ORIGINAL
PROF-1690

INDUCTION OF LABOUR

COMPARISON OF ORAL MISOPROSTOL WITH VAGINAL MISOPROSTOL FOR CERVICAL RIPENING

DR. GHAZALA NASREEN, FCPS
Department of Gynecology
Military Hospital, Rawalpindi

DR. ABEERA CHOUDRY, FCPS, FRCOG.
Department of Gynecology
Military Hospital, Rawalpindi

DR. MALIK AMJAD YASIN, MCPS, FCPS
Department of Surgery
Military Hospital, Rawalpindi

ABSTRACT... Objective: To determine the efficacy and safety of stepwise oral misoprostol with vaginal misoprostol for cervical ripening for induction of labour. **Study design:** Interventional Quasi - Experimental study. **Setting and duration:** The study was of 15 months (April to 30 June) duration conducted at Obstetrics and Gynaecology department Military Hospital Rawalpindi. **Subjects and methods:** 100 females between 37-42 weeks of gestation were randomly divided into two groups 1and 2. Patients in group -1 assigned to the stepwise oral misoprostol arm received 50 µg initially followed by 100 µg every 04 hours upto maximum 04 doses ; group-2 assigned to the vaginal misoprostol arm received 25 µg every 04 hours up to maximum 04 doses. Subsequent doses of misoprostol were withheld if adequate uterine activity ($\geqslant$ 3 contractions in 10 minutes) or a Bishop score $\geqslant$ 8 had been achieved, or active labour had begun. The main outcomes were the interval from first misoprostol dose to delivery and mode of delivery. Patients were also monitored for adverse events. **Results:** There was no difference in the average interval from the first dose of misoprostol to delivery in the oral (21.1 ± 7.9 hrs) and vaginal (21.5 ±11.0 hrs, p = NS) misoprostol groups. 9 patients in the oral group (18%) and 16 patients in the vaginal group (32%) underwent caesarean section ($p<0.05$). There were no significant differences in the occurrence of tachysystole, hypertonus, hyperstimulation or neonatal outcome between two groups. **Conclusions:** Oral misoprostol appears to be as effective as vaginal misoprostol for cervical ripening with a low incidence of hyperstimulation, no increase in side effects, and is associated with a lower cesarean section rate.

Key words: Misoprostol, Cervical ripening, Labour induction.

INTRODUCTION

Induction of labour has merit as a therapeutic option when the benefits of delivery outweigh the risks of pregnancy. Lack of adequate cervical ripening is a known obstacle to successful labour induction and expeditious delivery[1]. Obstetricians use a variety of agents and methods to ripen the uterine cervix, achieve a shorter induction to delivery interval, and potentially lower the cesarean section rate. One of the most widely used agents for cervical ripening is misoprostol, a synthetic methyl ester of prostaglandin E1 approved for the prevention and treatment of gastric ulcers associated with the use of non steroidal anti-inflammatory drugs. Since the early 1990s, misoprostol has found increasing interest by Obstetricians and Gynaecologists. Because of its uterotonic and cervical ripening activity, wide-ranging off-label uses have been introduced for misoprostol[2]. The manufacturer of misoprostol to date did not seek for approval for obstetric indications; in the opposite, warning statements were published in medical journals[3].

Misoprostol is rapidly absorbed orally[4] and, although not formulated for parenteral use, can also be administered sublingually[5], rectally[6], and vaginally. It is compared to other preparations of prostaglandins and does not require refrigerated transport or storage[7]. It has the potential for providing increased patient satisfaction because of its noninvasive route of administration. Moreover, the possibility of misplacement is eliminated. These characteristics make it particularly suitable for use in developing countries.

Vaginal, as well as oral misoprostol administration has been used for cervical ripening for induction of labour, but the optimal dose of oral misoprostol has not been established[8]. In general, higher doses of oral misoprostol are associated with improved efficacy but higher rates of hyperstimulations and maternal side effects than vaginal misoprostol[9,11].

Previous studies have shown rapid absorption of oral misoprostol with peak plasma concentration at 34 ± 17 minutes and a nadir at 120 minutes. In contrast, vaginal misoprostol peaks at 80 ± 27 minutes, and declines slowly[12].

Based on pharmacokinetics, previously published regimens and the incidence of side effects. It is hypothesized that stepwise dosing of oral misoprostol (50µg followed by 100 µg) would be as effective for cervical ripening as vaginal misoprostol in the ACOG approved dose of 25µg every 4 hours, without increasing the rates of hyperstimulation.

