A Comparative Trial of Labor Induction with Misoprostol Versus Oxytocin: Safety and Efficacy

DOĞUM İNDÜKSİYONUNDA MİSOPROSTOL VE OKSİTOSİNİN ETKİNLİK VE EMNİYET AÇISINDAN KARŞILAŞTIRILMASI

Argun TUĞRAN, MD,[a] Sebiha ÖZKAN, MD,[b] İzzet YÜCESOY, MD,[b] Birol VURAL, MD,[b] Semih ÖZEREN, MD,[b] Aydın ÇORAKÇI, MD,[b] Gülseren YÜCESOY, MD[b]

[a]Clinic of Obstetrics and Gynecology, Kırklareli Hospital, KIRKLARELİ
[b]Department of Obstetrics and Gynecology, Kocaeli University School of Medicine, KOCAELİ

Abstract

Objective: To compare the safety and efficacy of vaginally administered misoprostol with that of intravenous oxytocin infusion in term pregnant women undergoing labor induction.

Materıal and Methods: The study was designed as a prospective one in which term pregnant women were assigned to misoprostol (n= 44) and oxytocin groups (n= 46) in order to induce labor. Misoprostol subjects received 50 µg misoprostol tablets vaginally located in the posterior fornix and the same dose repeated 4 times, while participants assigned to oxytocin 4 hourly to a maximum dose of 20 mU/min group were managed according to the low standart oxytocin infusion protocol. Sociodemographic properties, Bishop scores, indications of labor induction, time interval till active labor process, time interval till delivery, interval till vaginal delivery, labor induction success rates, delivery route, intrapartum complications, apgar scores of 2 study groups were compared.

Results: Bishop score was significantly lower in misoprostol group ($p< 0.05$) while intrapartum variables such as time interval till active labor process, time interval till delivery, interval till vaginal delivery, route of delivery and labor induction success rates, apgar scores did not differ significantly between 2 groups (p= 0.11), (p= 0.40), (p= 0.39), (p= 0.65), (p= 0.65) (p= 0.6). Uterine hyperstimulation was demonstrated to be significantly increased in misoprostol group (p= 0.04).

Conclusıon: Misoprostol appears as an efficient agent of cervical ripening and subsequent labor induction that is also inexpensive and practical in use. Uterine hyperstimulation is a well-recognized adverse effect of misoprostol to be aware of during labor induction.

Key Words: Misoprostol; oxytocin; labor, induced

Özet

Amaç: Doğum indüksiyonu yapılan term gebelerde vaginal misoprostol ve intravenöz oksitosin uygulamalarını etkinlik ve emniyet açısından karşılaştırmak.

Gereç ve Yöntemler: Çalışma prospektif olarak tasarlandı. Doğum indüksiyonu uygulanacak term gebeler, misoprostol (n= 44) ve oksitosin (n= 46) grupları olmak üzere iki gruba ayrıldı. Misoprostol grubunda, 50 mg'lik misoprostol tabletleri arka vaginal fornikse yerleştirildi, aynı doz 4 saatte bir, toplam doz maksimum 200 mg olacak şekilde tekrarlandı. Oksitosin grubundaki hastalara ise standart 20 mU/dk. düşük doz oksitosin infüzyonu protokolü uygulandı. İki grup sosyodemografik özellikler, Bishop skorları, doğum indüksiyonu endikasyonları, aktif doğum eylemi gelişene kadar olan zaman aralığı, doğuma kadar olan zaman aralığı, vaginal doğuma kadar olan zaman aralığı, doğum indüksiyonu başarı oranları, doğum şekli, intrapartum komplikasyonlar. Apgar skorları açısından karşılaştırıldı.

