SECOND TRIMESTER PREGNANCY;
ORAL VERSUS VAGINAL MISOPROSTOL FOR TERMINATION

ORIGINAL
PROF-1742

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ABSTRACT:... Objective: To compare clinical efficacy and side effects of oral misoprotol with vaginal misoprostol for termination of second trimester pregnancy. **Design:** Interventional Quasi experimental. **Setting:** Gynae Unit III, Liaquat University Hospital, Hyderabad. **Period:** 1st March 2006 to 31st August 2006. **Methodology:** Sixty patients were selected with thirty in each group i.e thirty for oral route (group A) and thirty for vaginal route(group B). The patients included in this study were those having singleton pregnancy with gestational age between 12 to 26 weeks requiring termination of pregnancy. A dose of 100ug to 200ug was used with maximum of 1200ug in each group of patients. **Results:** The subjects of either group were similar with respect to mean age, height, weight, parity, gestational age and pre induction Bishop Score. The success rate in group A was 94.4% as compared to group B was 86.8%. intra uterine death was the commonest indication in both groups found in 46.7% women of vaginal misoprostol group and 50% women of oral misoprostol group. Surgical evacuation was needed in 36.7% women of oral misoprostol group and 16.7% women of vaginal misoprostol group. **Conclusions:** The present study shows misoprostol to be effective for mid trimester abortions, both orally and vaginally, the later route is preferable because it requires lesser doses and produces a shorter induction – abortion interval. However safety data are needed to guide the route choice and well designed studies are necessary.

Key words: Second Trimester Pregnancy, Misoprostol, Termination.

INTRODUCTION

Miscarriage or abortion is variously defined as the expulsion or extraction of fetus (embryo) weighing less than 500g and equivalent to approximately 20-22 weeks gestation (WHO 1977) or as termination before 24 weeks of gestation with no evidence of life[1]. According to World Health Organization (WHO), approximately 50 million pregnancies are terminated each year[2], emphasizing the need of safe and effective way for making it a global issue for the gynecologist and the patient. Mid trimester abortion are of great importance as the risk to the patient are so much higher than first trimester procedures[3]. Many maternal and fetal conditions exist in which there is a need to terminate pregnancy before patient goes into the spontaneous labor. Various indications for termination of pregnancy are fetal demise, risk to the pregnant woman, such as severe pre eclampsia, eclampsia, renal disease and uncontrolled gestational diabetes. Severe fetal congenital anomalies, intrauterine infection such as rubella, premature rupture of membranes, malignant diseases and other medical disorders like severe heart diseases[4,5,6,7].

Termination of pregnancy during second trimester has always been a difficult task and a matter of great controversy due to unripe cervix at this stage8. Different methods have been tried for mid trimester pregnancy termination with variable results.

Two options for termination of pregnancy are surgical evacuation and medical methods of termination[8,9]. Surgical evacuation has benefits of relieving psychological trauma and avoiding prolonged hospital stay but requires surgical skills and anaesthesia. On the other hand different abortificients are used for the medical termination of pregnancy such as oxytocin and prostaglandins.

Various prostaglandins have been widely used for pregnancy termination depending on the gestational

age, availability, cost as well as the preference of obstetricians and gynaecologists[10]. Medical termination takes longer time and causes more pain than surgical evacuation but patient satisfaction is high and misoprostol is effective and safe option for those women who avoid surgical treatment[11].

Prostaglandins like PG E2, PG E1 and PG F2 alpha are frequently used. Among them efficacy of PG E1 (cytotec) is tested throughout world including Pakistan. Misoprotol is a synthetic prostaglandin E1 analogue that was originally being used for treatment and prevention of peptic ulcer, but now it is being used for a wide range of indications in obstetrics and gynaecology and one of them is medical termination of pregnancy in second trimester[12].

