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ORIGINAL ARTICLE

Buccal Versus Vaginal Misoprostol Administration for the Induction of First and Second Trimester Abortions

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About the Author

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Abstract

Objectives To compare the effectiveness, side effects, and patient satisfaction of buccal versus vaginal misoprostol administration in first and second trimester induced abortions.

Methods In first trimester, women received oral mifepristone followed by misoprostol either by buccal or vaginal route. In second trimester, women received oral mifepristone followed by repeated doses of misoprostol either by buccal or vaginal route. A comparative analysis using SPSS was done.

Results In first trimester, success rate of medical abortion was 96 % in buccal group and 88 % in vaginal group. Nausea was the most common adverse effect which was similar in both groups. In second trimester, success rate was 96 % in buccal group and 80 % in vaginal group. A statistically higher incidence of nausea was noticed in buccal group. Patient satisfaction level was almost similar in both the groups in both trimesters.

Conclusions Buccal and vaginal routes of misoprostol administration have similar efficacy and patient satisfaction level for first and second trimester induced abortions. Hence, buccal route may serve as an alternative to vaginal misoprostol.

Keywords Abortions · Buccal · Vaginal · Misoprostol

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Introduction

Medical abortion is a safe alternative to surgical methods. MTP was legalized in India in the year 1971 [1]. In 2002 and 2003, an

amendment to the MTP Act sanctioned obstetrician-gynecologists to provide mifepristone and misoprostand after 6 weeks or in betweenol in a clinical setting up to 7 weeks of pregnancy.

Currently, most medical abortion protocols use mifepristone orally with misoprostol administered vaginally [2]. It was found in clinical studies that vaginal route of misoprostol administration was more effective than oral administration in medical abortions. Oral route is associated with extensive and rapid first-pass metabolism. Although effective, vaginal administration may require repeated vaginal examinations which are inconvenient and may be unacceptable for many patients. This has led to studies of other routes of misoprostol administration such as buccal and sublingual [3]. Additional benefits of the buccal route over the vaginal route include its ease of administration and lesser infection rate [4].

The purpose of this study is to determine the efficacy of buccal route of misoprostol as an alternative to vaginal administration of misoprostol for pregnancy termination in both first and second trimesters.

Materials and methods

One hundred women were selected for first and second trimester induced abortions. Patients were divided into two groups and each patient was assorted to one of the groups by random number tables. *Inclusion Criteria* (a) age 18 years and above (b) requesting for an elective termination of pregnancy well within the MTP Act. (c) an intrauterine pregnancy of less than or equal to 49 days for first trimester abortion and 14–20 weeks according to LMP for second trimester abortion, and also documented by ultrasonography. (d) willing to undergo required followup and surgical management when indicated. *Exclusion Criteria* (a) contraindication to mifepristone (chronic corticosteroid administration/adrenal disease) (b) contraindication to misoprostol (glaucoma, mitral stenosis, sickle cell anemia, poorly controlled seizure disorders or known allergy to prostaglandins) (c) any attempt of prior intervention in the present pregnancy. (d) known or suspected extrauterine pregnancy (e) known or suspected pelvic infection (f) Hemoglobin < 10 g/dl (g) known clotting defect/receiving anticoagulation therapy (h) cardiovascular disease (angina, valvular disease, arrhythmia or cardiac failure) (i) current breast feeding.

Rhesus negative subjects received anti-D immune globulin. After the approval of study by Institutional ethics committee, a written informed consent was taken from the patients who satisfied the inclusion criteria and each patient had the right to deny participation.

