Comparison of the Sublingual and Vaginal Misoprostol for Medical Termination of Pregnancy in Cases of First and Second Trimester Abortion: A Quasi Experimental Study

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ABSTRACT

Objective: To compare the success rate of sublingual and vaginal Misoprostol for medical termination of pregnancy in the first and second trimesters.

Study Design: Quasi-experimental study.

Place and Duration of Study: Department of Obstetrics and Gynecology, Combined Military Hospital, Malir Pakistan, from May 2019 to Nov 2019.

Methodology: Two hundred patients in their first or second trimester of pregnancy with different indications for termination of pregnancy were included through consecutive sampling. Spousal consent was also taken along with wife consent. Patients were randomly assigned to one of the two groups. Group-A received sublingual Misoprostol 600 mcg stat followed by 400 mcg four hourly and group-B received the same dose of Misoprostol vaginally. The success rate was assessed through complete termination of pregnancy within 72 hours. Age, parity, induction to expulsion interval (IEI) and each patient's medical history was also noted.

***Results*:** After 24 hours success rate was 93% in the sublingual group compared to 78% in the vaginal group. After 48 hours sublingual group achieved a 100% success rate compared to 84% in the vaginal group, which was improved to 92% after 72 hours. The difference in success rates of both groups remained significant at 24, 48 and 72 hours IEI (p-value = 0.003, p-value <0.001, p-value=0.004 respectively).

Conclusion: Both sublingually and misoprostol are effective for medical termination of pregnancy in the first and second trimesters. However, the sublingual route showed clear supremacy over the vaginal route, as evident by success rates in the present study.

Keywords: First and second trimester, Misoprostol, Sublingual route, Success rate, Vaginal route.

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INTRODUCTION

Most of the indications for termination of pregnancy can be picked up through non-invasive procedures like ultrasound. Not only fetal anomalies or intrauterine demise but also a threatening pregnancy to the mother's life justifies terminating the pregnancy using the most effective and safe method.[1,2] Medical termination of pregnancy involves using drugs given either orally, sublingually, vaginally or through parenteral routes. In most situations, medical treatment is preferred over surgical treatment due to its non-invasive nature, more patient compliance, less severe or fewer side effects, better success rate, and shorter induction to expulsion interval (IEI). Shorter stay in hospital and early resumption of daily activities make it a method of choice.[3,4]

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During the last two decades, Misoprostol has been approved to be an effective agent for the termination of pregnancy in various gestation, cervical ripening, labour induction, termination of pregnancy and possible management of postpartum haemorrhage. Interestingly, studies reported a 100% success rate in cases of sublingual Misoprostol with a shorter IEI, i.e. 24 hours,[5,6] Only 89% of the vaginal group aborted successfully in 24 hours. Although few studies reported a comparable success rate for the vaginal route, the difference between the two routes was statistically non-significant (p=0.189).[7] A systematic review of 36 studies showed no significant difference in success rates of the sublingual and vaginal routes of Misoprostol.[8,9]

Many studies showed promising results of Misoprostol for the termination of pregnancies during the first and second trimesters, but there is always a debate over the best route of administration for the drug. Therefore, the present study was conducted to

compare the success rate of sublingual Misoprostol with vaginal Misoprostol for medical termination of pregnancy in the first and second trimesters. It will further lead to viable, practical suggestions in routine practice guidelines for reducing the morbidity of our population.

METHODOLOGY

This was a quasi-experimental study design. This study was conducted from May 2019 to November 2019 at the Department of Gynecology and Obstetrics, CMH, Malir, after approval from the Institutional Review Board (58/2018/Trg/ERC). The sample size was calculated as per the reference parameters from the study by Hickey *et al,*[8] with a 95% confidence level, 5% margin of error and 80% power of the test. The magnitude of success rate was 93% with sublingual and 73% with the vaginal route. The estimated sample size came out to be 91 in each group.

