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TERMINATION OF PREGNANCY;
COMPARISON OF SUBLINGUAL AND VAGINAL MISOPROSTOL IN SECOND TRIMESTER

DR. UZMA HUSSAIN, FCPS
Assistant Professor of Gynaecology & Obstetrics
Fatima Jinnah Medical College /
Sir Ganga Ram Hospital, Lahore

DR. FARZANA LATIF, FCPS
Senior Registrar of Gynaecology & Obstetrics
Fatima Jinnah Medical College /
Sir Ganga Ram Hospital, Lahore

DR. TEHSEEN AKHTER, FCPS
Registrar Gynaecology & Obstetrics
Fatima Jinnah Medical College /
Sir Ganga Ram Hospital, Lahore

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ABSTRACT... Objective: To compare the efficacy of vaginal misoprostal with that of sublingual misoprostol in 2nd trimester of pregnancy by comparing the induction-expulsion interval between two groups of patients induced with vaginal and sublingual misoprostol. **Study design:** Interventional, quasi experimental study. **Settings:** Obstetrics & Gynaecology Unit 1, Sir Ganga Ram Hospital, Lahore. **Duration of study:** Thirteen months from October 2006 to November 2007. **Subjects and Methods:** Sixty women at 12-26 weeks of gestation which were selected for termination of pregnancy were assigned into two groups. Thirty women received sublingual misoprostol and thirty women received vaginal misoprostol. Dosage regimen was tablet Misoprostol 200µg 4 hours apart till expulsion of fetus (maximum 5 doses). Main outcome measures were: 1. Induction-expulsion intervals 2. Maternal side effects 3. Fever 4. Nausea/vomiting 5.Diarrhea. **Results:** Mean induction-expulsion interval in vaginal group was 11.8±8.3 hours and in the sublingual group was 12.8±8.5 hours. Percentage of complete expulsion was 53.3% in both groups. Cases of failed induction in vaginal group were 10% and in sublingual group were 13.3%. One case (3.3%) of fever and two cases (6.6%) of vomiting were observed in sublingual group and one case (3.3%) of vomiting was observed in vaginal group. **Conclusion:** Both routes appear to be equally efficacious for mid trimester pregnancy termination, without significant side effects.

Key words: Misoprostol, Pregnancy termination, mid trimester.

INTRODUCTION

Termination of pregnancy has been practiced world wide. Overall termination rates are similar in developing and the developed world butt illegal terminations are concentrated in developing countries[1]. Common indications for termination of pregnancy include substantial risk of a child being born with serious congenital anomalies, intrauterine fetal demise and presence of medical disorders that pose a real threat to the health or life of mother.

In Pakistan termination has been allowed legally for maternal and fetal indications. Annual abortion rate in Pakistan is 29 per 1000 women. An estimated 890,000 illegal terminations are performed annually[2].

Second trimester of pregnancy ranges between 13-

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Correspondence Address:
Dr. Farzana Latif, FCPS
Flat No. 5, 1-Waris Road
Lahore

26weeks. Second trimester termination of pregnancy is associated with three to five times higher maternal mortality and morbidity risks than termination during first trimester[3].

Both medical and surgical methods are used for termination of pregnancy[4]. Surgical termination carries its own risks to maternal life with advancing gestational age. It bears risk of pelvic infections[5], cervical injury, intrauterine adhesions, uterine perforations, excessive bleeding and risks associated with anesthesia[6,7]. Incomplete evacuation occurs in 2-3% of curettage procedures[8].

Medical evacuation has been largely accepted as an effective and safe management and also offers economic benefits from reduction in number of operations. Various preparations have been used largely for termination of pregnancy with different results.

As compared with surgical abortion, medical abortion does not increase risk of future spontaneous abortion, ectopic pregnancy, preterm birth or low birth weight and long term fertility potential is not compromised after medical treatment It is an appropriate method for mid trimester termination[9]. Among medical ones, prostaglandins are safe and have less risk as compared to surgical methods[10].

The synthetic prostaglandins E_1 (PGE_1) compounds currently used are misoprostol and gemeprost. Gemeprost is expensive, not widely available and is provided in vaginal pessary that requires refrigeration. In contrast misoprostol is inexpensive, can be sorted at room temperature. Other prostaglandin widely used before misoprostol was prostaglangin F ∞(PGF ∞) injections.