First Trimester Abortions

Fifty women were selected with pregnancy up to 49 days. Patients were divided into two groups (25 each) as follows: Group 1: Patients falling in this group received 200 mg mifepristone orally and were asked to report 48 h later for misoprostol administration by buccal route. Four tablets of misoprostol (200 mcg each) were placed in the buccal pouch i.e., between teeth and cheek (2 on each side). Subjects were instructed to swallow any remaining pill fragments after 30 minutes. Group 2: Patients falling in this group also received 200 mg mifepristone orally and were asked to report 48 h later for misoprostol administration by vaginal route. Four tablets of 200 mcg each (total 800 mcg) of misoprostol were inserted vaginally. Drug-related adverse effects and patient satisfaction were recorded. Followup: Subjects were asked to return for examination on 2nd, 14th day, and after 6 weeks or in between if they had any complaints. Vaginal sonography was carried out at day 14 to look for any retained products of conception. If the pregnancy was still viable at day 14, termination was done by surgical method. If there was a non-viable gestational sac, a choice to wait up to 42 days versus surgical abortion was offered. Patients reporting with incomplete abortion and hemorrhagic morbidity were offered immediate surgical evacuation. The main outcome was defined as successful if a complete abortion without surgical intervention was achieved.

Second trimester abortions

Fifty women were selected with pregnancy 14–20 weeks. Patients were divided into two groups (25 each) as follows: Group 1: Patients falling in this group were given 200 mg mifepristone orally and came for admission after 48 h. In this group, patients received first dose of 400 mcg of buccal misoprostol followed by 200 mcg of buccal misoprostol every 6 hourly until fetal expulsion or maximum 6 doses. Group 2: Patients falling in this group were given 200 mg mifepristone orally and came for admission after 48 h. In this group, patients were given 400 mcg intravaginal misoprostol every 6 hourly until fetal expulsion or maximum 6 doses. Once fetal expulsion occurred, all subjects received oxytocin, 20 U in 500 mL of lactated Ringer solution at 125 mL/h, until delivery of the placenta. USG was performed on day 2 of abortion to look for any retained products of conception, and check curettage was done in those found to have any retained products. Patients were asked for followup on day 14 and day 42 or in between for any complaints.

The outcomes measured in this study were the induction interval (the time from the initial misoprostol dose until fetal expulsion), drug-related adverse effects according to route of administration and patient's acceptability for route of administration. The main outcome was defined as successful if expulsion of the fetus with placenta occurred with 6 doses of misoprostol given 6 hourly (induction interval of 36 hours).

Women in the study were asked to complete a questionnaire which included inquiries about satisfaction level, gastrointestinal side effects, and intensity of pain perceived by the patient as measured on 11-point pain intensity numerical rating scale.

Statistical Analysis

The statistical analysis was carried out using Statistical Package for Social Sciences (SPSS Inc.). All quantitative variables were estimated using measures of central location (mean, median) and measures of dispersion (standard deviation and standard error). Normality of data was checked by measures of skewness and Kolmogorov–Smirnov tests of normality. For normally distributed data, means were compared using student's *t* test for two groups. For skewed data, Mann–Whitney test was applied for two groups. Qualitative variables were described as frequencies and proportions. Proportions were compared using Chi-square or Fisher's exact test whichever was applicable. All statistical tests were two-sided and were performed at a significance level of $\alpha = .05$.

Results

This prospective randomized controlled trial was carried out in 100 patients seeking abortion in first and second trimester (50 patients in each trimester). In each trimester, 25 patients were given misoprostol by buccal route and 25 by vaginal route. Various demographic parameters were comparable in both the groups in both trimesters and are shown in Table 1.

First Trimester the mean age of the women using buccal regimen was 29.96 ± 4.54 years and those using vaginal regimen was 30.20 ± 4.69. Mean period of gestation was 6.13 ± 0.58 weeks in buccal group and 5.97 ± 0.57 weeks in vaginal group which was comparable. The efficacy as judged by complete abortion was 96 % in buccal group and 88 % in vaginal group. At 2 weeks followup, one patient in the buccal group with retained products of conception was also given repeat misoprostol 400 mcg and had complete abortion at 1 week followup. In the vaginal group, three patients were found to be having retained products of conception. One patient underwent check curettage while two patients refused surgical intervention and were given repeat dose of misoprostol 400 μg and followed up after 1 week with complete abortion (Table 2).

