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Comparison of Effectiveness and Patient Satisfaction of Vaginal Versus Oral Misoprostol in Treatment of Missed Miscarriage

Elham Mohammadi[1*], Geetha Jayaprakash[2], Afshin Shiva[3], Nader Motallebzadeh[1]

[1]RR College of Pharmacy, Chikkabanavara, Bangalore, India; [2]Department of Pharmacy Practice, RR College of Pharmacy, Chikkabanavara, Bangalore, India; [3]Department of Pharmacy, Urmia University of Medical Sciences, Urmia, Iran

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***Correspondence:** Elham Mohammadi. RR College of Pharmacy, Chikkabanavara, Bangalore, India. E-mail: elhammohammady@ymail.com

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Abstract

BACKGROUND: In recent years' medical management with misoprostol is an effective alternative to surgical evacuation. But there is a dearth of evidence to reveal the effectiveness of the different routes of misoprostol and satisfaction rate among the patients treated with these routes.

AIM: This study was conducted to compare the effectiveness and patient's satisfaction rate of vaginal versus oral misoprostol.

METHODS: It was a prospective non-interventional study. One hundred women of having missed abortion confirmed by ultrasonography examination were enrolled in the trial. Fifty-eight subjects were administered 200 mcg of oral and 42 subjects received 200 mcg of vaginal misoprostol every four hours up to four doses. If complete expulsion did not occur 12 hours after the last dose, the surgical evacuation was done.

RESULTS: There was no significant statistical difference between the effectiveness of treatment with vaginal (78.57%) and oral misoprostol (79.31%) (p = 0.928). The difference between Patients' satisfaction at the time of discharge for the vaginal group (64.29%) and oral group (65.52%) was not statistically significant (P = 0.991). There was an increase in patients' satisfaction for both groups at the follow-up session, but still, the difference was not significant (P = 0.897).

CONCLUSION: This study confirms that there is no statistical difference between the effectiveness and patient satisfaction of oral and vaginal misoprostol in the treatment of missed abortion.

Introduction

In the past, treatment for miscarriage before 14 weeks consisted of aggressive surgery [1]. But surgery is associated with many complications, such as postoperative infection [2]. However, in recent years, medical management has been introduced which is effective, safe, and acceptable [3]. Till now, so many different regimens have been tried and used, more or less successfully and it is one of the most confusing aspects of medical treatment of abortion. More than one regimen may be effective at a particular stage of pregnancy [4]. Misoprostol is an effective agent commonly used in the treatment of miscarriages especially missed miscarriage, but optimal dose and route of administration of misoprostol have not been determined by randomised trials [5]. Even the World Health Organization has not recommended a standard regimen for administration of misoprostol in the treatment of missed miscarriage [6].

A study was performed to find out the effect of misoprostol route on its pharmacokinetic profile [7]. There was the best absorption of misoprostol following vaginal administration. Small drug doses administered vaginally were capable of inducing contraction of uterus slowly and maintaining it for induction of labour. Due to the higher peak in oral administration, the side effects were more compared to that of the vaginal route [7]. Although the studies performed there is no agreement among experts in the superiority of the effectiveness of oral misoprostol over vaginal misoprostol and vice versa. Some

studies revealed that vaginal misoprostol is more effective than oral one in the expulsion of uterine content [8]. However, some other studies showed that there is not any significant difference between oral misoprostol and vaginal form of that [9]. Another important issue that should be considered in the treatment of missed abortion is the acceptability and satisfaction of the patient with the administered treatment. Because patients of having missed abortion experience grief, anxiety and depression, the method of treatment may affect their emotional state [10]. Some trials have concluded that women have higher satisfaction with oral misoprostol [11] while some other findings were against the superiority of oral misoprostol over the vaginal form of that considering the patient's satisfaction [9].

Since there is no fixed standard regimen for the treatment of missed abortion and because the way of treatment can affect the patients emotionally, further studies can be helpful. So in this study, we investigated the effectiveness of 800 mcg oral misoprostol versus vaginal misoprostol in a tertiary care hospital in India. Also, patients' satisfaction treated with vaginal versus oral misoprostol was compared at the time of discharge and in a follow-up session.

Material and Methods

Study Design

The study was a non-interventional prospective trial conducted in Sapthagiri hospital, Bangalore. Women who were eligible for the study were thoroughly counselled, and informed consent was taken orally.