Misoprostol is an important medication for gynaecological practice[11]. It is not only widely used for medical abortion but also very effective for cervical priming before first trimester suction curettage[12] and before hysteroscopy in premenopausal women as well as it is equally effective for first second trimester termination with short induction to termination time with fewer side effects[13,14]. Misoprostol can play a very important role in the practice of obstetrics and gynaecology in resource poor countries like Pakistan where cost of other prostaglandins is high and temperature maintenance is a problem[15,16]. In proper dosage risk of complications is low. It can be given orally, vaginally and sublingually. Studies have shown that pharmacokinetic of these routes are different with slower absorption and longer onset of action for the vaginal route. Sublingual misoprostol has the shortest onset of action, the highest peak concentration and greatest bioavailability among all routes of administration[17].

Although a number of studies have been conducted abroad comparing vaginal and sublingual routes for mid trimester termination of pregnancy but limited studies has been done in Pakistan. So in our study we compared the efficiency of misoprostol administered vaginally with similar dose administered sublingually in our subject. By the result of these we are able to know that which route is affective and safe in termination of mid trimester pregnancy.

PATIENTS AND METHODS

This study was conducted at Obstertrics & Gynaecology Unit 1 of Sir Ganga Ram Hospital over a period of thirteen months starting from October 2006. Sir Ganga Ram Hospital is a tertiary care hospital affiliated with Fatima Jinnah Medical College Lahore.

Female presenting in Gynae Unit 1 having indications for second trimester termination of pregnancy, were included in this study. Sixty patients were divided into two groups. Group A received 200 µg misoprostol vaginally. Dose was repeated four hours apart till expulsion occurs. Maximum five doses were given (30 cases). Group B received 200 µg misoprostol sublingually. Dose was repeated four hours apart till expulsion occurs. Maximum five doses were given(30 cases).all women with mid trimester pregnancy having indication for termination were included and exclusion criteria was history of misoprostol hypersensitivity, presence of uterine contractions, grand multiparty, low lying placenta and previous classical cesarean section, myomectomy.

RESULTS

During the study period sixty women were assigned into two groups. Thirty women received vaginal misoprostol and thirty women received sublingual misoprostol. The groups were comparable with regard to maternal age , parity, gestational age and indication for pregnancy termination(Table I & II).

Mean induction-expulsion time was similar in both groups. In the vaginal group it was 11.8±8.3 hours and in the sublingual group were 12.8±8.5 hours. The difference was not statistically significant (P>0.05)(Table III).

Total number of doses of misoprostol used in both groups was also similar and did not exhibit any statistically significant difference (Table IV). Percentage of complete expulsion was same in both groups i.e53.3%. the difference was not statistically significant(Table IV).

Syntocinon was used for augmentation in 30% cases of vaginal group and 13.3% cases of sublingual group. However, the difference between the study groups did not reach statistically significance level (Table IV). Evacuation was done for RPOC's in 36.6% cases of vaginal group and 33.3% cases of sublingual group. The difference was not statistically significant(Table IV).

Regarding maternal side effects one cases (3.3%) of fever was noticed in sublingual group and no case of fever noticed in Vaginal group, where as 2 cases of vomiting (6.6%) in sublingual group and one case (3.3%) of vomiting observed in vaginal group (Table V).

Table-I. Patient Demographics

	Vaginal (n=30)	Sublingual (n-30)	Significance of difference
Maternal age (year)	26.9	25.3	NS
Parity	1.5	1.0	NS
Gestational age (weeks)	19.6	19.2	NS

N = Number, NS =Non significant

Table-II. Indications for termination (%)

	Vaginal (n=30)	Sublingual (n-30)	Significance of difference
Fetal demise (%)	86.6	70	NS
Structural anomaly	10	30	NS
Maternal reason (preedampsia)	3.3	-	NS

N = Number, NS =Non significant

Table-III. Induction-Expulsion interval (hour)

	No	Mean	Standard deviation	Standard error mean	95% confidence interval
Vaginal	30	11.8	8.3	1.5	8.8-14.8
Sublingual	30	12.8	8.5	1.6	9.6-16.0
P > 0.05					

Table-IV.