MATERIAL AND METHODS

This was an interventional Quasi - Experimental study conducted in Obstetrics and Gynaecology department, Military Hospital, Rawalpindi which is a tertiary care teaching hospital. Total duration of the study was 15 months from 1st April 2007 to 30 June 2008. A total of 100 patients were included in the study with 50 patients in each Group1 and 2. Sampling technique was Non-probability and purposive.

INCLUSION CRITERIA

Only multiparous patients with singleton pregnancy between 37 and 42 weeks of gestation were included.

1. Patients requiring induction of labour due to obstetric/medical reasons.
2. Patients with Bishop Score between 3 to 6 (two groups were matched for Bishop Score).
3. Cephalic presentation and reassuring fetal heart rate.
4. Approximate fetal weight between 2.5 kg-4.0 kg.

EXCLUSION CRITERIA

1. All Patients with severe systemic illness like uncontrolled Diabetes mellitus, preeclampsia, cardiac, renal or hepatic disease, intrauterine death, fetal anomaly and hypersensitivity to misoprostol or prostaglandin analogue.
2. Patients with any contraindication to induction and vaginal delivery eg cephalopelvic disproportion, malpresentation, fetal compromise, no reassuring fetal heart rate pattern, previous scar and ante partum hemorrhage. Patients below 18 or above 35 years of age.

DATA COLLECTION PROCEDURE

Study was started after taking approval from ethical committee of the hospital. Patients with singleton pregnancy between 37-42 weeks of gestation (by dates and confirmed by ultrasound) requiring induction of labour due to obstetrical and medical reasons like post date pregnancy, PROM, , oligohydramnios, controlled PIH, GDM, who met the inclusion criteria were included in the study and assessed through structured Performa.

These patients were admitted in the maternity ward after detailed history and examination (both systemic and vaginal). Ultrasonography and admission CTG was done, baseline haematological and biochemical investigations were sent. After written and informed consent, patients were divided into two groups (group-1 and group-2) on the basis of a computer- generated table of random numbers. Patients in group -1 assigned to the stepwise oral misoprostol arm received 50 microgram initially followed by 100 microgram every 04 hours upto maximum 04 doses; group-2 assigned to the vaginal misoprostol arm received 25 microgram every 04 hours up to maximum 04 doses. All women had strict and regular monitoring of fetal heart rate, uterine contractions and Bishop Score. Partogram was maintained. CTG was done before and after the dose of misoprostol and then intermittently during labour. Subsequent doses of misoprostol were withheld if adequate uterine activity ($\geqslant$ 3 contractions in 10 minutes) or a Bishop Score $\geqslant$ 8 had been achieved, or active labour had begun. If needed, oxytocin was initiated 4 hours after the last misoprostol dose. Amniotomy was used liberally when required.

Patients were monitored and documented for uterine contractions tachysystole, hyper stimulation syndrome, nausea, vomiting and diarrhea and other unwanted side effects. Tachysystole was defined as > 5 contractions in 10 minutes for 2 consecutive 10 minutes periods. Hyper tonus was defined as a single contraction lasting more than 2 minutes. Hyper stimulation syndrome was defined as tachysystole or hyper tonus with non reassuring fetal heart rate changes (late decelerations, variable decelerations, tachycardia or reduced variability). Mode of delivery, need for caesarean delivery were recorded.

The demographic data of patient's age, parity, gestational age, indications for inductions, and the following outcomes were measured, recorded and

compared.

1. Interval between first misoprostol dose and delivery.
2. Rate of vaginal deliveries.
3. Incidence of tachysystole, hypertonus and hyper stimulation of uterus.
4. Rate of caesarean section.
5. Maternal side effects like nausea, vomiting, diarrhea.
6. Neonatal outcomes (Apgar score<7, meconium passage, admission to neonatal ICU).

DATA ANALYSIS

Data was analyzed by using SPSS version 11. Relevant descriptive statistics; frequency, rate and percentage was computed for presentation of qualitative outcomes like parity, indications for induction, Bishop score, vaginal deliveries, cesarean section, hyper tonus, tachysystole, hyper stimulation, maternal side effects, (nausea, vomiting, diarrhea) and neonatal outcome (APGAR<7, meconium passage admission to NICU). Quantitative variables like age, gestational age, time interval between induction and delivery etc. was presented as mean ± standard deviation.

