Comparison of Sublingual and Vaginal Misoprostol for Second-Trimester Pregnancy Terminations

Forozan Milani, Seyede Hajar Sharami, Saeedeh Arjmandi

Reproductive Health Research center, Guilan university of Medical Sciences, Rasht, Iran

Received March 2013; revised and accepted Aprile 2013

Abstract

Objective: Comparing sublingual and vaginal misoprostol in second trimester pregnancy termination.

Materials and methods: In this study 268 women at 12-24 weeks of gestation candidate for pregnancy termination were enrolled. Women were randomly divided in two groups .The first group received 400 µg sublingual misoprostol and vaginal placebo and the second group received 400 µg vaginal misoprostol and sublingual placebo every 4 hours for a maximum of five doses. The course of misoprostol was repeated if the women did not abort within 24 hours.

Results: The median induction-to-abortion interval was shorter in sublingual group (12/72 hours in sublingual and 14/67 hours in vaginal).There was no significant difference in the success rate at 24 and 48 hours and in side effects. The preference for the sublingual route of administration was higher.

Conclusion: Both vaginal and sublingual misoprostol are effective for medical abortion in second trimester termination. But it appears from shorter induction interval in sublingual and higher acceptability that sublingual route is a better choice.

Keywords: Misoprostol, Vaginal, Sublingual, Second Trimester Termination

Introduction

Abortions during the second trimester represent only 10% to 15% of all induced abortions, but provoke two-thirds of all the serious complications and half of the deaths directlyrelated to this practice (1). With the wide-scale introduction of prenatal screening programs, the issue of second trimester abortion has become increasingly relevant, in particular for women whose pregnancies are complicated by a serious fetal anomaly (2). Prostaglandins and their analogues are widely used for medical Terminationof pregnancy. Misoprostol is a PGE1analogue available in a tablet form that is stable at room temperature and inexpensive (3). Two common routes of misoprostol administration are sublingual and vaginal; but they have different pharmacokinetics and effectiveness. Sublingual misoprostol reaches its peak concentration in a short time due to rapid absorption and has higher bioavailability; the vaginal route causes more prolonged regular uterine contractions. The vaginal route has less adverse effects such as nausea, vomiting and diarrhea after administration (4).Therefore in this paper we have compared the sublingual route to the vaginal route in the administration of misoprostol for second-trimester termination.

Correspondence:
Dr. SaeedehArjmandi, Reproductive Health Research Center, Department of Obstetrics and Gynecology, Alzahra Hospital, Rasht, Iran
Email: forozanmilani@yahoo.com , H_fertility@gums.ac.ir

Materials and methods

Our study is a double blinded randomized clinical trial

that was performed in Alzahra hospital of Rasht (IRAN), from September 2012 to January 2013. The study was approved by the ethics committee of Guilan University of Medical Sciences. Informed consent was obtained from patients. Indications for second trimester termination were intra uterine fetal death, chromosomal abnormalities, fetal anomaly and legal abortion based on maternal reasons. Exclusion criteria were contraindications to prostaglandins use (bronchial asthma, cough, appearance of skin signs, glaucoma),women with previous uterine surgery and cesarean section , multiple pregnancies, parity>3 , vaginal bleeding and placenta previa. Totally 268 pregnant women (between 12 and 24 weeks) were admitted. Four cases from vaginal and four cases from sublingual group withdrew before the study (fig. 1). Neither the investigator nor the patients were blinded to the treatment group. Women were randomly assigned to group A and B(130 patients in each group).Group A was given 400 µg sublingual misoprostol and vaginal placebo and group B was given 400 µg vaginal misoprostol and sublingual placebo at 4 hours interval (maximum of five doses) in 24 hours. The desire outcome was fetus expulsion and if did not occur, the same regimen was repeated 24 hours after the start of the first dose of misoprostol. A structured form was used to record age, previous obstetrics history (miscarriage, parity, gravidity), the time interval between misoprostol application and fetus expulsion, the number of tablets required, side effects such as fever, chills, diarrhea, nausea, vomiting, needing to analgesics and patient`s preference on the routes of application. Analysis was done using the SPSS 16.0 statistical package. This study was done with financial support of Vice chancellor of research Guilan University of Medical Sciences.

Statistical analysis

Data analysis was performed by using SPSS version16, All outcomes were assessed using Chi-squared test and independent t-test and mann-whitney. A level of 0.05 or less was considered significant.

Results

There was no statistically significant difference in women`s basic characteristics such as age, gestational age, parity, number of miscarriages between the two groups (table 1).The mean maternal age was 30.28± 6.78 years in the vaginal group and 29.72± 6.45 years in the sublingual group (p= 0.457).The mean gestational age was 16.11± 2.64 in the vaginal group and 15.91± 2.8 in the sublingual group (p= 0.555).The success rate at 24 hours was 72% in the sublingual group and 76% in the vaginal group(p= 0.39).There was no statistically significant difference between the two groups (table 2) And the success rate of fetus expulsion did not differ in the two groups(81.5% in the vaginal group and 74.6% in the sublingual group, p= 0.177) (table 2). The median induction-to-fetus expulsion intervalwassignificantly shorter in the sublingual group (table 2).