Misoprostol (cytotec) was first used in obstetrics in 1993 for labour induction[13], since then it has been used for different indications like ripening of cervix and control of postpartum hemorrhage[14]. Its use is associated with reduced blood loss, time duration and also rate of complications[15]. It has proved to be well absorbed after oral, sublingual, vaginal and rectal routes but best absorption has been seen through vaginal route[16] and most women prefer oral route[17]and clinical efficacy of sublingual route is poor as compared to vaginal route[18]. Cost effectiveness and easy administration are its main advantages[19].

These features make it ideal for use in third world countries, though the drug is not licensed for use in pregnant women but world wide it is being used in women for ripening of cervix[20].

The optimal dose of misoprostol for induction of labour in second trimester lies between 50ug to 1200ug. Higher dose may be needed to cause abortions early in the second trimester; where as lower dose may be sufficient late in the second trimester[21].

This study was conducted to see the efficacy of use of misoprostol for ripening of cervix. The use of misoprostal was compared with different routes (oral versus vaginal). The parameters which were taken into account for comparison were induction – delivery interval and use of additional oxytocin.

MATERIALS AND METHODS

This interventional Quasi experimental hospital based study was conducted at Gynae Unit III, Liaquat University Hospital, Hyderabad from 1st March 2006 to 31st August 2006. Sixty patients were selected with thirty in each group. Amongst them randomly, thirty were selected for oral route and thirty for vaginal route. The patients included in this study were those having singleton pregnancy with gestational age between 12 to 26 weeks requiring termination of pregnancy for intrauterine fetal demise and structural abnormalities not compatible with life, parity less than 4 and with no previous scar on uterus. Patients with known hypersensitivity to prostaglandins, liver disease and disturbed coagulation profile were excluded from the study.

After admission in the hospital the women fulfilling inclusion criteria were approached. Preformed proforma was used to collect the data after taking informed written consent from the patients. Hemoglobin percentage, platelet count and coagulation profile were checked and ultrasound was carried out. The dose of the drug was adjusted according to the gestational age and Bishop's score. The drug was repeated at 6 hours interval to maximum of 1200ug. Syntocinon infusion was used in cases where it was necessary. If the woman does not abort after the first course, same regimen was repeated 48 hrs after the start of the first dose of misoprotol.

Blood pressure, pulse rate, temperature and side effects were monitored every four hours. After expulsion of fetus, the products were examined and surgical evacuation of uterus preceded if required. Woman was discharged 24 hours after the abortion if no complication was noted.

Assessment of the median time to achieve abortion and unpleasant side effects were noted to see the efficacy acceptability and safety of misoprostol by either route. Frequency and percentages were calculated for all variables.

Chi square test was applied to compare these variables

between two groups and to test hypothesis at P<0.05 level of significance. Numeric response variables including age, parity, gestational age, dose used and induction to ripening time interval were presented by mean ± standard deviation and students t-test was applied to compare these variables between two groups at P< 0.05 level of significance.

RESULTS

A total 60 patients were included in the study. Of these 30 were randomly assigned to group A, who will receive orally and 30 in group B for vaginal administration of misoprostol. The subjects were similar with respect to mean age, parity, height, weight, gestational age and pre induction Bishop score.

A success noted more in group A (94.4%) as compared to group B (86.8%). Data revealed significant higher success rate in group A. Mean age of the women who underwent vaginal Misoprostol was 27.2± 4.55 years and of those who underwent oral Misoprostol group was 28.5±4.09 years. The difference of mean age between two groups was statistically insignificant (p=0.262). Mean gestational age of women who underwent vaginal Misoprostol was 22.6± 4.12 weeks and of those who underwent oral Misoprostol were 20.97±4.86 weeks.

Intrauterine death was the commonest indication for induction that was found in 14(46.7%) women of vaginal misoprostol group and 15(50%) women of oral misoprostol group. Missed abortion was the second commonest indication that was observed in 6 (20%) women of vaginal Misoprostol group and 7 (23.3%) women of oral Misoprostol group, this difference was also insignificant. Other indications were congenital anomaly, PIH eclampsia, chorio amnionitis, rupture membrane, HELLP syndrome, hydrops fetalis (Table-I).

