INTRODUCTION
Termination of Pregnancy (TOP), in our country is carried out only if there is a substantial risk of a fetus with serious congenital anomalies, intrauterine fetal death or in the presence of medical disorders that pose a real threat to the health or life of the mother.

Before the availability of misoprostol (a synthetic analogue of prostaglandins E₁), other prostaglandins such as prostaglandin E₂ and prostaglandin F₂ alpha (PGF₂α) were mostly used for second trimester terminations. These agents are efficacious but expensive, require refrigeration and needed higher doses, which is associated with side effects such as nausea, vomiting, diarrhea and fever in a high percentage of patients.¹,²

The abortifacient properties of misoprostol for second trimester termination have been reported in medical literature since 1993.³ Misoprostol is an inexpensive agent, can be stored at room temperature, stable for years and has few systemic effects.⁴

METHODOLOGY
This interventional quasi experimental study was conducted at the Department of Obstetrics and Gynaecology Unit-II, Fatima Jinnah Medical College/Sir Ganga Ram Hospital, Lahore, during a period of 14 months from August, 2003 to October, 2004. The study was approved by Institutional Committee.

In these days of financial constraints, misoprostol is an economical and effective abortifacient drug for second trimester pregnancy termination with shorter induction to abortion interval with few side effects.⁵ This agent is especially relevant for a country like ours because of scarce economic resources and high temperature.⁶ Misoprostol is well-absorbed by oral route, with peak plasma concentration achieved earlier and higher than vaginal administration, although the plasma concentrations are detectable for longer period by vaginal route.⁷,⁸ Although several studies have been carried out comparing misoprostol with other traditional methods of mid-trimester induction of labour but the optimal dosage and route of administration have not been delineated.⁹

The aim of the present study was to compare the efficacy of misoprostol by oral and vaginal route in similar dose for mid-trimester TOP in terms of induction-expulsion interval, need for surgical evacuation and failure of induction.

ABSTRACT
Objective: To compare the efficacy and safety of oral versus vaginal administration of misoprostol for second trimester pregnancy termination.

Study Design: Interventional, quasi experimental study.

Place and Duration of Study: The Department of Obstetrics and Gynaecology Unit-II, Fatima Jinnah Medical College /Sir Ganga Ram Hospital, Lahore, from August, 2003 to October, 2004.

Methodology: Sixty pregnant women at second trimester of gestation who were candidates for therapeutic termination of pregnancy were recruited for the study. Grandmultipara, women who had scarred uterus and history of hypersensitivity to prostaglandins were excluded. The subjects were assigned into two groups. Group 1 (n=30) had misoprostol orally, while the group 2 (n=30) received the drug by the vaginal route. Dosage regimen was similar in both groups that was 200 µg 4 hours apart till expulsion of fetus or maximum of upto 5 doses. Main outcome measures of the study were induction-expulsion interval, need for surgical evacuation and maternal complications.

Results: The mean induction-expulsion interval in the group 1 and 2 was 11.8±8.3 and 12.8±8.5 hours respectively, which was not different statistically. The process of expulsion was complete in 53.3% of subjects in both groups by misoprostol only, while 36.6% required surgical evacuation in oral group versus 33.3% in vaginal group. The rate of failed induction in groups 1 and 2 was 10% and 13.3% respectively. There was no reported case of nausea, diarrhea, headache, dizziness, shivering, pyrexia and hyperstimulation in both the groups. However, a case of vomiting (3.3%) was observed in the vaginal group.

Conclusion: Oral and vaginal misoprostol for second trimester pregnancy termination is equally effective and safe agent.


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A total of 60 women in their mid-trimester pregnancy, who were candidates for therapeutic TOP, were recruited in the study by non-probability convenient sampling technique. Those who were having uterine contractions, grandmultipara (parity five and above), scarred uterus or had hypersensitivity to prostaglandins were excluded. Written informed consent was taken in each case. All women had their blood group, hemoglobin estimation, coagulation profile and hepatitis B and C screening. One unit of blood was cross-matched.