Independent sample t test was used to compare age, gestational age, time interval between induction and delivery among two groups. Chi-Square test was used for comparing parity, indications for induction, Bishop Score, vaginal deliveries, cesarean section, hyper tonus, tachysystole, hyper stimulation, maternal side effects (nausea, vomiting, diarrhea) and neonatal outcome (APGAR < 7, meconium passage, admission to NICU). P ⩽ 0.05 was considered statistically significant.

RESULTS

Table-I. Base Line Demographics.

Characteristics	Oral misoprostol (n=50)	Vaginal misoprostol (n=50)	P-value
Maternal age (yrs)	28.1 ± 6.7	27.2 ± 6.4	P=NS
Gestational age (wks)	38.8 ± 1.9	39.1 ± 1.8	

The groups were similar with respect to age, gestational age, Bishop Score at entry.

The indications for induction are shown in Table-II. and were similar between both groups. The most common indications were postdates and hypertension.

Table-II. Indications for induction.

Indication	Oral misoprostol (N=50)	Vaginal misoprostol (N=50)	P-value
Postdates	16 (32%)	19 (38%)	P>0.05 NS
Hypertension	14 (28%)	13 (26%)	
Diabetes	5 (10%)	3 (06%)	
Oligohydraminos	4 (08%)	4 (08%)	
Others	11 (22%)	11 (22%)	

There was no difference in the average interval from the first dose of misoprostol to delivery in the oral (21.1 ± 7.9 hrs) and vaginal (21.5 ±11.0 hrs, p = NS) misoprostol groups. Considering the women who delivered vaginally, there was no difference in the average interval from first dose to vaginal delivery between oral (19.3 ± 6.7 hrs) and vaginal (18.0 ± 8.3 hrs, p = NS) groups. Among the women who delivered vaginally; there was no difference in the number that delivered within 12 hours and within 24 hours between the two groups (Table III).

Table-III. Time intervals to delivery.

Characteristics	Oral misoprostol (N=50)	Vaginal misoprostol (N=50)	P-value
1st dose to delivery (hrs)	21.1 ± 7.9	21.5 ± 11	P>0.05 NS
1st dose to vaginal delivery (hrs)	19.3 ± 6.7	18.0 ± 8.3	

The mean number of misoprostol doses given was 1.84 ± 0.8 in the oral group, and 1.55± 0.7 in the vaginal group (p < .01) The mean interval between the first and second doses of misoprostol was 4.8 ± 1.8 hours in the oral group versus 4.5± 0.8 hours in the vaginal group (p = NS

). Ten (10%) women made it to a Bishop score of ⩾ 8. The most common indication for withholding a subsequent dose was adequate contractions (56%) or active labor (31%). Oxytocin augmentation was started in 34(68%) women in the oral group, and in 29 (58%) women in the vaginal group (p =NS).

Table-IV. Mode of Delivery.

Characteristics	Oral misoprostol (N=50)	Vaginal misoprostol (N=50)	P-value
Vaginal deliveries	41 (82%)	34 (68%)	P < 0.05
Caesarean section	9 (18%)	16 (32%)	P < 0.05

The mode of delivery differed significantly between groups Table-IV. 9 patients in the oral group (18%) and 16 patients (32%) in the vaginal group underwent caesarean section (p <0.05). The indications for caesarean delivery are shown in Table –V.

Table-V. Characteristics of caesarian deliveries.

Indication	Oral misoprostol (N=9)	Vaginal misoprostol (N=16)	P-value
Failure to progress	6 (66%)	8 (49.6%)	P>0.05 NS
NRFHT*	2 (22.2%)	6 (37.2%)	
Others	1 (11.1%)	2 (12.4%)	

** non-reassuring fetal heart*

There were no significant differences in the indications between caesarean deliveries between the two groups. The number of women in each study arm that received only 1 dose of misoprostol before cesarean section differed significantly,11.1% in the oral vs 68.2% in the vaginal arm (p < .01), as majority of the women in the vaginal arm did not receive the second dose because they had achieved adequate uterine activity (⩾ 3 contractions in 10 minutes).

There were no significant differences in the occurrence of tachysystole, hyper tonus, and hyper stimulation between two groups Table -VI. Of the 4 cases of hyper stimulation syndrome only one women needed urgent delivery by caesarean section.

Table-VI. Maternal Outcomes and Side effects.