Inclusion Criteria: Patients with the gestational age between 4-24 weeks with a clear indication of termination of pregnancy like blighted ovulation, missed miscarriage, intrauterine fetal demise, anomalies, anencephaly, severe oligohydramnios due to PPROM and cases of chorioamnionitis were included in the study.

Exclusion Criteria: Patients with a history of major gynaecological surgeries and known allergies to Misoprostol, abnormal (molar) or ectopic pregnancies were excluded from the study.

A consecutive sampling scheme was employed. Patients admitted to the Department of Gynecology and Obstetrics, CMH Malir during the specified period for the study and fulfilling the inclusion criteria was enrolled in the study. These patients were randomly assigned to two groups, with an equal number of patients kept in each group.

There were 200 patients enrolled on the study. Informed written consent was obtained from each patient included in the study.

Group-A received sublingual Misoprostol 600 mcg stat followed by 400 mcg every four hours, and group-B received the same dose of Misoprostol vaginally, up to 4 doses in 24 hours.

Random distribution of samples was made using a computer-generated method into two groups, in group-A (sublingual group), tab Misoprostol 600 mcg stat followed by 400 mcg every four hours was given, up to 4 doses in 24 hours. In group-B (vaginal group), Misoprostol tab 600 mcg stat followed by 400 mcg every four hourly was given, up to a maximum of 4 doses in 24 hours. Success was measured in terms of complete abortion confirmed on ultrasound as an empty uterine cavity and absence of product of conception. Other variables like age, parity, educational status, medical history of diabetes, hypertension (HTN), obesity, anaemia and gestational age were also noted to see the effect of these parameters on success rate.

Data was entered in Statistical Packages for the Social Sciences (SPSS) version 22. Mean and SD was calculated for the continuous variable of age and IEI. Frequency and percentage were calculated for categorical variables of groups (Group A and Group B). The chi-square test was used to compare the success rate of both groups. The *p*-value of ≤0.05 was considered significant.

RESULTS

A total of 200 patients were included in this study, with equal numbers in each of the two groups. Mean age of the patients included in the study was 29.08 ± 5.34 years and ranged from 18-40 years. Mean gestational age was 13.19 ± 3.42 weeks. Only 22 (11%) patients were nulliparous, and the remaining 178 (91%) were parous. There were 91 (45.5%) patients with a history of previous LSCS. 11 patients (5.5%) were diabetic,[12] (6%) were hypertensive, 62 (31%) were anaemic, and 74 (37%) were obese.

In the sublingual group (group A), the mean age of patients was 29.30 ± 5.91 years and in the vaginal group (group B) was 28.86 ± 4.78 years. Mean gestational age was 13.54 ± 3.67 weeks in group-A and 12.85 ± 3.18 weeks in group-B. The majority of patients in both groups had formal education till higher secondary. In both groups, the rate of miscarriages was more in patients with low educational backgrounds.

In group-A (sublingual),[13] were nulliparous, and 41 were multiparous with three or more three children. Comparatively, in group-B (vaginal route),[9] were nulliparous while 25 were multiparous with three or more three children. The rest of the patients were multiparous, with 1 or 2 children in both groups. None of the patients had more than five children in any group.

In both groups, patients with previous uterine scars were included, with 48 in the sublingual group and 43 in the vaginal group. However, no complication of scar dehiscence or uterine rupture was seen in any patients. In the sublingual group, Misoprostol was more effective in ages 18-20 yearrs, first-trimester termination in multigravida and non-obsessed patients

(p<0.05). It was observed that 6 patients in the sublingual group and 5 in the vaginal group had uncontrolled diabetes, and pregnancy was terminated due to the presence of multiple anomalies. Among them, 2 fetuses had anencephaly with meningocele, and 4 had gross hydrocephalus. In hypertensive patients,[7] had severe oligohydramnios resulting in fetal demise, especially with uncontrolled hypertension. Figure-1 showd the medical and surgical history of the patients in each group.

