Misoprostol in Missed Abortion: Oral or Vaginal?

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Abstract: Miscarriage is very common, with nearly one in four women experiencing an early pregnancy loss in her lifetime. The aim of this study was to compare the efficacy, acceptability and side effects of the oral and vaginal misoprostol administration in facilitating cervical dilatation prior to surgical evacuation. A randomized controlled study was carried out in Al-Azhar university Hospitals. One hundred and twenty women with first trimester missed abortions were divided into 2 study groups, randomized for oral and vaginal (800 µg) misoprostol, and 2 control groups randomized for oral and vaginal placebo, before undergoing surgical evacuation of conception after 3 hours. Measured outcomes were: post medication cervical dilatation, time needed to dilate the cervix surgically, blood loss, and development of the side effects of misoprostol. The results werepost medication cervical dilatation was 7.77 ± 1.22 mm for the vaginal misoprostol group, 7.07 ± 1.36 mm for oral misoprostol, versus the control groups 2.43 ± 0.5 mm. Post medication cervical dilatation was significantly higher in the vaginal misoprostol group, compared to the oral group (p=0.032†). There were no significant differences in the amount of blood loss between oral (p=0.74), and vaginal misoprostol groups (p=0.629), and gastrointestinal side effects were significantly more in the oral misoprostol group (p=0.014). We concluded that misoprostol is an effective cervical priming agent when administered either orally or vaginally before evacuation of conception in the termination of the first trimester missed abortions.

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1. Introduction

Miscarriage is very common, with nearly one in four women experiencing an early pregnancy loss in her lifetime.(1) Cervical injury during surgical evacuation can be reduced by making the cervix softer and easier to dilate by using cervical priming agents.(2) Prostaglandins (PGs) have revolutionized the treatment of abortions.(3) Misoprostol, a prostaglandin E1 analogue, has been shown to be a better alternative to other prostaglandin preparation, as it is relatively inexpensive, stable at room temperature and associated with fewer side effects than the older prostaglandin analogues.(4)

Misoprostol for cervical ripening have been tried in different doses and routes. However, the data are not satisfactory. Hence, the purpose of this study was to compare the efficacy, acceptability and side effects of the oral and vaginal routes of misoprostol administration in facilitating cervical dilatation prior to surgical evacuation.

2. Patients and Methods

The study was carried out in the Department of Obstetrics and Gynecology in Al-Azhar university hospitals, over 1 year period from June 2012 to May 2013.It was prospective, randomized, controlled blind study. Patients with missed abortion or blighted ovum were admitted. Ultrasonography confirmed the clinical diagnosis. For the current study, the patients and the attendants were explained about the procedure and informed consent was obtained. Baseline investigations including Hb, bleeding time, clotting time, platelet count, blood grouping, and kidney function tests, liver function tests, urine examination were carried out.

A total of 120 patients with missed or blighted ovum were enlisted andrandomized into 4 groups, 2 study groups, and 2 control groups. Study group 1 (n=30) received 800ug vaginal misoprostol and study group 2 (n=30) received 800ug oral misoprostol. Control group 1 (n=30) received 4 vaginal placebo tablets and control group 2 (n=30) received 4 oral placebo tablets.

Patients had pelvic examination, with evaluation of basal cervical dilatation using Hegar dilators in descending order and those with cervical dilatation >4mm were excluded from the study.

A pad was placed after the application of medication, and the difference in its weight before, and 3 hours after the medication was calculated. An increase of one gram in the pad's weight was considered to be equivalent to one ml of blood namely, (specific gravity one gm.=ml), which was considered as pre-operative blood loss. The patients waited for 3 hours, no pre-medication was given, but they were told that analgesics and anti- emetics were