Statistically significant adverse effect noticed was altered taste which was perceived by 16 % of the patients in buccal group ($p - 0.037$). Nausea was perceived by 24 % of women in buccal group and 32 % in vaginal group. One patient had shivering in the buccal group and one had fever in vaginal group.

Mean pain score was 2.16 in buccal group and 1.80 in vaginal group, which was statically insignificant. As regards patient satisfaction, all the patients in buccal group were satisfied while in vaginal group 92 % of the patients were satisfied which did not reach statistical significance.

Second trimester the mean age of the women in the buccal group was 26.96 ± 5.09 and in the vaginal group was 25.04 ± 4.13. Mean period of gestation was 17.66 ± 2.11 weeks in buccal group and 17.78 ± 2.07 weeks in vaginal group, which was not statistically significant. The commonest indication for abortion was congenital malformations in the fetus in both the groups. Neural tube defects were the most common malformations seen in our study. Eugenic indication for abortion (premature rupture of membranes with absent liquor, congenital malformations, and conjoined twin) was present in 23 patients in buccal group and 21 in vaginal group. Social indications (contraception failure and limit number of children) were present in 2 patients in buccal and 4 in vaginal group Table 3.

Table 1 Demographic variables

		First trimester		Second trimester	
		Buccal	Vaginal	Buccal	Vaginal
Mean age (years)		29.96 ± 4.54	30.20 ± 4.69	26.96 ± 5.09	25.04 ± 4.13
Socio-economic status	Lower	0 (0 %)	1 (4.0 %)	3 (12.0 %)	6 (24.0 %)
	Lower middle	7 (28.0 %)	5 (20.0 %)	15 (60.0 %)	12 (48.0 %)
	Upper lower	0 (0 %)	0 (0 %)	0 (0 %)	1 (4.0 %)
	Upper middle	18 (72.0 %)	19 (76.0 %)	7 (28.0 %)	6 (24.0 %)
	Total	25 (100.0 %)	25 (100.0 %)	25 (100.0 %)	25 (100.0 %)
Background	Urban	24 (96.0 %)	22 (88.0 %)	10 (40.0 %)	9 (36.0 %)
	Rural	1 (4.0 %)	3 (12.0 %)	15 (60.0 %)	16 (64.0 %)
	Total	25 (100.0 %)	25 (100.0 %)	25 (100.0 %)	25 (100.0 %)
Mean BMI (kg/m^2)		24.51 ± 2.00	22.88 ± 3.65	21.90 ± 3.63	22.75 ± 3.08
Mean period of gestation (weeks)		6.1314 ± 0.58310	5.9771 ± 0.57244	17.6629 ± 2.11082	17.7886 ± 2.07844

Table 2 Indication of abortion

Group	Indication of abortion	Regimen		*p* value
		Buccal *n* (%)	Vaginal *n* (%)	
1st trimester	Contraception failure	25 (100.0)	25 (100.0)	
2nd trimester	Congenital malformations	22 (88.0)	18 (72.0)	0.171
	Limit number of children	2 (8.0)	2 (8.0)	
	Premature rupture of membranes with absent liquor	0 (0)	3 (12.0)	
	Contraception failure	0 (0)	2 (8.0)	
	Conjoined twin	1 (4.0)	0 (0)	
	Total	25 (100)	25 (100)	

Table 3 Drug-related adverse effects

Group	Regimen	Altered taste *n* (%)	Nausea *n* (%)	Vomiting *n* (%)	Diarrhea *n* (%)	Shivering *n* (%)	Fever *n* (%)
1st trimester	Buccal	4 (16.0)	6 (24.0)	0 (0)	0 (0)	1 (4.0)	0 (0)
	Vaginal	0 (0)	8 (32)	0 (0)	0 (0)	0 (0)	1 (4)
	p value	0.037	0.529	–	–	0.312	0.312
2nd trimester	Buccal	4 (16)	8 (32)	8 (32)	1 (4)	1(4)	1 (4)
	Vaginal	0 (0)	1 (4)	3 (12)	0 (0)	3(12)	0 (0)
	p value	**0.037**	**0.010**	0.088	0.312	0.297	0.312

Bold means the results are stastically significant with $p < 0.05$

The efficacy as judged by complete abortion was 96 and 80 % in buccal and vaginal group, respectively. Ultrasonography was done on day 2 of abortion to look for any retained products of conception (RPOC) and it was observed that 1 patient in buccal group and 5 in vaginal group had RPOC with *p* value > 0.05 (statistically insignificant).

