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Original Article

Comparison of sequential vaginal and sublingual misoprostol after a vaginal loading dose for second-trimester abortion

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ABSTRACT

Objective: To evaluate the effects of sequential vaginal and sublingual misoprostol after a vaginal loading dose for second-trimester abortion.
Materials and methods: From January 2006 to December 2011, 173 women received an 800-μg vaginal loading dose of misoprostol. After the loading dose, 103 patients received 800 mg of misoprostol vaginally and 70 patients received 400 mg of misoprostol sublingually every 12 h until the delivery of the fetus.
Results: In the vaginal group, the average abortion time was 1.07 ± 1.29 days; that was 0.82 ± 0.66 days in the sublingual group. Sequential sublingual misoprostol after a vaginal loading dose of 800 mg with an administration interval of 12 h had a similar abortion rate and time to abortion. In addition, this protocol reduced unnecessary digital pelvic examinations and speculum examinations.
Conclusion: This sequential sublingual misoprostol regimen might be a suitable regimen for mid-trimester abortion.

Introduction

Misoprostol is a prostaglandin E1 methyl ester that was originally described for the prevention of peptic ulcers. Misoprostol can also stimulate myometrial contractions and cervical ripening and it was first used to induce labor with a live fetus in 1991. Because misoprostol is inexpensive, easily available and stable at room temperature, it is now widely used for the off-label induction of abortion and labor or the treatment of postpartum hemorrhage [1–3].

Misoprostol was originally licensed for oral administration. However, for the purpose of terminating pregnancy, vaginal administration is more effective than oral route. Further potential administration routes include sublingual and buccal administration. Different doses and intervals of misoprostol were reported for mid-trimester termination [4–7]. According to the pharmacokinetics of different routes of administration, sublingual administration results in a higher peak serum concentration and increased bioavailability in comparison to vaginal administration [8,9]. Misoprostol also has the advantages of convenience and less discomfort for patients. Therefore, patients prefer sublingual administration for mid-trimester termination. Tang et al. showed the success rate after 24 h was significantly lower in the sublingual group (72%) than in the vaginal group (86%), especially among nulliparous women [3]. The result is due to local vaginal suppository of misoprostol might have a higher cervical concentration than sublingual systemic use and might induce rapid abortion.

To improve the efficacy of mid-trimester abortion, we designed a prospective clinical trial of sequential vaginal and sublingual misoprostol after a vaginal loading dose to compare the efficacy and safety of these two different regimens. We try to develop an efficient and safe model of misoprostol regimen for mid-trimester termination.

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Materials and methods

From January 2006 to December 2011, 203 pregnant women between 14 and 24 gestational weeks with fetal abnormality were recruited. This study has been carried out at the Department of Obstetrics and Gynecology of MacKay Memorial Hospital. A total of 30 patients who had previous cesarean section or uterine surgery, intrauterine fetal demise, premature rupture of membranes, Bishop score >4 or multiple pregnancies were excluded.

All 173 women were admitted to receive an 800-μg vaginal loading dose of misoprostol. After the loading dose, 103 patients received 800 mg of misoprostol vaginally and 70 patients received 400 mg sublingually every 12 h thereafter until the delivery of the fetus. A complete blood count and informed consent were obtained before the abortion process. Maternal pulse, body temperature and blood pressure were recorded every 4 h and soon after abortion. Pyrexia was defined as a persistent body temperature >38 °C for at least 2 separate checks, and acetaminophen wound be prescribed in such cases. Analgesics in the form of 50 mg of pethidine were administered intramuscularly on the patient's request.

The time to delivery was measured from vaginal loading dose administration to the expulsion of the fetus. The percentage of patients with a duration to delivery within 12, 24 and 48 h was analyzed, and failure of induction was defined as a duration of more than 48 h. Failed cases can be given the option of continuous medical abortion via different routes or other mechanical techniques. Due to the compliant of discomfort caused by pelvic examination, the total numbers of digital pelvic examinations and speculum examinations were also estimated for analysis.

Age, gestational weeks, the number of speculum examinations, the number of digital pelvic examinations, analgesics use, and the time to delivery in the two groups were analyzed using the Student's t test. Success rates (abortion within 48 h), fever, and parity were compared using the Fisher's exact test.

Results

All 173 patients included in this study, the age, gestational week and parity did not differ significantly between the two groups. The average abortion time was 1.07 ± 1.29 days in the vaginal group and 0.82 ± 0.66 days in the sublingual group. The abortion times of nulliparous and parous women were 1.05 ± 0.8 and 1.08 ± days in vaginal group, and 1.02 ± 0.82, 0.65 ± 04 days in sublingual group respectively. Although no significant difference was found, this abortion time was shorter in sublingual group, especial those of parous women. The failure rates were 7/103 (7%) in vaginal group and 5/70 (7%) in sublingual group (Table 1).

Table 1
Comparison of vaginal and sublingual misoprostol after a vaginal loading dose.