available if required. Their blood pressure, pulse rate, and body temperature were measured just before the surgical procedure. The side effects related to misoprostol in terms of nausea and vomiting, abdominal pain, headache, and elevation of body temperature were recorded. All patients underwent evacuation of conception products, 3 hours after the administration of tablets. The post-medication cervical dilatation was measured by passing Hegar's dilator in descending order starting with Hegar number 10. The size of the largest dilator that could pass through the cervical os without resistance was recorded as post medication cervical dilatation achieved. No further dilatation was performed when the cervix was dilated to 7 mm or greater, and evacuation of conception was carried out. If the cervical dilatation was less than 7 mm, the cervix was dilated up to 7 mm for evacuation. The change in cervical dilatation was calculated by subtracting basal cervical dilatation from post medication cervical dilatation achieved. The duration of the procedure was calculated as the time required for dilatation, when additional dilatation was necessary. Intra-operative blood loss was taken as the volume of blood measured after sieving away the products of conception from the uterine products. Patients were observed for 2 hours after the operation.

Statistical Analysis

Statistical analysis was computerized using the Statistical Program for Social Sciences (SPSS version 12). The t-test of significance was used to compare numerical values, and the Chi square test was used to compare percentages. A *p*-value less than, or equal to 0.05 were considered as statistically significant.

3. Results

Cervical ripening and dilatation was significant in the vaginal route as compared to the oral route (P<0.01) [Table 1]. Intra-operative blood loss was relatively more in the vaginal group as compared to the oral groups but without significant difference [Table 2]. Nausea, vomiting with gastrointestinal adverse effect was observed with the oral route of misoprostol [Table 3].

Table 1 - Comparison of basal cervical dilatation and mean change in cervical dilatation between study and control groups.(*non-significant, †significant)

Studied groups	Number	Basal cervical dilatation	P-value	Post medication cervical dilatation	P-value	Mean change in cervical dilatation	P-value
Oralplacebo	30	2.43 ± 0.5	1.0*	2.43 ± 0.5	0.00†	0.00 ± 0.00	
Oral misoprostol	30	2.43 ± 0.5		7.07 ± 1.36		4.7 ± 1.42	
Vaginal placebo	30	2.43 ± 0.5	0.61*	2.43 ± 0.5	0.00†	0.00 ± 0.00	
Vaginal misoprostol	30	2.5 ± 0.51		7.77 ± 1.22		5.23 ± 1.28	
Total	120						
Oral misoprostol versus oral misoprostol			0.61*		0.041†		0.032†

Table 2 - Comparison of preoperative blood loss and intra-operative blood loss between study and control groups.(*non-significant, †significant)

Studied groups	Number	Preoperativeloss± SD(mls)	*P*-value	Intraoperativeloss± SD (mls)	*P*-value
Oral placebo	30	0.00 ± 0.00		54.67 ± 31.46	0.00†
Oral misoprostol	30	3.27 ± 2.78		22.67 ± 19.64	
Vaginal placebo	30	0.3 ± 0.95	0.00†	52 ± 27.56	0.00†
Vaginal misoprostol	30	3.1 ± 2.54		19.6 ± 16.39	
Total	120				
Oral misoprostol versus vaginal misoprostol			0.74*		0.629*

Table 3: Comparison of development of side effects of misoprostol between the study and control groups (*non-significant, †significant)

Side effects	Oral placebo	Oral misoprostol	Vaginal placebo	vaginal misoprostol	P-value
Nausea	2 (6.7)	8 (26.7)	1 (3.3)	2 (6.7)	0.014†
Vomiting	0 (0)	4 (13.3)	0 (0)	0 (0)	0.006†
Headache	1 (3.3)	5 (16.7)	0 (0)	1 (3.3)	0.03†
Fever	1 (3.3)	4 (13.3)	1 (3.3)	1 (3.3)	0.0251*
Abdominal pain	0 (0)	14 (46.7)	0 (0)	0 (0)	0.00†
Diarrhea	0 (0)	5 (16.7)	1 (3.3)	1 (3.3)	0.03†

4. Discussion

Misoprostol E1 is cheap and stable at room temperature and available in different dosage forms.(5)

The present study observed that the cervical ripening effect and the mean time taken by misoprostol were favorable among the vaginal group. The observed difference can be attributed to the different absorption kinetics and subsequent more systemic bioavailability with the vaginal route than oral administration. Our results were consistent with the observations by Cakr et al (6) Saxena et al.(7) and Tang et al (5). However, the effects with the oral route were not as promising as observed in the earlier studies.