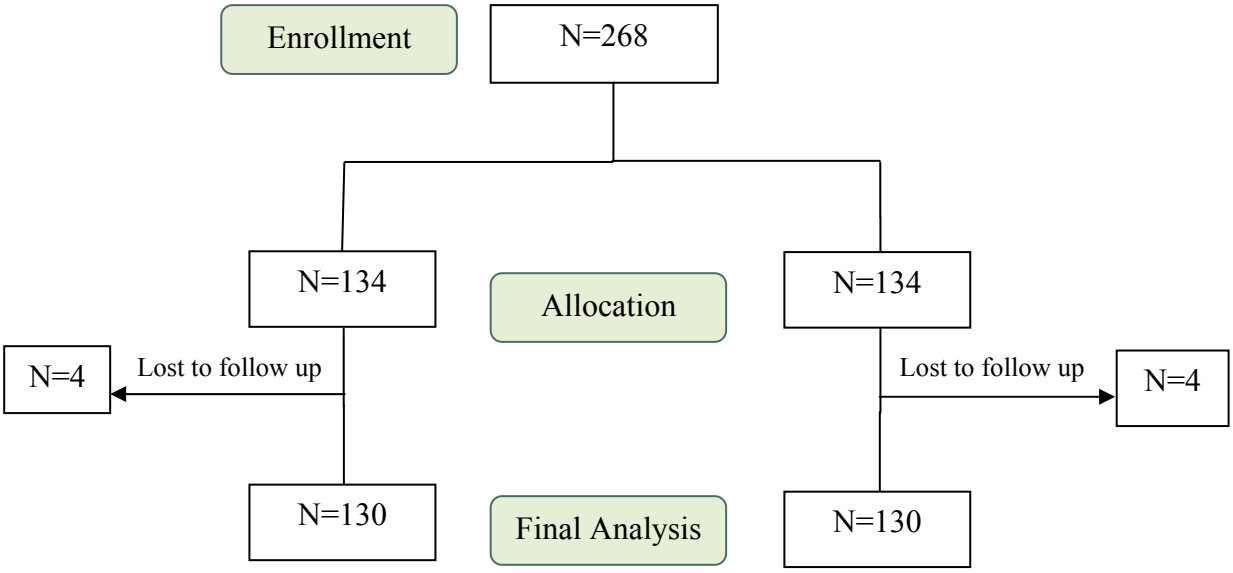

Fig. 1: Flow chart for the progress through the trial

Table 1: Demographic characteristics

	Sublingual n (%)	Vaginal n (%)	p Value
BMI			
<19	3(2.3)	2(1.5)	0.869
19-25	67(51.5)	62(47.7)	
25-30	49(37.7)	53(40.8)	
30<	11(8.5)	13(10)	
Previousabortion			
0	106(81.5)	105(80.7)	0.987
1	22(16.9)	23(17.7)	
2≤	2(1.5)	2(1.5)	
Parity			
1	89(68.5)	87(66.9)	0.532
2	25(19.2)	20(15.4)	
3	16(12.3)	23(17.7)	
Maternal age(years) (mean± SD)	29.72± 6.45	30.28± 6.67	0.495
Gestational age(weeks) (mean± SD)	15.91± 2.8	16.11± 2.64	0.555

Table 2: Effectiveness of sublingual versus vaginal misoprostol for fetus expulsion

	Sublingual group n=130	Vaginal group n=130	p value
Success rate in 24 hours [n (%)]	94 (72.3)	100 (76.9)	0.39
Success rate in 48 hours [n (%)]	97 (74.6)	106 (81.5)	0.177
Induction to abortion period (hour) (mean± SD)	12.72± 5.79	14.67± 6.16	0.22

The mean dose applied was 1311.34 µg in the sublingual group and 1593.62 µg in the vaginal group that shows the sublingual group needed lower dose of misoprostol for fetus expulsion in comparison with the vaginal group (p= 0.010).Side effects such as fever, chills, nausea, vomiting, diarrhea, headache and needing to analgesics were compared and we found no significant difference in the two groups (p> 0.05). Totally 74.6% of the sublingual group and 25.4% of vaginal group preferred the sublingual route. No serious complication such as uterine rupture was reported in both groups.

Discussion

Different studies were performed to compare sublingual versus vaginal misoprostol in second-trimester termination, but there were different results about the success rate of pregnancy termination in 24 hours, in 48 hours, the time interval between induction and fetus expulsion and the side effects in both groups.

In TANG ET AL study using 400 µg sublingual and vaginal misoprostol every 3 hours achieved similar success rate in 48 hours in both groups (>90%) but the success rate in 24 hours was significantly higher in the vaginal group (5). But in our study no significant differences were seen in the success rate of fetus expulsion in 24 and 48 hours in both groups. Finally, TANG ET AL`s study suggest that both routs of application are effective in second-trimester termination but, regarding to the side effects and patients acceptability, sublingual misoprostol is a better option.