The subjects were assigned into two groups. In group 1, 30 women were given misoprostol orally, while in group 2, equal number of women received misoprostol by vaginal route placed in posterior fornix. Dosage regimen was similar for both groups i.e. tablet misoprostol 200 µg 4 hours apart till expulsion of fetus or maximum upto 5 doses.

Regular monitoring of patients for blood pressure, pulse, temperature at hourly interval were carried out. Patients were observed for abdominal pain, uterine contractions and vaginal bleeding. Oxytocin infusion was given in those situations where process of expulsion did not start in spite of uterine activity and cervical dilatation to expedite the process of expulsion. Thirty units of oxytocin in 1 litre of normal saline were started at 10 drops/minute and increased at half hourly interval according to uterine contractions.

After abortion, the products of conception were inspected to confirm the complete expulsion. In cases of incomplete expulsion, surgical evacuation was carried out.

Patients were observed for maternal complications for 24 hours after expulsion and discharged subsequently.

Data was collected on pre-designed proforma in each case and analyzed by SPSS software version 10. Descriptive statistics was used for maternal age, gestational age and induction to expulsion interval and was calculated as mean±SD. The mean induction-expulsion interval in both the groups was compared. The student t-test was used as test of significance with p-value <0.05 as level of significance. For indications of induction and side effects of the drugs, proportions and percentages were calculated.

Complete expulsion, augmentation with oxytocin, need of surgical evacuation and failed termination was compared in both the groups; χ² was used as test of significance with p-value <0.05 as level of significance.

RESULTS

During the study period, 60 women were assigned into two groups. Group 1 received oral misoprostol, while in the group 2, misoprostol was administered vaginally. The groups were comparable with regard to age, parity, gestational age and indications for termination (Tables I and II).

The mean induction expulsion interval in the group 1 and 2 was 11.8±8.3 and 12.8±8.5 hours respectively, which was not different significantly (p>0.05). The mean dosage of misoprostol was 3.1±1.5 and 3.3±1.6 tablets (one tablet of 200 µg each) in oral versus vaginal protocol, which did not exhibit any statistically significant difference.

Complete expulsion was achieved with misoprostol in 16 (53.3%) patients in both groups. Augmentation with oxytocin was required in 3 (10%) cases of oral group versus 4 (13.3%) in vaginal group. However, the difference between the study groups did not reach statistically significance level. (χ²=0.162, df=1 p >0.05, Table III).

Surgical evacuation was carried out for retained products of conception in 11 (36.6%) cases of oral group versus 10 (33.3%) cases with vaginal protocol (χ²=0.07, df=1 p >0.05, Table III). Induction was failed in 3 (10%) cases of group 1 and 4 (13.3%) cases of group 2, which was also statistically insignificant (χ²=0.162 df=1, p >0.05, Table III).

Regarding maternal complications and side effects, there was not a single case of shivering, fever, nausea, diarrhea, dizziness, headache and hyperstimulation in both the groups. The only side effect noticed was vomiting in one patient (3.3%) of vaginal group.

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<tr>
<th>Table I: Demographic data of the study subjects.</th>
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<tr>
<td>Characteristics</td>
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<td>Maternal age (years)*</td>
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<td>Parity (range)</td>
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<td>Gestational age*(weeks)</td>
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*Data given as mean ± SD, n=Number of cases

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<th>Table II: Indications for termination of pregnancy in two groups.</th>
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<td>Indications (%) Group 1 Oral (n=30) Group 2 Vaginal (n=30) p-value</td>
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<tr>
<td>Fetal demise</td>
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<td>Structural anomaly</td>
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<td>Maternal reason (Medical grounds)</td>
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<th>Table III: Treatment outcome in the two groups.</th>
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<td>Outcome Group 1 Oral (n=30) Group 2 Vaginal (n=30) p-value</td>
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<tr>
<td>Complete expulsion</td>
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<td>Oxytocin required</td>
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<td>Evacuation</td>
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<td>Failed termination</td>
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DISCUSSION

The present study compares the oral and vaginal routes of administration of misoprostol for second trimester termination of pregnancy in local population. The study demonstrated that misoprostol is an effective and safe
drug for second trimester TOP. Both oral and vaginal routes for administration of the drug seems to be equally efficacious with no significant maternal complications.