	Oral misoprostol (N=50)	Vaginal misoprostol (N=50)	P-value
Tachysystole	8 (16%)	9 (18%)	P>0.05 NS
Hyper tonus	2 (4%)	3 (6%)	
Hyper stimulation syndrome	2 (4%)	2 (4%)	
Nausea vomiting	7 (14%)	8 (16%)	
Diarrhea	1 (2%)	1 (2%)	

Non-reassuring fetal heart rate pattern that needed urgent delivery were noted in 4 (8%) of the women in the oral group and 8 (16%) of the women in the vaginal group. Of these 2/4 and 6/8 underwent caesarean delivery. Treatment side effects and delivery complications were similar between the two groups.

There were no differences in neonatal outcomes (Table-VII) except in APGAR Score < 7 at one minute which were more frequent in the vaginal group(14% vs 4%, p <0.05).

Table-VII. Neonatal Outcomes.

	Oral misoprostol (N=50)	Vaginal misoprostol (N=50)	P-value
APGAR score <7			
At 1 min	3 (6%)	7 (14%)	<.05
At 5 min	0	1	NS
Meconium passage	4 (8%)	5 (10%)	NS
Admission to NICU	5 (10%)	6 (12%)	NS

DISCUSSION

The hunt for the ideal agent, timing, and dosage interval to convert an unfavorable cervix to one receptive to delivery is an ongoing process. Attention has focused on prostaglandins as effective pharmacologic adjuncts to

induction. Prostaglandin is an agent that has been shown to have utility in promoting cervical ripening and labor initiation. Dinoprostone (PGE_2) is currently the only medication specifically approved by the Food and Drug Administration for this purpose. Although effective, these agents are expensive and require refrigeration. Because of these issues, the search for alternatives of more cost effective cervical ripening has continued. One agent that has become intensely investigated is misoprostol, a PGE_1 analogue.

Misoprostol has been approved for the treatment of peptic ulcers. Initial studies attested to misoprostol's uterotonic abilities, and intravaginal application was successfully used to terminate first and second trimester pregnancies[15-16]. The first investigations using misoprostol in cervical ripening and cervical induction came from South America. Subsequent studies showed intravaginal misoprostol comparing favorably with other commonly used induction agents, including prostaglandins and oxytocin[17-18]. Misoprostol compares favorably with the currently approved agent dinoprostone in expense and storage requirements. The optimal dosing regimen, timing, and route of administration remain the focus of ongoing research. Although vaginal application of misoprostol has been validated as a reasonable means of induction, there is patient resistance to the digital exams necessary for placement of the agent. We designed this randomized trial to compare the safety and effectiveness of vaginal misoprostol with oral misoprostol for induction of labor.

However, others reported that intravaginal administration of misoprostol is associated with a shorter induction to delivery interval, lower number of doses, and lower oxytocin use[19]. We could not demonstrate this difference probably because of lower dose. Generally, the 50-mcg dose results in a shorter induction to delivery interval and a higher rate of vaginal delivery after one dose. However, a vaginal dose of 25 mcg is often recommended as the more prudent dose for labor induction because it is associated with a lower incidence of uterine hyper stimulation. We also used this dose in our study. In the large UK multicentric trial initial dose of 50ugm was used but in our study we used 25 ugm . Our rate of hyper stimulation was 2% compared to 6 % in the large multicentric trial[21]. It is also comparable to the 50-mcg dose in achieving delivery within 24 hours[22]. Doses higher than the 50 mcg have been associated with an increased risk of serious complications[23].

In the literature, the interval of administration of misoprostol ranged from every 3 to 6 h. However, because of the possible risk of tachysystole, many centers use 4- to 6-h dosing intervals in their protocol. We also followed this protocol. In 1996, Ngai et al[22]. Investigated the effectiveness of oral misoprostol as a cervical-priming agent for patients presenting with prelabor rupture of membranes at term and suggested that oral misoprostol is an effective agent for this group of patients. Similar results were published by Sanchez-Ramos et al. in 1997 and Shetty et al[23] in 2002. Case reports were published with regard to the risk of uterine rupture during induction of labor with misoprostol[24]. However, the safety profile of misoprostol use was demonstrated in the study by Bique et al 25. who used it on a group of grand multiparous women with no significant adverse maternal or neonatal outcome. However, vigilance should be exercised in these cases, as emphasized by the American College of Obstetricians and Gynecologists Bulletin[26]. In study by Jenice et al from Canada vaginal route was associated with lesser induction to delivery interval , whereas in our study no difference was observed . This could be attributable to lower dose 25 ug vaginal in our study. Jenice at al used 50ugm for both oral and vaginal routes. Like their study there was less dosing in vaginal route majority of patients required only one dose.

The purpose of my study was to find out the effectiveness and safety of a novel dosing regimen of oral misoprostol (50µg followed by 100 µg) compared with the standard regimen of vaginal (25 µg) misoprostol every 4 hours.