	Vaginal (n=30)	Sublingual (n=30)	Significance of difference
Total doses of misoprostol (mean)	3.1	3.3	NS
Complete explusion (%)	53.3	53.3	NS
Augmentation with oxytocin (%)	30	13.3	NS
Evacuation (%)	36.6	33.3	NS
Failed Induction (%)	10	13.3	NS

Table-V. Maternal side effects (%)		
Side effects	**Vaginal (n=30)**	**Sublingual (n=30)**
Fever	Nil	3.3
Nausea / vomiting	3.3	6.6
Diarrhea	Nil	Nil
N = number		

DISCUSSION

Medical termination in the second trimester is the best method of choice to accomplish the pregnancy termination. Misoprostol is a known safe and efficacious agent for pregnancy termination, produces the least number of complications, the least amount of stress for the patient and is most effective[18] .

In this study, We have compared the vaginal route with the sublingual route to offer patients and health care providers, an easier alternative for pregnancy termination.

The demographics of the two groups showed no difference in gestational age, parity or indication for pregnancy termination. These are important factors to consider because the uterus becomes more sensitive to uterotonic agents as gestational age increases. It is also well known that abortion is more easily accomplished in multiparous compared with primiparous women, and when the fetus is already dead[19].

Several studies involving the use of vaginal and sublingual misoprostol in mid trimester termination have used doses of 100-800 µg with dosing intervals of every 3-12 hours[20,21]. Herabuttya found that although the rate of successful abortion increased with increasing doses, but the frequency of side effects also increased. So in this study, a dose of 200 µg was chosen for both groups[22].

Induction expulsion interval was found to be similar in both vaginal and sublingual groups. In our study the induction expulsion intervals is shorter as compared to some studies. This may be due to the induction of termination of pregnancy as majority of cases were terminated due to fetal demise than in the study by Feldman et al[23]. Also different studies showed that second trimester pregnancy termination that is complicated by fetal demise, is usually more predictable with shorter induction expulsion interval than that conducted when the fetus is alive due to increased sensitivity of the uterus to prostaglandins and the release of tissue factor following fetal demise. The effect has been demonstrated in a randomized control trial[24].

Dr Heleno Van Herzan and colleagues conducted a study comparing vaginal and sublingual misoprostol where misoprostol was administered by both routes at 3 hourly and 12 hourly interval in order to find the best route and interval. There was no significant difference in the results among the sublingual and vaginal groups when misoprostol was administered 3 hourly as compared to 12 hourly interval, where vaginal misoprostol was found to be more successful. This study showed that sublingual misoprostol is effective and results are comparable to the vaginal route when administered every 3-4 hourly interval in repeated doses[25]. Similar results were found in our study.

In our study misoprostol (200 µg) was administered by both sublingual and vaginal routes at 4 hourly intervals and maximum at 5 doses were given. Induction expulsion interval was almost similar in both groups which showed that the sublingual route can be used as effectively for second trimester termination of pregnancy as vaginal route, its effectively is more as compared to oral route, at the same time it is easy to administer and avoids repeated pelvic examinations and risk of infection as compared to vaginal route.

No significant maternal side effect were noted except one case of fever and two cases of vomiting in sublingual group and one case of vomiting observed in vaginal group.

No case of uterine rupture was observed in either of study groups. Although there are case reports of uterine rupture with misoprostol in the second trimester, it appears to be a much less frequent event than induction

at term[26,27]. It is possible that, because the lower uterine segment has not thinned out to the extent as seen at term and the cervix does not need to dilate as much to achieve the expulsion of fetus, so fewer uterine ruptures occurred in the mid trimester. So misoprostol is a safe drug for mid trimester pregnancy termination.

CONCLUSION

The study concluded that:

- Both routes appear to be equally efficacious for second trimester pregnancy termination with no significant side effects.
- The sublingual route provides an easier alternative for pregnancy termination, is preferable to patients as well as health care providers because it limits the number of vaginal examinations and the medication can be administrated by nursing staff.
- Misoprostal is effective and safe drug, so it should be used with confidence for termination of pregnancy.

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PREVIOUS RELATED STUDIES

- Tasnim Tahira. Termination of pregnancy; During second trimester by PGF2α in patients with caesarean scar. Professional Med J 2007; Vol: 14, No. 3, 403-406.