Bulgular: Bishop skoru misoprostol grubunda anlamlı olarak düşük bulundu ($p< 0.05$). Aktif doğum eylemi gelişene kadar olan zaman aralığı, doğuma kadar olan zaman aralığı, vaginal doğuma kadar olan zaman aralığı, doğum şekli ve doğum indüksiyonu başarı oranları gibi intrapartum değişkenler ve Apgar skorları iki grup arasında anlamlı olarak farklı bulunmadı (p= 0.11), (p= 0.40), (p= 0.39), (p= 0.65), (p= 0.65) (p= 0.6). Uterin hiperstimülasyon misoprostol grubunda anlamlı olarak artmış olarak saptandı (p= 0.04).

Sonuç: Misoprostol, servikal olgunlaştırma ve doğum indüksiyonunda etkin olmanın yanı sıra ucuz ve pratik kullanımlı bir ajandır. Uterin hiperstimülasyon ise misoprostol ile doğum indüksiyonunda dikkat edilmesi gereken önemli bir yan etkidir.

Anahtar Kelimeler: Misoprostol; oksitosin; doğum indüksiyonu

Turkiye Klinikleri J Gynecol Obst 2007, 17:361-367

Geliş Tarihi/*Received:* 26.05.2007 **Kabul Tarihi/*Accepted:*** 19.07.2007

Yazışma Adresi/*Correspondence:* Sebiha ÖZKAN, MD
Kocaeli University School of Medicine
Department of Obstetrics and Gynecology, KOCAELİ
sozkan1972@yahoo.com

Artificial initiation of uterine contractions prior to spontaneous onset resulting in progressive cervical dilatation and effacement with subsequent delivery is called as labor induction.[1] It may be required in a variety of

maternal and fetal indications. 3-25% of all live births are reported to be pharmacologically or mechanically induced.[2,3]

Synthetic oxytocin has been the most frequently used induction agent in viable pregnancies since 1953 it has been first described.[1] In spite of its favourable safety and efficacy profiles, success depends mainly on Bishop score which involves cervical dilatation, effacement, consistency, position and the station of the presenting fetal part.[4,5] Failure of oxytocin induction leading to increased rates of abdominal delivery with inadequately ripened cervices and other associated risks related with fetal well-being led to looking for alternative labor induction agents.

Within a variety of cervical ripeners, yet none seems to be the ideal agent nor the regimen. Among prostaglandins, the most frequently preferred cervical ripening agents PGE1, PGE2 and PGF2α have been investigated extensively. They act through changing cervical stroma by means of recruitment of both hyaluronic acid and extracellular matrix destructing component. Those result in altered cervical submucosal water content and subsequent cervical effacement. Significant uterotonic activity of prostaglandins creates a potent synergy in cervical ripening and labor induction.[6,7]

PGE2 (dinoprostone) has been shown to increase Bishop score, decrease induction-delivery interval, decrease additional oxytocin amount and decrease the rates of induction failure. However due to expensiveness and requirement for refrigeration in use of PGE2, misoprostol that is a synthetic PGE1 analogue has gained widespread acceptance as a labor induction and cervical ripening agent.[8-10] Several meta-analyses have compared misoprostol with other labor induction agents.[11-14] Misoprostol which is first described as a gastric cytoprotective agent is cheap, available as tablet, can be broken and administered orally, vaginally or sublingually.[2,9] It further requires no refrigiration and does not restrict patient mobility in early labor. The ideal dose and regimen still remain to be determined. On the other hand, uterotonic activity may result in potentially excessive and irreversible adverse effects such as uterine rupture, intrapartum fetal death, meconium passage, neonatal acidemia and increased cesarean section rates due to fetal distress which require further randomized controlled studies.[15]

In this study, we aimed to compare safety and efficacy of vaginally aministered misoprostol with that of intravenous continous oxytocin infusion in term and postterm pregnant women undergoing labor induction.