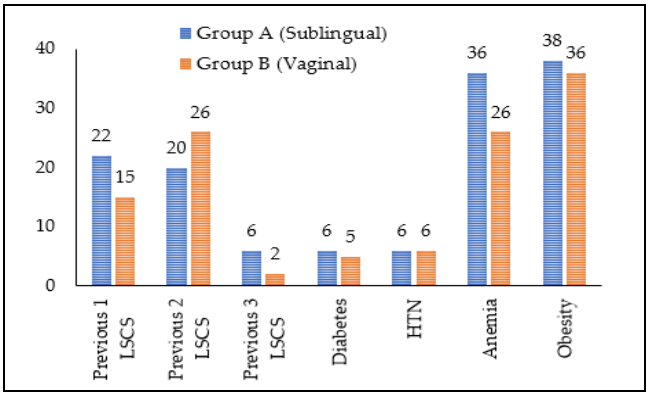

Figure-1: Surgical and Medical history of the patients included in the present study.

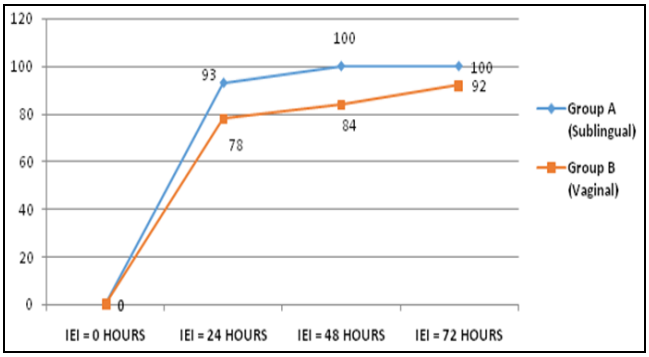

Figure-2: Success rate (percentage of patient with complete termination of pregnancy) with corresponding IEI (Induction to Expulsion Interval) in group A and group B.

Success was defined as complete expulsion of product of conception, and success rates were estimated for each group at 24, 48 and 72 hours. Figure-2 showed the success rates achieved in groups A and B with time. It was evident that sublingual groups showed promising results, and 100% success was achieved within 48 hours. Group B could not show up to 100% success even after 72 hours, and the patients underwent surgical intervention. The surgical evacuation was required in only four patients in the sublingual group (group A) after 24 hours and none after 48 hours. However, the surgical evacuation was required in 7 patients in the vaginal group (group B), four after 48 hrs and two after 72 hours.

The difference between the two groups' success rates was highly significant at 24, 48 and 72 hours IEI (p-value=0.003, p-value <0.001, p-value=0.004, respectively). Table-I showed that the difference between the two groups is significant (p-value <0.05). Table-II showed a difference in success rates ranging from 1-13%.

Table-I: Comparison of success rates in group A and group B at different IEI (24 hours, 48 hours, 72 hours).

Induction to Expulsion Interval (IEI)		Study Groups		Chi Square Test (p-value)
		Group A (Sublingual) n (%)	Group B (Vaginal) n (%)	
24 Hours	Yes	93 (93.0%)	78 (78.0%)	0.003
	No	7 (7.0%)	22 (22.0%)	
48 Hours	Yes	100 (100%)	84 (84.0%)	0.003
	No	0 (0.0%)	16 (16.0%)	
72 Hours	Yes	100 (100%)	92 (92.0%)	0.004
	No	0 (0.0%)	8 (8.0%)	

Patients in both the groups were categorized based on age, parity, and presence of co-morbid (diabetes, hypertension, obesity, anaemia). Comparison was made between these categories of patients in each group.

Table-II: Comparison of success rates in categories of patients of both the group A and group B.

Parameters	Categories of patients	Success Rate in Group A (Sublingual) n (%)	Success Rate in Group B (Vaginal) n (%)	p-value
Age (in Years)	18-29	53 (53%)	53 (53%)	0.521
	30-40	47 (47%)	39 (39%)	
Parity	Nulliparous	13 (13%)	9 (9%)	0.297
	Primiparous	20 (20%)	27 (27%)	
	Multiparous	67 (67%)	56 (56%)	
Medical History of co Morbid	Obesity	38 (38%)	33 (33%)	0.810
	Diabetes	6 (6%)	5 (5%)	
	Hypertension	6 (6%)	6 (6%)	
	Anemia	36 (36%)	23 (23%)	

DISCUSSION

In our study the sublingual route showed clear supremacy over the vaginal route. More importantly, the sublingual route also showed comparatively shorter IEIs and a 100% success rate was achieved within 48 hours.