Inclusion and exclusion criteria

Patients were recruited for the study based on the following inclusion criteria:

1. Females of age group 18 to 45 years, 2. Women with a gestational age of < 13 weeks of gestation from LMP, 3. Diagnosis of missed abortion by USG, 4. Mild vaginal bleeding or spotting or no bleeding and spotting at all, 5. Close cervix on pelvic examination, 6. Haemoglobin ≥ 9 gm/dl, 7. No history of asthma, liver disease on known allergy to misoprostol

Woman with any degree of cervical dilation, excessive uterine bleeding, twin gestation sac, molar pregnancy, BP ≥ 160/ 90 mmHg, signs and symptoms of infection, long-term corticosteroid therapy, and patients with high risk of uterine rupture and women who refused compliance with follow up schedule are excluded from the trial.

During a one-year study from September 2016 to September 2017, we enrolled 100 women, each with a documented missed abortion < 13 weeks of gestation through ultrasound examination. The subjects were administered mifepristone on day one followed by oral or vaginal misoprostol on day 3. Out of 100, 42 patients received 200 mcg of vaginal misoprostol, and 58 subjects received 200 mcg of oral misoprostol every four hours up to four doses. The patients were examined for complete expulsion of uterine content. If complete expulsion did not occur 12 hours after the last dose, the surgical evacuation was done.

Study Procedure

All patients were monitored for vaginal bleeding and expulsion of uterine content. In case of any expulsion, the POCs were examined by the gynaecologists. Also, a bimanual pelvic examination was performed to determine any retained gestational material. If complete abortion occurred before the completion of all doses, the next doses were not given.

Clinical outcomes had been considered before the initiation of the trial as:

- The effectiveness of trail had been defined as the expulsion of uterine content completely without the need for surgery.

- Failure was defined as the need for surgery for completing the course of treatment.

Clinical outcomes were recorded 12 hours after the last dose of misoprostol. The surgical evacuation was done in case of severe pain, infection, heavy vaginal bleeding or failure of complete expulsion of POCs after administration of the last dose of misoprostol.

Subjects were observed for 12 hours after complete abortion and then discharged. All women were then asked to return to hospital 14 days after discharge for examination with USG to make sure that there was no retention of any conception product in the uterine, also for assessing their satisfaction. The subjects were asked to fill a multiple- choice questionnaire by themselves at two-time points: one at the time of discharge from hospital and one at follow-up session 14 days after their discharge from the hospital.

Statistical analysis

The data were recorded in mean ± SD. Statistical significance was determined by Chi-square test for complete evacuation and patient satisfaction. $P < 0.05$ was considered statistically significant. The SPSS 16.0 statistical package was used for analysing the data.

Results

As mentioned in Table 1, baseline characteristics of both groups in terms of age, parity and period of gestation were comparable.

Table 1: Characteristics of the patients

Characteristics	Vaginal group (n = 42)	Oral group (n = 58)
Age (years)		
18-27	14 (33.33)	20 (34.48)
28-37	22 (52.38)	30 (51.72)
38-45	6 (14.28)	8 (13.79)
Mean ± SD	32.41 ± 3.52	34.61 ± 3.14
Parity		
1	8 (19.04)	11 (18.96)
2	10 (23.80)	14 (24.13)
3	20 (47.61)	25 (43.10)
4	4 (9.52)	8 (13.79)
mean± SD	2.47 ± 0.90	2.51 ± 0.95
Gestation duration (weeks)		
5-6	1 (2.38)	0 (0)
7-8	9 (21.43)	23 (39.66)
9-10	22 (52.38)	17 (29.31)
11-12	10 (23.81)	18 (31.03)
Mean ± SD	9.35 ± 1.34	9.34 ± 1.52

Values are given a number or number (percentage) unless otherwise indicated.

There was no significant difference between oral and vaginal route (Table 2) in success of treatment ($\chi 2 = 0.008$; P = 0.928; df = 1).

Table 2: Effectiveness of vaginal and oral misoprostol in the treatment of missed abortion

	Success	Failure	$\chi 2$ (p-value)
Vaginal	33 (78.57)	9 (79.31)	0.008
Oral	46 (21.43)	12 (20.69)	(P= 0.928)

Values are given a number or number (percentage) unless otherwise indicated.

There was no significant difference of patient's satisfaction between oral and vaginal misoprostol (Table 3) at time of discharge ($\chi 2 = 0.0162$; P = 0.991; df = 2).