Material and Methods

This prospective survey was carried out at Kocaeli University, School of Medicine, Department of Obstetrics and Gynecology after approval by Local Ethics Committee of the university. Inclusion criteria consisted of gestational week of 38-42 weeks, singleton pregnancy with vertex presentation, reassuring fetal heart pattern, presense of maternal, fetal or elective indication for labor induction, a Bishop score ≤5, no active labor with regular uterine contractions, no cephalopelvic disproportion or previous uterine surgery. Patients with antepartum hemorrhage, abnormal fetal heart pattern, history of asthma, cardiopulmonary, renal or hepatic disease, glaucoma, known hypersensitivity to prostaglandins, active labor and grandmultiparity were excluded. Ninety pregnant women with informed consents fulfilling the inclusion criteria were recruited.

Study subjects were assigned to misoprostol (n= 44) or oxytocin groups (n= 46). The cases of misoprostol group received 50 μg misoprostol (1/4 of 200 μg Cytotec® tablet, Searle GD, Chicago) vaginally located in the posterior fornix and the same dose repeated 4 hourly to a maximum dose of 200 μg (4 doses). Oxytocin infusion was not begun in misoprostol patients in whom the active labor could not be initiated. Oxytocin group received controlled continous intravenous infusion initiated at 2 mU/min, stepped up by 2 mU/min every 15 minutes until the optimal uterine contraction pattern was achieved or to a maximum dose of 20 mU/min and maintained at the same rate until delivery. Labor was induced following determination of Bishop score and cervical examination was repeated with 4 hour intervals. Continous fetal heart

rate monitorization was done for the assesssment of fetal well-being. Amniotomy was performed at cervical dilatation of 5 cm.

Active labor was defined as recording minimum 3 uterine contractions of 40-50 seconds duration in 10 minutes.

Labor induction was accepted to be successful if vaginal delivery occured in 24 hours of induction while unsuccessful if active labour could not be initiated.

Fetal tachycardia, bradycardia, late decelerations or loss of variability determined by electrocardiotocography were reported to be fetal distress.

Tachysystole was defined as at least 6 contractions in 10 minutes for 2 consecutive 10 minutes. A single contraction or more of at least 2 minutes was determined as uterine hypertonus. Tachysystole or hypertonus associated with nonreassuring fetal heart tracings was named as uterine hyperstimulation.[16] In case of those intrapartum complications, changing maternal position to the left lateral side, nasal oxygen administration, sublingual use of 10 mg of nifedipine, using saline to flush vaginal misoprostol or stopping oxytocin infusion were undertaken.

Age, parity, gestational age, Bishop score, route of delivery, time interval to initiation of active labor, time interval to delivery, time interval to vaginal delivery, intrapartum complications such as uterine hyperstimulation, fetal distress and meconium-stained amnios, apgar scores, admission to neonatal intensive care unit (NICU), fetal birth weights were recorded. Two study groups were compared by means of those variables in order to determine safety and efficacy of misoprostol and oxytocin for labor induction.

Statistical analysis was done by SPSS programme (Chicago IL 11). Continous and categoric variables were assessed by Student's test and Chi square tests respectively. $P < 0.05$ was considered to be statistically significant.

Results

A total of 90 pregnant women were involved in the study, 44 cases in misoprostol group and 46 patients in oxytocin group. Age, gestational age, parity did not seem to be significantly different between 2 groups while Bishop score was found to be significantly higher in oxytocin group (Table 1).

In misoprostol group, indication for labor induction was elective in 20 cases (45.5%), premature rupture of membranes in 11 cases (25%), preeclampsia in 4 cases (9.1%) and oligohydramnios in 2 cases (4.5%), maternal indication in 2 cases (4.5%), intrauterine fetal growth restriction in 1 patient (2.3%), postterm pregnancy in 1 case (2.3%) and multiple reasons in 3 cases (6.8%). In the other study group, indication for labor induction was elective in 24 cases (52.2%), premature rupture of membranes in 9 cases (19.6%), preeclampsia in 5 cases (10.9%), postterm pregnancy in 2 cases (4.3%) and oligohydramnios in 2 cases (4.3%), intrauterine fetal growth restriction in 1 patient (2.2%) and multiple reasons in 3 cases (6.5%).

