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ORIGINAL ARTICLE

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Medical abortion by mifepristone with oral versus vaginal misoprostol

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OBJECTIVE(S) : To compare oral with vaginal administration of misoprostol for induced abortion in women treated initially with mifepristone.

METHOD(S) : We administered 200mg of mifepristone to 128 women seeking termination of pregnancy within 9 weeks of amenorrhea. Forty eight hours later, they were assigned to receive 800 ?g misoprostol either orally or vaginally.

RESULTS : The complete abortion rates in vaginal group and oral group were 96.7% and 86.2% respectively. Median induction to abortion interval was significantly longer in women in the oral group compared to that in the vaginal group (P=0.04).

CONCLUSION(S) : Mifepristone followed by vaginal misoprostol was more effective at inducing an abortion up to 9 weeks of pregnancy than followed by oral form.

Key words : medical abortion, mifepristone, misoprostol

Introduction

Medical abortion of pregnancy with a combination of mifepristone and prostaglandin is a relatively safe and effective alternative to suction evacuation upto 9 weeks of gestation. Mifepristone 600 mg followed two days later by oral misoprostol 400 ?g for termination of pregnancy up to 7 weeks of gestation has been approved by the US Food and Drug Administration. In India the combination was approved for clinical use in 2001. Multicenter trials conducted by the World Health Organization demonstrated that the effectiveness of a 600 mg dose of mifepristone could be equalled with a reduced dose of 200 mg [1]. Although misoprostol is licensed for oral administration it is now often administered vaginally. A pharmacokinetic study has shown that systemic bioavailability of vaginally administered misoprostol is three times higher than that of orally administered misoprostol when determined by the area under plasma concentration time curve (AUC) for 360 minutes [2]. The marked difference in AUC between oral and vaginal administration is likely to be the result of presystemic gastrointestinal or hepatic metabolism that occurs with oral but not with vaginal administration. Although misoprostol is more effective when given vaginally, most women prefer the oral route because this can avoid the uncomfortable vaginal examination. We conducted this prospective clinical trial to compare oral with vaginal administration of the misoprostol for abortion up to 9 weeks of amenorrhea in women treated initially with 200 mg of mifepristone.

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Methods

Between May 2002 and March 2004, 128 women requesting termination of pregnancy within 9 weeks from the onset of amenorrhea were recruited for the study. Exclusion criteria were - (i) suspected ectopic pregnancy, (ii) contraindications for use of mifepristone including chronic systemic corticosteroid administration or adrenal disease, (iii) known coagulopathy or concurrent anticoagulant therapy, and (iv) inherited porphyria. The study was approved by the ethics committee. Women who enrolled gave written informed consent and agreed to have suction evacuation should the pregnancy be viable at the follow-up visit or anytime if heavy bleeding occurred. The

gestational age was confirmed in all women by ultrasound examination. The women were given mifepristone 200 mg orally and allowed to go home. If the patient's blood type was Rh negative, she also received anti D 50 ?g intramuscularly. They were then assigned sequentially to receive the misoprostol either orally or vaginally. Patients assigned to oral group were asked to swallow at home four tablets (800 ?g) of misoprostol, 48 hours after mifepristone. Patients assigned to vaginal misoprostol were asked to come back to the hospital 48 hours later and four tablets of 200 ?g misoprostol were inserted into the posterior vaginal fornix. Patient's vitals were monitored for one hour after the administration before allowing her to go home. Patients were asked to record the onset of bleeding, timing of passage of products of conception, duration of bleeding, and side effects for the next 14 days. They came for a follow-up visit on day 15 when vaginal examination and pelvic ultrasound examination were carried out. For each woman, the outcome was classified into one of the following categories - (i) complete abortion, (ii) incomplete abortion, (iii) missed abortion, and (iv) continuing pregnancy. Women with treatment outcomes in the last three categories were further managed by suction evacuation of the uterus. Success was defined as complete expulsion of the products of conception with no need for surgical intervention. The induction-abortion interval was defined as the time interval from administration of prostaglandin to the passage of products of conception. In presenting the results, continuous variables were presented as means with standard deviations and ranges. Differences in continuous variables were analysed with Student t test. Comparison between discontinuous variables were made using the Fisher exact or chi square test as appropriate. Differences were regarded as statistically significant if $P < 0.05$.

Table 1. Baseline characteristics.

Characteristics	Vaginal misoprostal (n=63)	Oral misoprostal (n=65)
Age (years)		
Mean ± SD	29.8 ± 4.4	29.2 ± 4.9
Range	18 - 44	18 - 44
Parity		
Primigravidas	10 (15.9)	8 (12.3)
Multigravidas	53 (84.1)	57 (87.7
Gestational age (weeks)		
≤7	48 (76.2)	52 (80)
7 - 9	15 (23.8)	13 (20)
Previous voluntary abortion	8 (12.7)	7 (10.8)
Previous cesarean section	13 (20.6%)	17 (26.1)

Figure in brackets represent percentages.