	Vaginal group (n = 103)	Sublingual group (n = 70)	p value
Age	32.15 ± 4.68	33.04 ± 4.79	0.22
Gestational week	19.50 ± 3.33	20.05 ± 3.30	0.28
Parous	51 (50%)	31 (44%)	0.76
Time to delivery (days)	1.07 ± 1.29	0.82 ± 0.66	0.10
Nulliparous	1.05 ± 0.80	1.02 ± 0.82	0.84
Parous	1.08 ± 1.65	0.65 ± 0.40	0.08
Abortion within 12 h	57 (55%)	43 (61%)	0.44
Abortion within 24 h	85 (82%)	58 (83%)	0.95
Abortion within 48 h	93% (96)	65 (93%)	0.93
Pyrexia	14 (14%)	10 (14%)	0.90
Analgesics use	63 (61%)	39 (56%)	0.53
Doses of pethidine	0.97 ± 0.98	0.89 ± 0.97	0.58
Speculum examinations	1.54 ± 0.71	1.12 ± 0.47	<0.01
Digital pelvic examinations	2.65 ± 1.86	2.19 ± 1.34	0.04

In addition, pyrexia, analgesics use, and the total dose of pethidine using did not differ significantly between the two groups, either. Nevertheless, the number of speculum examinations was 1.12 ± 0.47, and the number of digital pelvic examinations was 2.19 ± 1.34 were significantly lower in the sublingual group.

In this study, 100 patients, including 57/103 (55%) in the vaginal group and 43/70 (61%) in the sublingual group, aborted successfully after a single vaginal loading dose of 800 μg misoprostol without a further sequential dose. There were 73 cases, including 46 in the vaginal group and 27 in the sublingual group, required a sequential dose. 39 (85%) patients in vaginal group and 22 (81%) in sublingual group have successful abortion within 2 days. Age, gestational week, parity, pyrexia, analgesics use, and the total dose of pethidine did not differ significantly in the two groups with sequential doses. However, is significantly different in the number of speculum examinations of 2.46 ± 0.91 in the vaginal group and 1.37 ± 0.79 in the sublingual group. The sublingual group had fewer speculum examinations. But the number of digital examinations did not show significant difference in both groups (Table 2).

Discussion

Dinoprostone is a prostaglandin E2 vaginal tablet that is used for the induction of labor. This tablet can be dissolved and absorbed via the vagina and works by binding and activating the prostaglandin E2 receptor. Misoprostol is designed as an oral prostaglandin E1 tablet rather than a vaginal suppository. However, a number of different misoprostol regimens are used for mid-trimester termination, but no standard regimen of doses, intervals and administration routes is currently available. Vaginal and sublingual administration have a shorter duration to abortion than the oral route [10]. During vaginal administration, the tablet sometimes does not dissolve, even when combined with wet gauze, which indicates that vaginal administration may result in unstable pharmacokinetics and efficacy. On the other hand, after sublingual administration, misoprostol can be rapidly absorbed through the oral mucosa. A pharmacokinetics study revealed that sublingual administration had a higher peak serum concentration than those of vaginal and oral routes. In conclusion, sublingual administration has great potential for medical abortion [8].

Sublingual administration is more convenient than vaginal administration and also has significantly higher patient satisfaction and preference [3,11]. Moreover, recent clinical trials demonstrated similar outcomes after vaginal and sublingual administration [10]. A study reported a lower successful abortion rate within 24 h after sublingual administration in comparison to vaginal administration

Table 2
Comparison of the efficiency of sequential vaginal and sublingual misoprostol after a vaginal loading dose.

	Vaginal group (n = 46)	Sublingual group (n = 27)	p value
Age	31.76 ± 4.60	33.67 ± 3.98	0.078
Gestational week	19.98 ± 2.92	21.16 ± 2.81	0.09
Parous	17/46	10/27	0.99
Time to delivery (days)	1.59 ± 1.69	1.32 ± 0.78	0.36
Nulliparous	1.34 ± 0.82	1.49 ± 0.85	0.54
Parous	2.02 ± 2.56	1.02 ± 0.55	0.14
Success rate within 48 h (%)	39 (85%)	22 (81%)	0.48
Pyrexia	7 (15%)	6 (22%)	0.53
Speculum examinations	2.46 ± 0.91	1.37 ± 0.79	<0.01
Digital pelvic examinations	3.59 ± 2.21	3.07 ± 1.57	0.29

We analyzed 46 and 27 cases that received sequential vaginal and sublingual misoprostol, respectively. The results revealed no significant differences between the two groups, except for the number of speculum examinations.

[3]. It showed that a vaginal suppository may have a more local effect than systemic use via oral or sublingual administration.

As that of Tang et al. showed, the results of our study also revealed that both sequential sublingual and vaginal misoprostol after vaginal loading have similar results. 100 women (58%) of 173 women enrolled in this study, 57 (55%) in the vaginal group and 43 (61%) in the sublingual group, expelled the fetus after a single vaginal loading dose of 800 mg of misoprostol. In addition, 85 (82%) women in the vaginal group and 58 (83%) women in the sublingual group had abortion within 24 h. A total of 143 women had abortion with one vaginal loading dose plus one sequential sublingual or vaginal dose of misoprostol. The dosage of sublingual misoprostol is half that of the vaginal route. However, the success rates were not significantly different. The abortion rate within 48 h was 93% in both groups.

Vaginal administration caused patients' discomfort during speculum examination and wet gauze insertion. Sublingual administration had the benefits of less pelvic examinations and speculum use. In this study, the sublingual group had significantly lower rates of pelvic examination and speculum examination.

The administration interval had been designed as 12 h to prevent adverse effects. The pyrexia rate was only 14% in each group, which is lower than other reports. In addition, the administration interval was longer than those used in other trials of 3-h to 6-h interval. The abortion rates and the time to abortion between the study and others were similar. Sequential sublingual misoprostol after a vaginal loading dose of 800 mg with an administration interval of 12 h had low rates of pyrexia and similar abortion rates and time to abortion. The vaginal loading dose caused a local effect, and sequential sublingual administration was easy and avoided unnecessary pelvic examinations. This sequential sublingual regimen might be an alternative regimen for mid-trimester abortion.

Conflict of interest

All authors declare that that have no conflict of interest.

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