Three patients had continued pregnancy after maximum of 6 doses of misoprostol (36 h after first dose). Decision for therapeutic rest for 24 h was taken for these patients. Two patients in buccal group had spontaneous abortion after 4 h (40 h) and 9 h (45 h), respectively, and one patient in vaginal group aborted spontaneously after 4 h (total 40 h).

Mean induction to abortion interval in second trimester in buccal group was 14.64 ± 11.42 and 11.85 ± 8.16 h in vaginal group. This was found to be statistically insignificant (*p* value -0.326).

Analgesia requirement was almost same by either route i.e., 36 % in buccal and 32 % in vaginal group.

The incidence of nausea was higher (32 %) in buccal group versus 4 % in vaginal group, and this difference was statistically significant (*p* value 0.010). Vomiting was seen in 32 % in the buccal group and 12 % in the vaginal group, which was statistically insignificant. In buccal group, one patient had fever and one had diarrhea as drug-related adverse effect.

Mean pain score in buccal group was 4.84, and in vaginal group it was 5.12, and patient satisfaction level was 88 % in buccal group and 96 % in vaginal group (Table 4).

Table 4 Patient satisfaction level

Group	Satisfaction level	Regimen		*p* value
		Buccal *n* (%)	Vaginal *n* (%)	
1st trimester	Satisfied	25 (100.0)	23 (92.0)	0.149
	Unsatisfied	0 (.0)	2 (8.0)	
	Total	25 (100)	25 (100)	
2nd trimester	Satisfied	22 (88.0)	24 (96.0)	0.297
	Unsatisfied	3 (12.0)	1 (4.0)	
	Total	25 (100)	25 (100)	

Discussion

Induced abortion has a long history and has been facilitated by various methods including herbal abortifacients, the use of sharpened tools, physical trauma, and other traditional methods. The health risks of abortion depend on whether the procedure is performed safely or unsafely. Medical abortions are a safe alternative to surgical methods.

In our study, we randomized patients of both first and second trimester into two groups to receive misoprostol by either buccal or vaginal route, 48 h after oral mifepristone, based on computer generated random tables who fulfilled the inclusion criteria. The patients were comparable in terms of age, height, weight and BMI, mean period of gestation, and socio-economic status.

First Trimester Abortion

Large retrospective analysis of medical abortion safety conducted by PPFA, Inc, since 2001 showed a decrease over time in the serious infection rate with a change from vaginal to buccal misoprostol and similar efficacy [5]. In our study, efficacy in buccal group was 96 and 88 % in vaginal group in first trimester. The difference was not statistically significant. Our results were comparable with an open label randomized trial conducted by Middleton et al. in which efficacy rate for complete abortion with 800 mcg misoprostol was 95 % in the buccal group and 93 % in the vaginal group [3]. Another study in which 10 metropolitan centers were audited, success rate of 98.3 % for medical abortion with 200 mg of mifepristone combined with 800 mcg of self-administered buccal misoprostol within 24–48 h was demonstrated [6].

There were no significant differences in the rates of drug-related adverse effects between the two groups. Nausea was the most commonly reported adverse effect in both groups. This was consistent with study by Middleton et al. in which nausea and weakness were the most common adverse effects [3]. Altered taste was an additional side effect of buccal route of administration.

Analgesia was required in 1 patient in each group, which was administered orally. The overall satisfaction rate as determined by a questionnaire was 100 % in buccal group and 92 % in the vaginal group. Thus, the buccal regimen has an acceptable success rate and may provide a new treatment alternative for women uncomfortable with inserting misoprostol vaginally in the first trimester.