Surgical evacuation was needed in 5 (16.7%) women of Group A and 11 (36.7%) women of Group B however, this difference of proportion regarding need of surgical evacuation between two groups was statistically insignificant (X^2=3.07, p=0.080).

There were four cases of failed induction (13.2%) in group B and one in group A (33.3%). Average time (hours) taken for induction to abortion in vaginal group was comparatively less than group B (35.4 ± 16.2), but statistically insignificant difference was observed.

Table-I. Comparison of indications of induction between two groups of termination of pregnancy

Indications	Route Misoprostol		P-value
	Vaginal (n=30)	Oral (n=30)	
Intrauterine death	14 (46.6%)	15 (50%)	0.796
Abortion/Missed abortion	6 (20%)	7 (23.3%)	0.754
Anencephaly	2 (6.6%)	1 (3.3%)	0.999
Congenital anomaly	1 (3.3%)	3 (10%)	0.612
Pregnancy induced hypertension	2 (6.6%)	3 (10%)	0.999
Eclampsia	2 (6.6%)	-	0.492
Others^	5 (16.6%)	2 (6.6%)	0.424

Mean dose required for complete induction in group A was 557.3 ± 213 ug and 726.7 ± 192.9 ug in group B. Data revealed significantly higher number of doses required in group B for complete induction.

Nausea and vomiting were noted more frequent in group A than group B (53.3% vs. 10%, p=0.030), diarrhea was slightly high in group B than group A (23.3% vs. 13.3%), however the difference was statistically insignificant (p=0.410) (Table-II).

Table-II. Comparison of side effects between two groups of termination of pregnancy

Side effects	Route of Misoprostol		P-value
	Vaginal (n=30)	Oral (n=30)	
Nausea/vomiting	3 (10%)	11 (53.3%)	0.030
Diarrhea	7 (23.3%)	4 (13.3%)	0.410
Lower abdominal pain	7 (23.3%)	3 (10%)	0.371
Headache	-	2 (6.7%)	0.492

Need of augmentation was required more in oral misoprostol group than vaginal Misoprostol group (16.7% vs. 3.3%, p=0.195), however this difference of proportion was statistically insignificant (Table-III).

Table-III. Comparison of complications between two groups of termination of pregnancy

Complications	Route of Misoprostol		P-value
	Vaginal (n=30)	Oral (n=30)	
Augmentations	1 (3.3%)	5 (16.7%)	0.195
Failed induction	1 (3.3%)	4 (13.2%)	0.999

DISCUSSION

The medical management of mid trimester pregnancy termination is centered on the use of prostaglandin compounds, other alone or in combination with either abortificient agent (e.g mifepristone) in recent years misoprostol a synthetic analogue of prostaglandin E1,has attracted attention as an effective and cost effective agent for the medical interruption in mid trimester pregnancy. The aim of this study was to determine efficacy and safety of two different routes oral versus vaginal for termination of second trimester pregnancy.

The success of induction depends upon cervical status at the start of induction process[22]. Bishop scoring system is most widely used for induction[23]. Patient included in the study for termination of pregnancy had poor Bishop score prior to induction i-e (0-5) comparable to the poor Bishop score observed in another study by Nazli Hossain[14].

Mean maternal age in this study was 27.98 years. In study conducted by Maymon et al[24]. Mean age was higher i.e 31 years. This difference might be due to the fact that termination of pregnancy was done only due to fetal anomalies which increase due to advancing maternal age. Mean gestational age was found 19 weeks and 20 weeks in study by Nazli Hossain[14], which is consistent with the present study.

The induction to abortion interval is an important aspect in termination of pregnancy. Longer time interval is associated with more pschycological trauma. Prolonged time also necessitates the use of intravenous hydration, increased analgesic requirement and use of augmentation oxytocin .Average time (hours) taken for induction to abortion in vaginal group was comparatively less than oral misoprostol group (35.46+16.3 VS 37.6+16.2) when compared to study of Ashok PW[25]. Priming to abortion interval was significantly shorter in the vaginal group compared with the oral group (23.3vs3.5 hours respectively)[26].