Labor induction in pregnant women of 40 weeks of gestation without maternal and fetal risk factors was defined to be elective. Postterm pregnancy was accepted to be pregnancies over 41 weeks of gestation. Maternal indications were maternal cardiac disease in 1 case and gestational diabetes mellitus in another subject. Indications of

Table 1. Baseline characteristics of misoprostol and oxytocin groups are demonstrated.

	Misoprostol (n= 44)(mean ± SD)	Oxytocin (n= 46)(mean±SD)	p
Age	25.3 ± 6.0	24.9 ± 4.8	0.50
Gestational age (weeks)	39.4 ± 1.2	39.5 ± 1.1	0.60
Gravidity	2.2 ± 1.9	1.7 ± 0.9	0.55
Parity	0.9 ± 1.5	0.5 ± 0.8	0.65
Bishop score	1.9 ± 0.8	4.5 ± 0.8	< 0.001*

*p< 0.05 Statistically significant

labor induction for two groups were not found to be differing significantly (p> 0.05).

Twelve pregnant women of misoprostol group were given 2 doses of misoprostol (100 μg) while 29 women received only 1 dose of misoprostol. In 3 patients 4 doses were required. Mean misoprostol amount to be given was calculated to be 68.18±24.33 μg. In oxytocin group maximum oxytocin infusion rate was 20 mU/min and mean oxytocin dose that was used was determined to be 6250.3±1562.8 mU.

Induction-active labor interval, induction-delivery interval, induction-vaginal delivery interval were calculated in 41 cases of misoprostol group and 44 cases of oxytocin group since active labor could not be initiated in 3 misoprostol cases and 2 oxytocin cases. Those time intervals did not seem to be significantly different between 2 groups (p= 0.11, p= 0.40, p= 0.39 respectively) (Table 2).

Labor induction was successful in 35 cases of misoprostol group (79.5%) and in 39 cases of oxytocin group (84.7%) (p= 0.65). Induction was unsuccessful in 3 cases of misoprostol (6.8%), in 2 cases of oxytocin (4.3%) (p= 0.60). Induction was repeated next day and of 3 cases of the first group 2 were delivered abdominally while 1 was delivered vaginally. Of 2 oxytocin patients 1 was delivered vaginally while the other one underwent cesarean section. Of 41 misoprostol cases in whom active labor was achieved by induction, 35 were delivered vaginally (85.4%) while 6 had to be delivered abdominally due to fetal distress (14.6%). Of 42 oxytocin cases who underwent active labor 39 were delivered vaginally (88.6%) while 5 were delivered by cesarean section (11.4%). Success of induction and route of delivery did not seem to be significantly different (p= 0.65) (p= 0.65) (Table 3).

Intrapartum variables were as follows:

In misoprostol group uterine hyperstimulation developed in 8 patients (18.2%). Fetal distress and meconium stained amnios were diagnosed in 6 and 4 cases respectively (13.4%, 9.1%). In oxytocin group those variables were found to be 4.3%, 10.9% and 4.3% respectively. Uterine hyperstimulation was demonstrated to be significantly higher in misoprostol group (p= 0.04) while the others did not differ significantly (p= 0.7, p= 0.3) (Table 3).

Table 2. Intrapartum variables are demonstrated.

	Misoprostol (n= 44)(mean ± SD)	**Oxytocin (n= 46)(mean±SD)**	**p**
Dose (misoprostol)(μg)	68.18 ± 24.33		
Dose (oxytocin)(mU)		6250.3 ± 1562.8	
Induction-active labor interval (min)	179.75 ± 102.87	151.36 ± 48.93	0.11
Induction-delivery interval (min)	498.90 ± 230.36	459.09 ± 209.55	0.40
Induction-vaginal delivery interval (min)	489.28 ± 221.20	445.64 ± 214.47	0.39

*p< 0.05 Statistically significant

Table 3. Induction success rates and intrapartum complications are demonstrated.