In the present study, there was no significant difference in the induction-expulsion interval in both groups, a finding, which is similar to the study of Feldman et al. However, in the later study, the interval was longer as compared to this study in spite of the higher doses of misoprostol used in their study. This may be due to the different indications of TOP in both studies. Fetal demise was the main indication for termination in the present study. Second trimester pregnancy termination that is complicated by fetal demise is usually more predictable with a shorter induction-expulsion interval than that conducted when the fetus is alive, an observation revealed by Nagina et al. This could be due to the increased sensitivity of the uterus to prostaglandins and the release of tissue factors following fetal demise.

Bebbington et al., Dickinson and Ho et al. revealed a shorter induction-expulsion interval for vaginal route of the drug as compared to oral route for misoprostol. The reason for the difference in the results from this study may be due to the uneven allocation of patients, different indications for termination and different dosage schedule used in their studies. Ho et al. used mifepristone as a pre-induction agent and none of pregnancy in their study were terminated because of fetal demise or fetal anomalies, whereas in the present study pregnancies were terminated mainly because of fetal demise and structural anomalies.

Complete expulsion was achieved with misoprostol in 53.3% patients in both groups in the present study, while it was achieved in 78.2% by oral versus 86.2% in vaginal protocol in the study of Iqbal. Surgical evacuation was required in about 37% of cases in oral group versus 33% in vaginal group in this study, while Iqbal quoted the need of surgical evacuation in 21.4% in oral protocol versus 13.8% in vaginal protocol. The difference in the results could be due to higher dosage schedule as compared to this study, which also resulted in decreased failure rate in their study compared to present observation. Naz reported 12% failed induction by vaginal misoprostol comparable to our subjects of vaginal protocol, although the initial dose in their protocol was 400 µg, instead of 200 µg.

In the present study, no significant maternal side effects were noted in both groups. Vomiting was reported in one case (3.3%) of vaginal group. However, vomiting commenced after starting the oxytocin infusion, therefore, it may be due to the side effect of oxytocin. Javed reported nausea and vomiting in 4% of the vaginal protocol of the study subjects. Nausea and vomiting was much higher in the study of Iqbal, in addition to headache, fever and chills, reason of which could be comparatively higher dose.

Gilbert and Reid also reported no significant difference in side effects between both groups of oral and vaginal misoprostol. However, Bebbington et al. reported increased febrile morbidity in patients who received misoprostol by vaginal route. This may be due to high dose of the drug (400 µg) in their study. Dickinson et al. also noticed more side effects with higher dosage of vaginal misoprostol, while Kamal reported no significant difference between side effects of misoprostol while comparing vaginal with orovaginal route. There was not a single case of rupture of uterus in this study. Although, there are reports of rupture of uterus with misoprostol in the second trimester, it appears to be a less frequent event than with induction at term. The lower uterine segment has not thinned out to the extent as seen at term and the cervix does not need to be dilated as much to achieve expulsion of the fetus in second trimester. Therefore, the drug can be used safely for second trimester TOP. This data suggests that misoprostol can be considered for mid-trimester pregnancy termination. Both oral and vaginal routes are equally effective so oral route can be a convenient option as it will be preferable for patients as well as health care providers because it limits the number of vaginal examinations and the medication can be administered by the patient herself or by the nursing staff. Small sample size in this study was a limitation, therefore, large multicentre randomized control trials are needed before adopting routine use of misoprostol for second trimester TOP.

**CONCLUSION**

Misoprostol is an effective and safe agent so it may be used for second trimester termination of pregnancy. Both oral and vaginal routes of administration appear to be equally efficacious with no significant maternal complications in the studied patients.

**REFERENCES**