Mid-trimester abortion accounts for 10-15% of induced abortions. Misoprostol is used either through the sublingual (oral) or vaginal route or both for termination of pregnancies. It is considered safe even in complications like previous uterine scars and other comorbidities.[10,11] Although combination therapy with mifepristone is preferred, Mifepristone's high cost

restricts the use of combination therapy, particularly in developing countries like Pakistan.[12,13]

Many studies were conducted to compare sublingual and vaginal misoprostol for termination of first and second-trimester pregnancies. Different outcomes were reported regarding the pregnancy suc-cess rate in 24, 48, and 72 hours IEI,[14,15,16] von Hertzen *et al*,[13] (2009) reported higher effectiveness of vaginal administration than sublingual administration in terminating second-trimester pregnancies, but nulliparous women mainly drove this result. Moreover, success rates of both the modes of treatment vary due to certain variables, including previous LSCS, parity, co-morbid like diabetes, hypertension, anaemia and obesity etc. Iftikhar *et al*,[15] (2017) concluded that lower gravidity, higher gestational age, and previous LSCS were associated with longer IEI when oral Misoprostol was used in one hundred and six pregnancies mid-trimester abortion. Young *et al*,[17] reported no significant difference between oral and vaginal Misoprostol in labour induction in a randomized controlled trial.

Milani *et al*,[4] reported both sublingual and vaginal misoprostol as successful modalities for medical abortion in the second trimester. However, the sublingual route remained a preferable option due to shorter IEI, better compliance and fewer side effects.[17,18]

There have been few randomized controlled trials on sublingual misoprostol for medical abortion.[19,20,21] Alfirevic *et al*,[18] conclusion based on six hundred and eleven studies reported Misoprostol safe and cost-effective, but the efficacy has a high degree of uncertainty compared with other drugs for induction of labour. Lapuente-Ocamica *et al*,[20] concluded that Misoprostol has high efficacy and suitable safety protocol. In another clinical trial, Tanha *et al*,[21] found that sublingual administration of Misoprostol is the best choice due to its high response, patient compliance, and fewer side effects but the efficacy of the oral Misoprostone is the same as that of vaginal administration. Another study also demonstrated in their study results that sublingual misoprostol is an effective and favourable cervical ripening agent for first-trimester abortion as compared to vaginal and oral dosage forms.[19]

Akkenapally *et al*,[22] suggested that equivalence between vaginal and sublingual administration could not be demonstrated overall. Moreover, some studies reported superiority of sublingual treatment over vaginal treatment when used in conjunction with surgical intervention to facilitate cervical dilatation. Ingrid Saav*et al*,[23] conducted a double-blind clinical trial on one hundred and eighty-four nulliparous women admitted for first-trimester abortion. They concluded that the efficacy of oral misoprostol is higher than vaginal misoprostol. Hamoda *et al*,[24] found sublingual misoprostol highly effective for cervical priming before the surgical abortion. Few studies also emphasised better efficacy of combined sublingual and vaginal routes.[25]

LIMITATION OF STUDY

A more comprehensive strategy was necessary where different cohorts of patients based on their demographics, medical and gynaecological/obstetrical history can be studied. Experiments with different doses of misoprostol should have been conducted to provide clear guidelines to the clinicians.

CONCLUSION

Both sublingually and misoprostol are effective for medical termination of pregnancy in the first and second trimesters. However, the sublingual route showed clear supremacy over the vaginal route, as evident by success rates in the present study.

Conflict of Interest: None.

Authors' Contribution

UIK: Data collection, writing, BI: Supervision, SSJ: Literature review, NAA: Data analysis, BS:, AF: References.

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