	Misoprostol (n= 44) (n,%)	**Oxytocin (n= 46) (n,%)**	**p**
Successful labor induction	35 (79.5%)	39 (84.7%)	0.65
Unsuccessful labor induction	3 (6.8%)	2 (4.3%)	0.60
Uterine hyperstimulation	8 (18.2%)	2 (4.3%)	0.04*
Fetal distress	6 (13.4%)	5 (10.9%)	0.7
Meconium-stained amnios	4 (9.1%)	2 (4.3%)	0.3

*p< 0.05 Statistically significant

Apgar scores, admission to neonatal intensive care unit and fetal birth weights were not shown to be significantly different (p= 0.7, p= 0.6, p= 0.11).

Discussion

A growing amount of clinical data points out that misoprostol (Prostaglandin E1 analogue) appears to be a reasonable alternative cervical ripener and an effective pharmacological agent to be used in labor induction with adequate maternal and fetal safety.[5,7,12,17-23] Primary outcomes of the present study were time interval to delivery, time interval to vaginal delivery, success rates of labor, delivery route and maternal-neonatal complications related with the agent used in labor induction.

Sanchez-Ramos et al[21] compared vaginally administered misoprostol (50 μg 4 hourly) with oxytocin infusion in 129 term pregnant subjects. Time interval to delivery was found to be 11 hours and 18 hours in misoprostol and oxytocin groups respectively, significantly decreased in misoprostol group while tachysystole was reported to be 3 times higher with misoprostol administration. Delivery route and incidence of maternal-fetal complications were not determined to be significantly different. In our study, time interval to delivery was demonstrated to be 8.4 hours and 7.7 hours in misoprostol and oxytocin groups respectively. Shorter time interval to delivery in oxytocin group although not significantly different in our cases was attributed to higher initial Bishop scores of oxytocin group subjects. In spite of unfavorable cervical findings in misoprostol group, similar time interval to delivery with oxytocin cases points out that misoprostol may be an effective alternative agent for labor induction. Another similar finding with this study was 4 times increased uterine hyperstimulation following misoprostol administration in our study. No other parameter was determined to be significantly differing in our cases either.

Kramer et al[22] randomized 130 term pregnant women into 2 groups in order to compare the efficacy and safety of misoprostol (4 hourly 100 μg) with that of oxytocin infusion for labor induction. Time interval to delivery was significantly shortened in misoprostol group while uterine hyperstimulation was detected to be occuring more frequently in the same group. Delivery route and maternal-neonatal complications did not differ significantly. All data of this study were consistent with our findings except shorter time interval to delivery in our oxytocin cases although not significant. This finding was again assigned to higher Bishop scores of our oxytocin cases.

A meta-analysis regarding misoprostol administration in labor induction in comparison with oxytocin, PGE2 and combined oxytocin and PGE2 concluded that time interval to delivery, time interval to vaginal delivery, rates of abdominal delivery and additional oxytocin dose requirement were decreased while rates of induction success and uterine hyperstimulation frequency were increased significantly in misoprostol group.[12] Maternal-neonatal complications did not differ significantly. Cumulative misoprostol dose used in those studies included in this meta-analysis was determined to be ranging between 50-600 μg since different misoprostol regimens were chosen (25 μg two hourly-a single dose of 100 μg). Two different studies of Wing et al[24,25] included in this meta-analysis compared two different regimens of misoprostol with PGE2 administration (50 μg 3 hourly, maximum 6 doses of misoprostol versus PGE2, 25 μg 3 hourly, maximum 8 doses of misoprostol versus PGE2). 25 μg misoprostol use was demonstrated to be associated with decreased risk of uterine hyperstimulation but unfortunately increased time intervals to delivery and vaginal delivery. Optimal dose and regimen regarding misoprostol use in labor induction still remain obscure.