Results

Table 1 shows the baseline data of the 128 women who underwent medical abortion with mifepristone and vaginal or oral misoprostol. The two groups were comparable in age, parity, gestational age, previous voluntary termination of pregnancy, and previous cesarean section. Of the 128 women enrolled, two in the vaginal misoprostol group had abortion after the administration of mifepristone but before the administration of misoprostol. They were excluded from further analysis. Complete abortion occurred in 96.7% of the women in the vaginal group and 86.2% in the oral group (Table 2). The treatment outcome in the vaginal misoprostol regimen was significantly better (P=0.03 by Fisher exact test). The induction-abortion interval was significantly longer in women in the oral group when compared to that in the vaginal group (3.72 ± 1.5 vs 3.16 ± 1.1 hours. P=0.04 by Student t test). There was no significant difference in the number of days of vaginal bleeding in the two groups [9.32 ± 2.49 (vaginal group) vs 9.67 ± 3.22 (oral group); P=0.05].

Table 2. Treatment outcome.

Outcome	Vaginal misoprostol (n=63) Number (Percent)	Oral misoprostol (n=65) Number (Percent)
Complete abortion	59 (96.7)	56 (86.2)
≤ 7 weeks	46 (97.8)	45 (86.5)
> 7-9 weeks	13 (86.7)	11 (84.6)
Incomplete abortion	3 (3.3)	8 (12.3)
≤ 7 weeks	1 (2.2)	6 (11.5)
> 7 - 9 weeks	1 (7.1)	2 (15.4)
Ongoing pregnancy	0 (0)	1 (1.5)
≤ 7 weeks	0 (0)	1 (1.9)
> 7 - 9 weeks	0 (0)	0 (0)

Figures in brackets represent percentages.

Table 3 gives the side effects observed in the two groups. Among the 126 participants, the symptom questionnaire was completed by 122 women. The reported incidence of vomiting was 45.6% in the vaginal misoprostol group, which was significantly higher than the 26.2% incidence in the oral misoprosol group (P=0.04 by chi square test). Remaining side effects were comparable in the two groups. No hospitalization or blood transfusion was needed for excessive bleeding.

Table 3. Adverse effects.

Adverse effects	Vaginal misoprostol (n=61) [a]	Oral misoprostol (n=61) [b]	P value
Abdominal pain requiring analgesia	2 (3.2)	3 (4.9)	0.51
Tolerable abdominal pain	23 (37.1)	26 (42.6)	0.51
Nausea	24 (38.7)	27 (44.3)	0.51
Vomiting	27 (45.6)	16 (26.2)	0.04
Diarrhea	3 (4.8)	5 (8.2)	0.34
Dizziness	0 (0)	2 (3.3)	-

Figures in brackets represent percentages.

[a] Two women out of 63 had aborted after taking mifepristone only.
[b] Four women out of 65 did not complete the symptom questionnaire.

Discussion

The vaginal rather than oral administration of misoprostol may extend the use of medical abortion up to 9 weeks. The complete abortion rate in this study is in agreement with that reported by El Rafaey et al[3]. In their study, 95% aborted with the vaginally administered misoprostol and 87% aborted with oral misoprostol. Ashok et al [4] reported the complete abortion rate after mifepristone administration alone as 2%. Two of our 128 women aborted with mifepristone alone.

El Refaey et al [3] reported that the incidence of gastrointestinal side effects was higher when misoprostol was given orally than when it was administered vaginally. They reported that one woman in the vaginal group bled heavily and required a blood transfusion. Although this complication is uncommon, the possibility of hemorrhage with medical abortion highlights the need for vigilance and ready access to medical help.

Kant and Taneja [5] administered misoprostol orally in the out patient department in doctor's presence. Our study demonstrated that misoprostol can be self administered at home without sacrificing safety. Pymar and Creinin [6] provided evidence that vaginal misoprostol is more effective than the oral form in achieving complete abortion between 7 and 9 weeks gestation. The limitation of our study is that only 28 women requested for medical abortion just after seven weeks gestation. So we could not demonstrate a better outcome with vaginal administration in this gestational age group.

Conclusion

Our study demonstrated that 200mg mifepristone followed by vaginal misoprostol is more effective at inducing abortion upto 9 weeks of pregnancy than oral misoprostol.

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References

1. WHO Task Force on Post-ovulatory Methods in Fertility Regulation. Comparison of two doses of mifepristone in combination with misoprostol for early medical abortion: a randomized trial. *Br J Obstet Gynecol 2000;107:524-30.*
2. Zieman M, Fong SK, Darney PD et al. Absorption kinetics of misoprostol with oral or vaginal administration. *Obstet Gynecol 1997;90:88-92.*
3. El-Rafaey H, Rajasekar D, Abdalla M et al. Induction of abortion with mifepristone (RU 486) and oral or vaginal misoprostol. *N Engl J Med 1995; 332: 983-7.*
4. Ashok PW, Penney GC, Flett GM et al. An effective regimen for early medical abortion: a report of 2000 consecutive cases. *Hum Reprod 1998;13:2962-5.*
5. Kant A, Taneja I. Low dose mifepristone for early abortion. *J Obstet Gynecol India 2004;54:173-4.*
6. Pymar HC, Creinin MD. Offering mifepristone as an abortion option. *Contemporary OB/GYN 2001;46:113-9.*