods**: Fifty nine women with medical or obstetric indications for labor induction with undilated, uneffaced cervices were assigned randomly to receive 100 µg of oral or 25 µg of vaginal misoprostol every 4 hours for 24 hours. Intravenous oxytocin was then given using a standardized protocol. **Results:** Among 59 subjects, 29 received oral and 30 received vaginal misoprostol. The mean interval from start of induction to delivery was 1240 ± 845 minutes for orally treated women and 1381±802 minutes for vaginally treated women (P = .06). More orally treated women delivered vaginally in 24 hours than vaginally treated women 17 versus 16 (P= .14). Twenty five women (86.2%) who received oral misoprostol delivered vaginally, compared with 26 women (86.7%) who received vaginal misoprostol (P = .07). Oxytocin was given to 14 (49.6%) orally treated and 16(53.3%) vaginally treated subjects. More women in oral group had tachysystole, three compared with one (P = .06) and hyperstimulation. Frequencies of intrapartum complications and birth outcome were similar between groups.
Conclusion: Oral misoprostol 100 µg and vaginal misoprostol 25 µg were similarly effective for cervical ripening and labor induction. Oral administration was associated with trends toward higher likelihood of vaginal delivery and more uterine tachysystole.
Key Words: Misoprostol, cervical ripening, labor induction.

For cervical ripening and labor induction, acceptance of misoprostol, a prostaglandin (PG) E1 analogue is growing[1,2,3,4]. Previously focus was on vaginal administration of misoprostol for labour induction. Oral misoprostol offers convenience and higher patient acceptability and promises outpatient administration if proved safe and effective for cervical ripening and labor induction. In a previous study oral misoprostol (50µg) was compared to vaginal misoprostol (25µg) every 4 hours for labour induction and found no adverse events with oral administration. However, there was a longer mean time from start of induction to delivery and more oxytocin used in women who received oral misoprostol[5]. We hypothesized that a higher dose of oral misoprostol would more effectively induce cervical change and initiate labor. This study compared the efficacy of a 100-µg dose of oral misoprostol with 25µg of vaginal misoprostol for cervical ripening and labor induction.

Methods

From August 2006 to January 2007, women with medical or obstetric indications for labor induction at Lady Willingdon Hospital Lahore, were evaluated for participation. Those who met the study criteria signed written informed consents.

Fifty nine women were invited to participate. Among those, 29 received oral (n=29, 49%) and 30 received vaginal (n=30, 51%) misoprostol. During the study the patients were enrolled, randomized, offered treatment and fetal heart rate and uterine activity monitoring was done. The patients included were primi and second gravidae with a Bishop score of less than 4.Women with ruptured membranes were also participated.The exclusion criteria was multigravidity, previous scar and Bishop score of more than 4.

According to the treatment assignment, 100 µg of misoprostol was given orally, or 25µg was placed intravaginally by a senior house officer. If the subject did not have adequate uterine contraction frequency (three or more contractions in 10 minutes), the same dose was repeated every 4 hours to a maximum of six-doses in 24 hours (600µg in the oral treatment group, 150µg in the vaginal treatment group). Oxytocin could be administered 2 hours or more after misoprostol when necessary.

The primary outcome measure was successful induction, defined as vaginal delivery within 24 hours from the start of induction. Induction failure was defined as failure to achieve cervical dilatation of 4 cm or more after oxytocin infusion. Other variables concerning the conduct of labor and delivery, and neonatal outcome, were assessed. Data was analyzed by using chi- square and student t test with P=0.05.

Results

Study group included fifty nine subjects, which were similar in mean age, gravidity, parity, height, and indications for induction (Table1). Thirteen (43.3%) of the orally treated and 12(41.4%) of the vaginally treated women were nulliparous. The mean gestational age at entry was 38.4±1.9 weeks for orally treated subjects and 38.7±1.8 weeks for vaginally treated subjects. The median preinduction Bishop score was 2 in each group (range 0-5). The median Bishop score before redosing was 3 in the oral group (range 0–7), and 7 in the vaginal group (range 0–6).