Escudero Contreras[7] carried out a randomized trial in 123 term pregnant women in order to compare efficacy and safety of misoprostol (50 μg 4 hourly to a maximum dose of 600 μg) and oxytocin in labor induction. Uterine hyperstimulation was determined to be more frequent in misoprostol group although fetal complications and delivery route did not seem to be significantly differing in the same group. Interval to vaginal delivery was shown to be significantly shorter in oxytocin group consistent with findings of Chuckaro and Huffak-

ker[26] while some other studies demonstrated shorter interval to vaginal delivery in misoprostol group in comparison with oxytocin, placebo or PGE2.[12,22] This difference was explained by an increased oxytocin sensitivity in study subjects of former investigators.

Compelling data point out that misoprostol use is clearly associated with higher frequency of uterine contraction abnormalities and subsequently higher likelihood of uterine rupture.[4,15] Yet with misoprostol the main clinical concern appears to be the significantly increased risk of uterine hyperstimulation which is demonstrated to be dose-related. We should be cautious that this powerful uterotonic drug should be absolutely used in a hospital setting with continous maternal-fetal monitoring and maximum care under supervision of trained health care providers. On the other hand, in spite of higher incidence of uterine hyperstimulation with misoprostol use, acute intervention due to fetal distress and meconium passage were not found to be significantly more frequent in our cases consistent with literature data.[4,7] This may be attributed to close monitorization and immediate diagnosis of uterine hyperstimulation that was resolved as soon as detected by undertaking correct measures.

As a conclusion, misoprostol seems to be an effective agent for cervical ripening and labor induction altough the optimum dose and regimen still remain to be controversial. It is demonstrated to be a viable alternative technique of labor induction since it is efficaous, easily administered, not expensive, stable at room temperature, needs no refrigeration with a longer shelf-life. Misoprostol does not require mixing, tubing or infusion pumps like oxytocin that is an advantage to reduce drug errors. It allows ambulation in early labour and avoidance of an intravenous access and subsequent better patient acceptibility. Although uterine hyperstimulation is the main concern with misoprostol use, close maternal-fetal monitorization and timely undertaken measures would prevent devastating adverse effects during labor induction and increase tolerability of the drug by both the mother and fetus. Further randomized controlled studies are mandatory in order to finally conclude about safety and the ideal dose and regimen of misoprostol use in labor induction.