Our study has demonstrated that stepwise oral misoprostol appears to be as effective as vaginal misoprostol for cervical ripening before induction of labor. The average interval from first dose to vaginal delivery was similar between two groups, and the same number of women in each group achieved vaginal

delivery in 24 hours. There was a low incidence of hyper stimulation in both groups (4% p = NS) , comparable to a generally accepted incidence of hyper stimulation of 7% with vaginal administration[26].

We found that stepwise oral misoprostol to be well tolerated , with no increase in maternal side effects compared with vaginal misoprostol. There was also a trend towards more fetal safety in the oral arm. Perhaps the most significant finding of our study is the lower cesarean section rate in the women who received the oral regimen .Detailed analysis revealed the difference in the number of misoprostol doses administered before delivery .The majority of the patients in the vaginal arm received only 1 dose of misoprostol for ripening because they were found to be contracting $\geqslant$ 3 times in 10 minutes when the next dose was due . Probably the patients tolerated the initial 50 g oral misoprostol dose better than the 25 µg vaginal dose . Although the later provided adequate uterine activity, it may paradoxically have been less effective in cervical ripening , as excess uterine contractions prevented further dosing . Probably the initial 50 µg oral dose prepared the cervix and the uterus to tolerate further doses resulting in higher rate of vaginal delivery. Other hypothesis to explain the lower cesarean section rate in the oral group include a dose related or bioavailability effect, more effective priming of the myometrium to endogenous/exogenous oxytocin.

Our protocol might be considered conservative in that it called for discontinuation of misoprostol after $\geqslant$3 uterine contractions in 10 minutes regardless of the strength of the contractions .While some patients with very mild contractions might safely benefit from additional misoprostol doses. It also had the limitations of lack of blindness like other studies with similar routes of administration[27].Caution is advised in extrapolating the data to high risk patients like previous scar and intrauterine growth restriction to make subgroup analysis.

REFERENCES

1. Mazouni C, Vejux N, Menard JP, Bruno A, Boubli L, d'Ercole C, Bretelle F. **Cervical preparation with laminaria tents improves induction-to-delivery interval in second- and third-trimester medical termination of pregnancy.** Contraception. 2009;80:101-4.
2. Mahjabeen, Khawaja NP, Rehman R. **Comparison of oral versus vaginal misoprostol for mid-trimester pregnancy termination.** J Coll Physicians Surg Pak. 2009;19:359-62.
3. Behrashi M, Mahdian M. **Vaginal versus oral misoprostol for second-trimester pregnancy termination: a randomized trial.** Pak J Biol Sci. 2008;11:2505-8.
4. Abbassi RM, Sirichand P, Rizvi S. **Safety and efficacy of oral versus vaginal misoprostol use for induction of labour at term.** J Coll Physicians Surg Pak. 2008;18:625-9.
5. Hill JB, Thigpen BD, Bofill JA, Magann E, Moore LE, Martin JN Jr. **A randomized clinical trial comparing vaginal misoprostol versus cervical Foley plus oral misoprostol for cervical ripening and labor induction.** Am J Perinatol. 2009 ;26:33-8.
6. Bricker L, Peden H, Tomlinson AJ, Al-Hussaini TK, Idama T, Candelier C, Luckas M, Furniss H, Davies A, Kumar B, Roberts J, Alfirevic Z. **Titrated low-dose vaginal and/or oral misoprostol to induce labour for prelabour membrane rupture: a randomised trial.** BJOG. 2008;115:1503-11.
7. Powers BL, Wing DA, Carr D, Ewert K, Di Spirito M. **Pharmacokinetic profiles of controlled-release hydrogel polymer vaginal inserts containing misoprostol.** J Clin Pharmacol. 2008;48:26-34.
8. Rasheed R, Alam AA, Younus S, Raza F. **Oral versus vaginal misoprostol for labour induction.** J Pak Med Assoc.2007 ;57:404-7.
9. Cheung PC, Yeo EL, Wong KS, Tang LC. **Oral misoprostol for induction of labor in prelabor rupture of membranes (PROM) at term: a randomized control trial.** Acta Obstet Gynecol Scand. 2006;85:1128-33.
10. Alfirevic Z, Weeks A. **Oral misoprostol for induction of labour.** Cochrane Database Syst Rev. 2006.19; CD001338.
11. Dodd JM, Crowther CA. **Misoprostol versus cervagem for the induction of labour to terminate pregnancy in the second and third trimester: a systematic review.** Eur J Obstet Gynecol Reprod Biol. 2006 ;125:3-8.