Table 1. Demographics and indications for labor induction

Characteristics	Oral misoprostol (n = 29)	Vaginal misoprostol (n = 30)
Age (y)	27.8 ± 5.8	28.8 ± 6.6
Gravidity	2.9 ± 1.9	3.0 ± 2.1
Parity	1.4 ± 1.6	1.4 ± 1.5
Height (in)	65.5 ± 3.7	62.8 ± 4.
Indications for induction		
Oligohydramnios	4 (13.8%)	3 (10.0%)
Preeclampsia	8 (27.6%)	9 (30.0%)
Prelabour rupture of membranes	2 (6.8%)	1 (3.3%)
Diabetes mellitus	2 (6.8%)	2 (6.6%)
Postdate	10 (34.5%)	9 (30.0%)
Abnormal fetal heart rate tracing	0	2(6.6%)
Fetal growth restriction	0	3 (10.0%)
Chronic hypertension	2(6.8)	1 (3.3%)

More subjects in the oral treatment group than in the vaginal treatment group delivered vaginally within 24 hours,17 of 25(68.0%)and 14 of 23(60.9%) respectively. The mean (±SD) intervals from start of induction to delivery, regardless of route, were 1240±845 minutes and 1381±802 minutes for orally and vaginally treated subjects, respectively (Table 2).

Table 2. Time to delivery

	Oral misoprostol (n = 29)	Vaginal misoprostol (n = 30)	P
Mean time from induction to delivery (min)	1240.3± 845.0	1381.1± 802.1	.06
Mean time from induction to vaginal delivery (min)	1240.3± 845.0	1381.1 ± 802.1	.10
Vaginal delivery within 24 hours	17/25 (68%)	16/25 (64%)	.14

Twenty five women (86.2%) who received oral misoprostol and 26(86.7%) women who received vaginal misoprostol had vaginal deliveries. Nine caesarean sections were performed, of which four were induced orally and five vaginally. Indications for cesarean section were similar, including failed induction, arrest disorders, uterine hyperstimulation and fetal distress in both groups.

Subjects who received oral misoprostol required a median (SD) of 1.9±1.2, doses and vaginally treated women required a mean of 2.3±1.3 doses (P=.04). Oxytocin augmentation was used in 14(49.6%) and 16 (53.3%) orally and vaginally treated subjects, respectively. Among orally and vaginally treated women, indications for oxytocin augmentation were failure to enter active labor after the maximum number of doses, failure to enter active labor after more than 24 hours of cervical ripening, inadequate uterine activity in the active phase of labor, adequate cervical ripening with fewer than the maximum number of doses of misoprostol, spontaneous rupture of membranes and abnormal FHR tracings.

Uterine tachysystole occurred in three (10.3%) orally treated and one (3.3%) vaginally treated subjects. Two cases of hyperstimulation were in the oral treatment group (Table 3). Abnormal CTG occurred in 5(17.2%) orally treated subjects and 3(10.0%) vaginally treated subjects.

Table 3. Complications

	Oral misoprostol (n =29)	Vaginal misoprostol (n =30)	P
Tachysystole	3 (10.3%)	1 (3.3%)	.06
Hyperstimulation	2 (6.9%)	0	.25
Nausea or vomiting	2 (6.8%)	0	

There was no difference in frequency of presence of meconium-stained amniotic fluid between groups. Side effects of misoprostol were seldom reported (Table3). Neonatal outcome also did not differ between groups (Table 4).

Table 4. Neonatal outcome

	Oral misoprostol (n = 29)	Vaginal misoprostol (n = 30)
Apgar score <7		
1 minute	2	3
5 minutes	2	4
Resuscitation	9 (31%)	10 (33.3%)
NICU admission	5 (17.2%)	4 (13.3%)

NICU = neonatal intensive care unit.

Discussion

For cervical ripening and labor induction trend towards oral misoprostol is growing[6,7,8,9,10]. In this study we found that giving 100 µg of oral misoprostol every 4 hours was as effective as vaginal administration of 25µg every 4 hours, with no difference in maternal or neonatal outcome. There was shorter induction - delivery mean interval and higher tendency towards vaginal delivery within 24 hours in subjects treated with 100-µg doses of oral misoprostol, although it was not statistically significant.