REFERENCES

1. Durodola A, Kuti O, Orji EO, Ogunniyi SO. Rate of increase in oxytocin dose on the outcome of labor induction. Int J Gynecol Obstet 2005;90:107-11.
2. Ferguson JE, Head BH, Frank FH, et al. Misoprostol versus low-dose oxytocin for cervical ripening: a prospective, randomized, double masked- trial. Am J Obstet Gynecol 2002;187:273-80.
3. Elhassan EM, Mirghani OA, Adam I. Misoprostol vs. oxytocin for induction of labor. Int J Gynecol Obstet 2005; 91:254-5.
4. Wing DA, Fassett MJ, Guberman C, Tran S, Parrish A, Guinn D. A comparison of orally administered misoprostol to intravenous oxytocin for labor induction in women with favorable cervical examinations. Am J Obstet Gynecol 2004;190:1689-96.
5. Lemancewicz A, Urban R, Skotnicki MZ, Kapiuk A, Urban J. Uterine and fetal Doppler flow changes after misoprostol and oxytocin therapy for induction of labor in postterm pregnancies. Int J Gynecol Obstet 1999;67:139-45.
6. Riskin-Mashiah S, Wilkins I. Controversies in labor management: Cervical ripening. Obstet Gynecol Clin 1999;26: 243-57.
7. Escudero F, Contreras H. A comparative trial of labor induction with misoprostol versus oxytocin. Int J Gynecol Obstet 1997;57:139-43.
8. Goldberg AB, Greenberg B, Darney PD. Misoprostol and pregnancy. N Engl J Med 2001;344:38-46.
9. Wing DA, Ham D, Paul R. A comparison of orally administered misoprostol with vaginally administered misoprostol for cervical ripening and labor induction. Am J Obstet Gynecol 1999;180:1155-60.
10. Elhassan E, Mirghani O, Adam I. Intravaginal misoprostol versus dinoprostone as cervical ripening and labor-inducing agents: Int J Gynaecol Obstet 2004;85:285-6.
11. Mozurkewich E, Horrocks J, Suzanne D, et al. The misoPROM study: A multicenter randomized comparison of oral misoprostol and oxytocin for premature rupture of membranes at term. Am J Obstet Gynecol 2003;189:1026-30.
12. Sanchez-Ramos L, Kaunitz AM, Wears RL, Delke I, Gaudier FL. Misoprosol for cervical ripening and labor induction: A metaanalysis. Obstet Gynecol 1997;89:633-42.
13. Sanchez-Ramos L, Kaunitz AM. Misoprostol for cervical ripening and labor induction: A systematic review of the literature. Clin obstet Gynecol 2000;43:475-88.
14. Butt KD, Bennett KA, Crane JMG, Hutchens D, Young DC. Randomized comparison of oral misoprostol and oxytocin for labor induction in term prelabor membrane rupture. Obstet Gynecol 1999;94:994-9.
15. Alfirevic Z. Oral misoprostol for induction of labour. Cochrane Database Syst Rev 2001;2:CD001338.

16. American College of Obstetricians and Gynecologists. Fetal heart rate patterns: Monitoring, interpretation, and management. Washington (DC): The College 1995. Technical bulletin No:207.
17. Wing DA, Paul RH. A comparison of different dosing regimens of vaginally administered misoprostol for preinduction cervical ripening and labor induction. Am J Obstet Gynecol 1996;175:158-64.
18. Bennett KA, Butt K, Crane JM, Hutchens D, Young DC. A masked randomized comparison of oral and vaginal administration of misoprostol for labor induction. Obstet Gynecol 1998;92:481-6.
19. Adair CD, Weeks JW, Barrilleaux S, Edwards M, Burlison K, Leis DF. Oral or vaginal misoprostol administration for induction of labor: A randomized, double-blind trial. Obstet Gynecol 1998;92:810-3.
20. Wing DA, Park MR, Paul RH. A randomized comparison of oral and intravaginal misoprostol for labor induction. Obstet Gynecol 2000;95.905-8.
21. Sanchez-Ramos L, Kaunitz AM, DelValle GO, Delke I, Schroeder PA, Briones DK. Labor induction with prostaglandin E1 methyl analogue misoprostol versus oxytocin: a randomized trial. Obstet Gynecol 1993;81:332-6.
22. Kramer RL, Gilson GJ, Morrison DS, Martin D, Gonzales JL, Qualls CR. A Randomized Trial of Misoprostol and Oxytocin for Induction of labour: Safety and Efficacy. Obstet Gynecol 1997;89:387.
23. Stitely ML, Browning J, Fowler M, Gendron RT, Gherman RB. Outpatient cervical ripening with intravaginal misoprostol. Obstet Gynecol 2000;96:684-8.
24. Wing D, Rahal A, Jones M, Goodwin M, Paul R. Misoprostol: An effective agent for cervical ripening and labor induction. Am J Obstet Gynecol 1995;172:1811.
25. Wing DA, Jones MM, Rahal A, Goodwin TM, Paul RH. A comparison of misoprostol and prostaglandin E2 gel for preinduction cervical ripening and labor induction. Am J Obstet Gynecol 1995;172:1804.
26. Chuck FJ, Huffaker BJ. Labor induction with intravaginal misoprostol versus iIntracervical prostaglandin E2 gel: Randomized comparison. Am J Obstet Gynecol 1995;173: 1137-42.