The mean intra-operative blood loss was less in the oral group, however without significant difference, this is in agreement with the results reported by Saxena et al. (8), and not in agreement with the results reported by Caker et al (6) who found statistical significant difference in the amount of blood loss between the vaginal and oral misoprostol groups.

The observed side effects like abdominal pain, nausea, vomiting and vaginal bleeding were quite different from the earlier studies by Tang et al. (5) where the incidence was high which may be because of the higher and the frequent dosing used in the first study (9). Vaginal bleeding in our study was more in the vaginal group than the oral group which could be attributed to the sustained peak plasma concentration in this route.

Ho et al. (10) in 1997 conducted a comparative study between oral and vaginal administration and concluded that oral administration is convenient and more acceptable to women and Ngai et al.(11) showed that oral administration of 400 μg of misoprostol 3 h before vacuum aspiration is as effective as a similar regimen of vaginal misoprostol. However, administration of oral drug with water 3 h before operation may cause problems especially if general anesthesia is needed for surgical evacuation. These, clinical studies have shown that the vaginal route is superior to oral misoprostol in termination of first trimester pregnancies.

Conclusion

From the present study, it can be concluded that vaginalmisoprostol is an effective and favorable cervical ripening agent for first trimester abortion prior to surgical evacuation as compared to oral dosage forms.

References

1. Chen BA, Creinin MD. Contemporary management of early pregnancy failure. Clin Obstet Gynecol. 2007;50(1):67–88.
2. Meckstroth KR, Darney PD. Prostaglandins for first-trimester termination. Best Pract Res Clin Obstet Gynaecol. 2003;17(5): 745e763.
3. Kulier R, Gülmezoglu AM, Hofmeyr GJ, Cheng LN, Campana A. Medical methods for first trimester abortion. Cochrane Database Syst Rev 2004;2:CD002855.
4. Schaub B, Fuhrer P, Sainte-Rose D. Randomized study of sulprostone versus misoprostol in the cervical preparation before elective abortion in nulliparous women. J Gynecol Obstet Biol Reprod (Paris).
5. Tang OS, Miao BY, Lee SW, Ho PC. Pilot study on the use of repeated doses of sublingual misoprostol in termination of pregnancy up to 12 weeks gestation: Efficacy and acceptability. Hum Reprod 2002;17:654-8.
6. Caker L, Dilbaz B, Caliskan E, Dede FS, Dilbaz S, Haberal A. Comparison of oral and vaginal misoprostol for cervical ripening before manual vacuum aspiration of first trimester pregnancy

under local anesthesia: A randomized placebo-controlled study. Contraception 2005;71:337-42.
7. Saxena P, Sarda N, Salhan S, Nandan D. A randomised comparisons between sublingual, oral and vaginal route of misoprostol for pre-abortion cervical ripening in first-trimester pregnancy termination under local anaesthesia. Aust N Z J Obstet Gynaecol 2008;48:101-6.
8. Saxena P, Salhan S, Sarda N. Comparison between the sublingual and oral route of misoprostol for pre-abortion cervical priming in first trimester abortions. Hum Reprod 2004;19:77-80.
9. Tang OS, Lau WN, Ng EH, Lee SW, Ho PC. A prospective randomized study to compare the use of repeated doses of vaginal with sublingual misoprostol in the management of first trimester silent miscarriages. Hum Reprod 2003;18:176-81.
10. Ho PC, Ngai SW, Liu KL, Wong GC, Lee SW. Vaginal misoprostol compared with oral misoprostol in termination of second-trimester pregnancy. Obstet Gynecol 1997;90:735-8.
11. Ngai SW, Chan YM, Tang OS, Ho PC. The use of misoprostol for pre-operative cervical dilatation prior to vacuum aspiration: A randomized trial. Hum Reprod 1999;14:2139-42.

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