In previous studies[5,9] 50µg of oral misoprostol given every 4 hours was associated with longer intervals to delivery compared with vaginal misoprostol. Another group of researchers compared repeated doses of 100µg of oral misoprostol with repeated doses of 100 µg of vaginal misoprostol and found greater efficacy but more maternal and neonatal complications like FHR and uterine contraction abnormalities with vaginal administration of such a high dose[8]. Repeated 200µg oral doses of misoprostol were associated with greater efficacy but higher rates of uterine tachysystole and hyperstimulation when compared with repeated vaginal doses[6,10]. These

results suggest that, although oral misoprostol is effective for labor induction, but an intermediate dosing regimen should be used to minimize side effects. More women in the oral group received oxytocin, although it was not statistically significant[11].

In our study uterine hyperstimulation was more frequent in women treated with 100µg doses of oral misoprostol, although the abnormalities did not differ significantly from those of women who received vaginal misoprostol.

The timing of hyperstimulation was found to be nearly one hour after ingestion of misoprostol, coincided with peak maternal serum levels after oral administration of misoprostol[12] and it is likely that the dose might have been excessive for those women.

In no instances did the detection of hyperstimulation lead to immediate cesarean delivery. The effectiveness in terms of failed induction and safety were comparable between intravaginal and oral misoprostol[13].

Conclusion

Our limited data supports the use of 100µg doses of oral misoprostol for preinduction cervical ripening and labor induction. That approach offers convenience, higher patient acceptance, ease of administration, and reduction of nursing interventions. The potential exists for overdose with oral misoprostol[14] so we believe further studies on safety with larger numbers of women need to be conducted before we advocate routine oral misoprostol.

References

1. Sanchez-Ramos L, Kaunitz AM, Del Valle GO, Delke I, Schroeder PA, Briones DK. Labor induction with the prostaglandin E1 methyl analogue misoprostol versus oxytocin: A randomized trial. Obstet Gynecol 1993;81:332–6.
2. Wing DA, Rahall A, Jones MM, Goodwin TM, Paul RH. Misoprostol: An effective agent for cervical ripening and labor induction. Am J Obstet Gynecol 1995;172:1811–6.
3. Sanchez-Ramos L, Kaunitz AM, Wears RL, Delke I, Gaudier FL. Misoprostol for cervical ripening and labor induction: A meta-analysis. Obstet Gynecol 1997;89:633–42.
4. Mundle WR, Young DC. Vaginal misoprostol for induction of labor: A randomized controlled trial. Obstet Gynecol 1996;88: 521–5.
5. Wing DA, Ham D, Paul RH. A comparison of orally administered misoprostol with vaginally administered misoprostol for cervical ripening and labor induction. Am J Obstet Gynecol 1999;180:1155–60.
6. Ngai SW, To WK, Lao T, Ho PC. Cervical priming with oral misoprostol in pre-labor rupture of membranes at term. Obstet Gynecol 1996;87:923–6.
7. Windrim R, Bennett K, Mundle W, Young DC. Oral administration of misoprostol for labor induction: A randomized controlled trial. Obstet Gynecol 1997;89:392–
8. Toppozada MK, Anwar MYM, Hassan HA, El-Gazaerly WS. Oral or vaginal misoprostol for induction of labor. Int J Gynaecol Obstet 1997;56:135–9.
9. Bennett DA, Butt K, Crane JMG, Hutchens D, Young DC. A masked randomized comparison of oral and vaginal administration of misoprostol for labor induction. Obstet Gynecol 1998;92: 481–6.
10. Adair CD, Weeks JW, Barrilleaux S, Edwards M, Burlison K, Lewis DF. Oral or vaginal misoprostol administration for induction of labor: A randomized, double-blind trial. Obstet Gynecol 1998;92: 810–3.
11. Shetty A, Livingstone I, Acharya S, Rice P, Daniellan P, Templeton A. Oral misoprostol(100 microg) vs. vaginal misoprostal (25 microg) in term labor induction: a randomized comparison. Acta Obstet Gynecol Scand. 2003 Dec;82(12):1103-6.
12. Nopdonrattakoon L. A comparison between intravaginal and oral misoprostol for labor induction: a randomized controlled trial. J Obstet Gynaecol Res. 2003 Apr;29(2):87-91.
13. 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.
14. Bennett BB. Uterine rupture during induction of labor at term with intravaginal misoprostol. Obstet Gynecol 1997;89:832–3.

Corrigendum:

The name of Dr. Muhammad Shafiq was wrongly printed in the article "Role of Intravenous Magnesium Therapy in Short Term Risk Factors of Acute Myocardial Infarction" published in Annals Vol. 12, No.3, Jul-Sep 2006 issue.