Another study showed that after pre-treatment with mifepristone , vaginal misoprostol (200mg) caused a significantly shorter induction abortion interval than when the same dose was given orally (15.2 hours v 32.0 hours, (P<0.05).However patient preferred the oral route because they felt it was more convenient[26].

Women in the oral group were more likely to experience nausea while vaginal administration of misoprostol may minimize the side effects experience by women[25]. Our study prove that nausea and vomiting was the most frequent side effect that was significantly high in oral misoprostol group than 5.3%vs 10%, (p =0.030), while those in vaginal group were more likely to complain of tiredness ,lower abdominal pain and diarrhea. These differences did not seem to affect women satisfaction with the route of misoprostol administration used.

Apart from this, common side effects which are more pronounced with the oral route of drug[27], Misoprostol is well absorbed through all route of administration. It appeared natural as well as convenient .We did not observe the unpleasant side effects like nausea vomiting and diarrhea with vaginal route. Bulgaho et al also reported virtually no side effects with intra vaginal doses of 50-200ug[28].Vaginal administration also allows the body to be exposed to more of the drug active metabolite .The peak plasma level after vaginal route of administration is achieved within 60-80 minutes.

Vaginal route is preferred in first and second trimester, oral route may be advisable in set ups with limited medical staffing[29,30].Cost effective of the drug is added advantage of the use of misoprostol. The cost

effectiveness is highly suitable for developing countries and it has been well recognized in developed countries too[31,32].

In Pakistan Hossain N and Somroo N had studied misoprostol in small number (30) of women for cervical ripening and induction of labour and they found misoprostol effective in all three trimester of pregnancy[14]. In above study we did not use any fixed dose regimen for Tab Misoprostol. The drug is quite new for use in our area so a cautious attitude is to be adopted. Most of the studies quoted in the reference have used fixed dose schedule of either 600 µg every 12 hours interval. Mean dose required for complete abortion was significantly higher in Group B than Group A (Vaginal 7267 µg vs. 557.3 µg oral).

The need for augmentation with oxytocin was the variable which was taken into consideration that was required more in oral misoprostol group than vaginal misoprostol group 16.7% vs. 3.3%. This was considered significant, as it required use of intravenous access.

CONCLUSIONS

This study suggests that oral administration misoprostol in an effective alternative to vaginal administrators in the context of medical abortion. Oral administration offers additional choice to women in particular those wishing to avoid vaginal administration. Women should however, be counseled about the increase prevalence of side effects with this route of administration.