Results of Delavari`s study, that compared vaginal and sublingual routs by giving 400 µg misoprostol every 6 hours,reported that there were similar effects in second-trimester termination. The median induction to abortion period was 16 hours that is longer than our study(<15 hours) which is maybe due to longer interval between drugs application (4).

Similar toBartusevicus`s study (6), our study demonstrated that induction to abortion period is significantly shorter in the sublingual group and this group needed lower dose of drug for abortion. It can be due to different pharmacokinetics profile of two routes. Because of absent intestinal-hepatic passage in vaginal application, it seems that drug activity and bioavailability is higher in vaginal route (7-10),but one study that investigated pharmacokinetics of vaginal and sublingual misoprostol, demonstrated that maximum plasma concentration was higher in sublingual application (1). Sublingual misoprostol can achievesthe higher peak concentration and bioavailability very quickly. Sustained and long-lasting effect is seen in vaginal absorption (7- 9), but the absorption is disturbed by local factors such as vaginal bleeding (7).

Some previous studies suggested that side effects such as fever , chills, diarrhea and vomiting are more common whit the sublingual route of administration(10,11),but our study was not supported these findings. In our study, similar to Von Hertzen H`s study (12), the side effects were comparable in the two groups.

It seems that sublingual administration is a more preferable way of giving misoprostol (13- 15). In our study,all patients experienced both vaginal and

sublingual routes(misoprostol and placebo) and higher percentage of women preferred the sublingual route (74.6% versus 25.4%).The sublingual route appears to be more convenient and less uncomfortable.

This study concludes although both vaginal and sublingual routes have similar effectiveness and side effects in second-trimester termination, but sublingual route is a better option because of its quicker response and better acceptability.

Acknowledgements

This investigation was based on a thesis submitted by the third author to the Guilan University of Medical Sciences. This study was done with financial support provided by Vice Chancellor of Research Center of Guilan University of Medical Sciences. There is no conflict of interest in this study.

References

1. Cabrera Y, Fernández-Guisasola J, Lobo P, Gámir S, Alvarez J. Comparison of sublingual versus vaginal misoprostol for second-trimester pregnancy termination: A meta-analysis. Aust N Z J ObstetGynaecol 2011; 51:158-65
2. Wildschut H, Both MI, Medema S, Thomee E, Wildhagen MF, KappN. Medical methods for mid-trimester termination of pregnancy. Cochrane Database Syst Rev 2011; 19: CD005216.
3. Ho PC, Blumenthal PD, Gemzell-Danielsson K, Gómez Ponce de León R, Mittal S, Tang OS. Misoprostol for the termination of pregnancy with a live fetus at 13 to 26 weeks.Int J GynaecolObstet 2007; 99Suppl 2:S178-81.
4. Tanha FD, Golgachi T, Niroomand N, Ghajarzadeh M, Nasr R. Sublingual versus vaginal misoprostol for second trimester termination: a randomized clinical trial. Arch GynecolObstet2013;287:65-9.
5. Tang OS, Lau WN, Chan CC, Ho PC. A prospectiverandomised comparison of sublingual and vaginal misoprostol in second trimester termination of pregnancy. BJOG 2004;111:1001-5.
6. Bartusevicius A, Barcaite E, Nadisauskiene R.Oral,Vaginal and sublingual misoprostol for induction of labor. Int J Gynaecol Obstet 2005;91:2-9.
7. Tang OS, Xu J, Cheng L, Lee SW, Ho PC. Pilot study on the use of sublingual misoprostol with mifepristone in termination of first trimester pregnancy up to 9 weeks gestation.Hum Reprod 2002;17:1738-40.
8. Tang OS, Ho PC. Pilot study on the use of sublingualmisoprostol for medical abortion. Contraception. 2001; 64:315-7.
9. Bhattacharjee N, Saha SP, Ghoshroy SC, Bhowmik S, BaruiG.Arandomised comparative study on sublingual versus vaginal administration of misoprostol for termination of pregnancy. Aust N Z J ObstetGynaecol 2008; 48:165-71.
10. 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.
11. Tang OS, Gemzell-Danielsson K, Ho PC. Misoprostol: pharmacokinetic profiles, effects on the uterus and side-effects.Int J GynaecolObstet 2007; 99(Suppl 2): S160–7.
12. Von HertzenH, PiaggioG, WojdylaD, Nguyen TM, MarionsL, OkoevG, et al. Comparison of vaginal and sublingual misoprostol for second trimester abortion: randomized controlled equivalence trial. Hum Reprod2009;24:106-12.
13. Tang OS, Lau WN, Chan CC, Ho PC. A prospectiverandomised comparison of sublingual and vaginal misoprostol in second trimester termination of pregnancy. BJOG 2004; 111:1001-5.
14. Saxena P, Salhan S, Sarda N.Role of sublingual misoprostol for cervical ripening prior to vacuum aspiration in first trimester interruption of pregnancy. Contraception 2003;67:213-7.
15. Singh K, Fong YF, Prasad RN, DongF. Does an acidic medium enhance the efficacy of vaginalmisoprostolfor pre-abortion cervical priming? Hum Reprod 1999; 14:1635-7.