12. Capilla Montes C, Bermejo Vicedo T. **Efficacy and safety of misoprostol in obstetrics.** Farm Hosp. 2005 ;29:177-84.

13. Coln I, Clawson K, Hunter K, Druzin ML, Taslimi MM. **Prospective randomized clinical trial of inpatient cervical ripening with stepwise oral misoprostol vs vaginal misoprostol.** Am J Obstet Gynecol. 2005;192:747-52.

14. Langenegger EJ, Odendaal HJ, Grové D. **Oral misoprostol versus intracervical dinoprostone for induction of labor.** Int J Gynaecol Obstet. 2005;88:242-8.

15. Muzonzini G, Hofmeyr GJ. **Buccal or sublingual misoprostol for cervical ripening and induction of labour.** Cochrane Database Syst Rev. 2004. 18; :CD004221.

16. Grimes DA, Smith MS, Witham AD. **Mifepristone and misoprostol versus dilation and evacuation for midtrimester abortion: a pilot randomised controlled trial.** BJOG. 2004;111:148-53.

17. Farah LA, Sanchez-Ramos L, Rosa C. **Randomized trial of two doses of the prostaglandin E1 analog misoprostol for labor induction.** Am J Obstet Gynecol 1997; 177:364–369.

18. Sanchez-Ramos L, Kaunitz AM, Wears RL. **Misoprostol for cervical ripening and labor induction: a meta-analysis.** Obstet Gynecol 1997; 89:633–642.

19. Wing DA, Tran S, Paul RH. **Factors affecting the likelihood of successful induction after intravaginal misoprostol application for cervical ripening and labor induction.** Am J Obstet Gynecol 2002; 186:1237–1240.

20. Majoko F, Nystrom L, Lindmark G. **No benefit, but increased harm from high dose (100 mcg) misoprostol for induction of labour: a randomized trial of high vs. low (50 mcg) dose misoprostol.** J Obstet Gynaecol 2002; 22:61614–61617.

21. Opdonrattakoon L. **A comparison between intravaginal and oral misoprostol for labor induction: a randomized controlled trial.** J Obstet Gynaecol Res 2003; 29:87–91.

22. Goldberg AB, Greenberg MB, Darney PD. **Misoprostol and pregnancy.** N Engl J Med 2001; 344:38–47.

23. Friedman MA. **Manufacturer's warning regarding unapproved uses of misoprostol.** N Engl J Med 2001; 344:61.

24. Zieman M, Fong SK, Benowitz NL. **Absorption kinetics of misoprostol with oral or vaginal administration.** Obstet Gynecol 1997; 90:88–92.

25. Tang OS, Schweer H, Seyberth HW. **Pharmacokinetics of different routes of administration of misoprostol.** Hum Reprod 2002; 17:332–336.

26. Khan RU, El-Refaey H. **Pharmacokinetics and adverse-effect profile of rectally administered misoprostol in the third stage of labor.** Obstet Gynecol 2003; 101:968–974.

27. Dallenbach P, Boulvain M, Viardot C, Irion. **Oral misoprostol or vaginal dinoprostol for labour induction.** Am J Obstet Gynecol 2003; 188:162-7.

Article received on: 17/08/2010 Accepted for Publication: 27/01/2011 Received after proof reading: 16/05/2011

Correspondence Address:
Dr. Ghazala Nasreen, MBBS, FCPS.
Consultant Gynecologist,
Combined Military Hospital,
Skardu 4600, Pakistan.
drghazalanasreen@yahoo.com
dramjidyasin@yahoo.com

Article Citation:
Nasreen G, Yasin MA, Choudry A. Efficacy and safety of stepwise oral misoprostol with vaginal misoprostol for cervical ripening in induction of labour. Professional Med J Apr-Jun 2011;18(2): 181-188.

PREVIOUS RELATED STUDIES

Maimoona Hafeez, Waseem Talib, Saadia Siddique. Induction of labour; comparison of efficacy of different methods. Professional Med J Mar 2007; 14(1): 144-152.

Misbah Kausar Javaid, Samia Hassan, Tayyaba Tahira. Management preterm rupture of the membranes at term; induction of labour compared with expectant. Professional Med J Jun 2008; 15(2): 216-219.

Tayyiba Wasim, Saqib Siddiq. Comparison of prostaglandin E2 with misoprostol for induction of labour at term. Professional Med J Sep 2008; 15(3): 344-34.