REFERENCE

1. Grudzinskas JG. **Miscarriage, ectopic pregnancy and trophoblastic disease.** In: Edmonds DK, Dewhurst J, eds. Dewhurst's textbook of obstetrics and gynaecology for postgraduates. 6th ed. London: Blackwell Science. Publishing Group, 1999: 61-75.
2. Scott A, Glassier A. **Failed medical and surgical termination of pregnancy.** JOG 2002; 4:222-4.
3. **Operative procedures for therapeutic abortion.** In: Monaghan JM, Lopes T, Kaik R, Bonney V. Bonney's gynaecological surgery. 10th ed. London: Blackwell Publishers, 2004: 253-6.
4. Induction of labour "BCRCP" revised (serial online) 1999 April (cited 2002 Nov 2); 1, 2, 3: (10 screens). Available form http://www.Rep.bc.Ca/Guidelines/obstetrics/master%5B1%5D-OBI.
5. Pastorek II JG, Yankowitz J. **Maternal and fetal viral infections including listeriosis and toxoplasmosis.** In: James KD, Steer PJ, Weiner CP, Gonik B. High risk pregnancy management options. 2nd Ed. London: WB Saunders, 1999: 525-58.
6. Chia P, Chia H, Subramaniam R. **Failed medical and surgical termination of pregnancy.** JOG 2002; 4: 212-6.
7. Thomason JS S. **Elective induction of labour.** Why, when and how? JOG 1999: 1:20-5.
8. El-Refaey H, Rajasekar D, Abdullah M, Calder L, Templeton A. **Induction of abortion with mifepristone (RU 486) with oral and vaginal misoprostol.** N Eng 1 J Med 1995; 332: 983-7.
9. **Second trimester miscarriage.** In: Cambell S, Lees C. Obstetrics by ten teachers. 17th ed. London: Hodder Arnold, 2000: 263-71.
10. MacKenzie IZ. **Labor induction including pregnancy termination for fetal anomaly.** In: James DK, Steer PJ, Weiner CP, Gonik B (eds). High risk pregnancy management options. 2nd Ed. London: WB Saunders. 1999:1079-101.
11. Wagaarachchi PT, Ashok PW, Narvekar NN, Smith NC, Templeton A. **Medical management of late intrauterine death using a combination of mifepristone and misoprostol.** BJOG 2002; 109:443-7.
12. Hossain N, Soomro N, Umar A. **Medical management of second trimester fetal demise using misoprostol.** J Coll Physicians Surg Pak 2002;12:735-7.
13. Vimala N, Mittal S, Kumar S. **Sublingual misoprostol for pre abortion cervical repining in first-trimester pregnancy termination.** Contraception 2003; 67: 295-7.
14. Tang OS, Schweer H, Seyberth HW, Lee SW, Ho PC. **Pharmacokinetics of different routes of administration of misoprostol.** Hum Reprod 2002; 17:332-6.
15. Hossain N, Soomro N. **Use of misoprostol for cervical ripening and induction of labour.** Med Channel 2000; 6(3): 36-8.
16. Goldberg AB, Greenberg MB, Darney PD. **Misoprostol and pregnancy.** N Engl J Med 2001; 344: 38-47.

17. Mazhar SB, Imran R, Alam K. **Trial of extra amniotic saline infusion with oxytocin versus prostaglandin E2 pessary for induction of labour.** JCPSP 2003; 13: 317-20.

18. Bishop EJ. **Pelvic scoring for elective induction.** Obstet Gynaecol 1964; 24:266-8.

19. Maymon R, Sharon M, Reish O, Schneider D. Halperin R, Herman A. **Fetal abnormalities leading to termination of pregnancy. The experience at the Assaf Haroteh Medical Centre between the years 1999-2000.** Harefuah 2003; 142: 405-9, 488.

20. Ashok, P.W and Templeton A. **Randomised controlled study comprising oral and vaginal misoprostol for cervical priming prior to surgical termination of pregnancy.** BJOG: 2003, 110:1057-1061.

21. Nagai SW, Tang OS, HoPc. **Randomized comparison of vaginal (200mg every 3 hours) and oral (400mg every 3 hours). Misoprostol when combined with mifepristone in termination of second trimester pregnancy.** Hum Report 2000: 15; 2205-8.

22. Shetty A. Daniclian P. Templeton A. **Sublingual misoprostol for induction of labour at term.** Am J Obstet Gynaecol 2002; 186: 72-6.

23. Herabutya Y, O-Prasertswat P, **Second trimester abortion using intra vaginal misoprostol.** Int J Gynecol Obstet 1998; 60: 161-165.

24. Le Roux PA, Pahal GS, Hoffman L, Nooh R, El Rafey H, Rodeck Ch. **Second Trimester termination of pregnancy for fetal anomaly or death. Comparing mifepristone / misoprostol to gemeprosts.** Eur J obstetct Gynaecol Reprod Biol 2001; 95:53-4.

25. Carlan SJ, Blust D, O'Brien WF. **Buccal versus intra vaginal misoprostol administration for cervical ripening.** Am J Obstet Gynaecol 200; 186:229-33.

26. 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 dinoprostone.** BJOG: 2001; 108:1255-62.

27. Ashalatha Shetty, MRCOG, MRCP (Ireland), Peter Danielian, MD, MRCOG, and Allah Templeton, MD, FRCOG, **Sublingual misoprostol for the induction of labour at term.** AM J Obstet Gynaecol 2002; 186:72-6.

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