Second Trimester Abortion

Medical abortion is a safe option even for second trimester abortions in indicated cases. It is an option for women who are poor surgical candidates and also for those who live in areas where surgical termination is not available.

In Cochrane review 2011, medical abortion in the second trimester using the combination of mifepristone and misoprostol was found to have the highest efficacy and shortest abortion time interval. If mifepristone is not available, misoprostol alone is a reasonable alternative [7].

Both the World Health Organization and the RCOG recommend regimens in which mifepristone in combination with misoprostol offers the safest and most expeditious method to induce abortion in the second trimester [8, 9].

In our study, patients seeking abortion in second trimester were given 200 mg mifepristone followed by misoprostol 6 hourly for maximum of 6 doses by buccal or vaginal route. The success rate was 80 % in buccal group and 76 % in vaginal group at 24 h. At 48 h, the success rate increased to 96 and 80 % in buccal and vaginal group, respectively. Three patients had continued pregnancy after maximum of 6 doses of misoprostol (36 h after first dose). Decision for therapeutic rest for 24 h was taken for these patients. Two patients in buccal group had spontaneous abortion after 4 h (40 h) and 9 h (45 h), and one patient in vaginal group aborted spontaneously after 4 h (total 40 h).

The mean induction to abortion interval was 14.64 ± 11.42 h in buccal group and 11.85 ± 8.16 h in vaginal group. No statistically significant difference in induction time between buccal and vaginal administration of misoprostol for repeat doses was demonstrable (p value − 0.326).

Our results are comparable to study by Ellis et al. in which mean time to abortion was 15 h in buccal group and 12 h in vaginal group [10].

The safety and efficacy of misoprostol in second trimester termination of pregnancy in patients with previous cesarean section have been documented in various studies [11, 12]. In our study, five patients had delivery by cesarean section in previous pregnancy. Out of these, four patients received buccal misoprostol and aborted in 4 h 30 min, 5 h, 12 h 30 min, and 15 h, and one patient received misoprostol by vaginal route and aborted in 11 h 30 min. There were no uterine ruptures, need for hysterotomy or excessive bleeding in these patients.

The reported side effects of misoprostol are primarily gastrointestinal. In our study, adverse effects in both the groups were comparable except for altered taste and nausea which were more common in buccal group. Diarrhea was reported by only 1 patient in the buccal group. The side effects were comparable to those noted in previous studies where nausea and vomiting were reported with use of buccal misoprostol.

Previous studies demonstrate that approximately 2 to 10 % of women who have a medical abortion will require a surgical procedure for completion because of a continuing pregnancy, incomplete abortion, or the need for hemostasis. In our study, surgical procedure was carried out in 10 % of the patients in the second trimester, while 1 patient with retained products of conception on day 2 responded to 400 mcg of misoprostol vaginally. Mean pain score of 4.84 was found in buccal group, which was comparable to that in the vaginal group of 5.12. Analgesia requirement was almost same by either route (36 % in buccal and 32 % in vaginal group).

In buccal group, 88 % of the patients were satisfied, while in vaginal group 96 % reported satisfaction. This difference was not found to be statistically significant.

Thus, acceptance of misoprostol delivery was high with both routes of administration in both the trimesters but small sample size in our study remains the limiting factor.

Conclusion

Buccal and vaginal routes of misoprostol administration have similar efficacy for first and second trimester induced abortions. Thus, buccal misoprostol may serve as an alternative route to vaginal misoprostol for first and second trimester induced abortions.

Compliance with ethical standards The study was conducted among the patients selected from out patient department of Government Medical College and Hospital, Sector 32, Chandigarh and requesting for medical abortions. A written and informed consent was taken from all. The interventions involved in the present study are routinely practiced in Obstetrics and Gynecology and are safe. The patients were given the right to opt out of the study at any time they want. The defined guidelines of Central Ethics Committee for Biomedical Research on Human subjects by ICMR and guidelines as per Helsinki Declaration were strictly adherent in the present project.

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