Table 3: Patients satisfaction at the time of discharge

	Satisfied	Unsatisfied	Don't know (P value)	$\chi 2$
Vaginal	27 (64.29)	6 (14.29)	9 (21.43)	0.016
Oral	38 (65.52)	8 (13.79)	12 (20.69)	(0.991)

Values are given a number or number (percentage) unless otherwise indicated.

There was no significant difference of patient's satisfaction between oral and vaginal misoprostol (Table 4) at follow-up session ($\chi 2 = 4.822$; P = 0.897; df = 2).

Table 4: Patient satisfaction at a follow-up session

	Satisfied	Unsatisfied	Don't know $\chi 2$ (P value)
Vaginal	31 (73.81)	2 (4.76)	9 (21.43)
Oral	49 (84.48)	5 (8.62)	4.82 (0.897) 9 (6.90)

Values are given a number or number (percentage) unless otherwise indicated.

The complete abortion rate in the vaginal group was 78.57%, while it was 79.31% in the oral group. The abortion rate was higher in the oral group. However, the difference was not statistically significant (P = 0.928)

The questionnaires filled by the patients at two times of discharge showed 64.29% patients' satisfaction for vaginal treatment and 65.52% for oral treatment. But the difference was not significant statistically (P = 0.991). Patients' satisfaction for both groups increased at follow-up session and at this time point the result of patients' satisfaction of oral treatment (84.48%) was higher than that of the vaginal group (73.81%), but the difference was not statistically significant (P = 0.897).

Discussion

Misoprostol is an effective agent commonly used in the treatment of miscarriages but in spite of the studies that have been conducted the optimal dose and route of administration of misoprostol have not been determined yet [5]. Studies showed that the degree of absorption of misoprostol and its effect on uterine contractility after vaginal misoprostol was more long-lasting and more continuously increasing uterine contractility comparing to the time when oral misoprostol was administered After vaginal administration [3]. The difference between AUC values of orally and vaginally administered misoprostol is likely due to pre-systemic gastrointestinal or hepatic metabolism of oral misoprostol that will not happen in vaginal route [12]. So higher efficacy of vaginal misoprostol is expected due to the greater bioavailability of this route.

However, in spite of the logical explanation that vaginal misoprostol may be more effective than oral misoprostol due to their pharmacokinetic differences, in our study, there was no statistically significant difference in terms of response to treatment between oral misoprostol and vaginal misoprostol (P = 0.928). Although there are some studies that their results are contrary to our findings [1], [8], [13], [14], [15], [16], [17], there are some studies that support our findings [9], [18].

It was stated that age of gestation could influence the effectiveness of oral and vaginal misoprostol [27], but in our study, the subjects of two groups were very similar in the gestation duration (mean ± SD = 9.35 ± 1.34 for the vaginal group and mean ± SD = 9.34 ± 1.52 for the oral group).

Patient satisfaction is an important factor to be considered in the treatment of missed abortion because except the physical pain that these patients have, they are emotionally involved because of the loss of their child. They also suffer grief and depression [9]. Our study does not show a significant difference between patients' satisfaction of vaginal group and the oral group at the time of discharge (p = 0.991). Patients' satisfaction result at the second time point has increased for both groups (73.8% for the

vaginal group and 84.48% for the oral group). But still, the difference between the satisfaction of subjects of both groups is not statistically significant (P = 0.897).

From the results that we have obtained, we can infer that the emotional status of the patients in both groups may affect their response while completing the questionnaire at the time of discharge. It can be claimed so because the patient's satisfaction in both groups has increased after 14 days which is a good time for coming out of their grief. It has been stated that due to less privacy of vaginal misoprostol, patient show less satisfaction towards this route of administration [14] but our study is not in line with this finding because both groups of vaginal and oral misoprostol showed similar satisfaction towards their treatment. This similarity in the satisfaction of the subjects can be justified by considering the effectiveness of the treatment by these routes. As the difference in the effectiveness of both vaginal and oral misoprostol was not statistically significant, we can conclude that the success of the treatment is one important factor affecting patient satisfaction.

Therefore, it can be concluded that there is no difference between the vaginal and oral route of administration of misoprostol in the success of the treatment and patient satisfaction when used in the treatment of missed abortion.

The small sample size was one of the limitations of this study. Also, this study was not a controlled one. Further double-blind controlled studies with larger sample size are needed to elucidate the optimal route of misoprostol and patient satisfaction.

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