Misoprostol and first trimester pregnancy termination

X. Grapsas, V. Liberis, G. Vassaras, P. Tsikouras, G. Vlachos, G. Galazios

Department of Obstetrics and Gynecology, Democritus University of Thrace, General Hospital of Alexandroupolis, Alexandroupolis (Greece)

Summary

Objective: To investigate the efficacy of vaginal administration of 800 μg misoprostol as a single dose without performing post expulsion systematic curettage in first trimester pregnancy termination. *Method:* 113 women, aged 16-44, who requested first trimester pregnancy termination, received 800 μg of vaginal misoprostol. All examined women were divided into two groups depending on gestation age. The first group included of 67 women with up to nine weeks and the second of 46 with up to 12 weeks of pregnancy. *Results:* Abortion occurred within 24 hours and was completed in 74.3% of the cases. The mean induction-abortion interval was 5.9 ± 1.7 hours (median 5.5 hours). Side-effects were experienced by 24 women (21.2%). There was no significant difference between groups in the success rate, induction-abortion interval, number of previous deliveries and side-effects. *Conclusion:* Misoprostol is an effective agent for first trimester medical termination.

Key words: Misoprostol; Prostaglandins; Medical abortion; Surgical abortion; Uterine bleeding.

Introduction

Misoprostol is a synthetic prostaglandin E1 analogue that is commonly used for medical abortion. It can given orally vaginally and sublingually [1]. It was first developed in 1973 for the prevention or treatment of peptic ulcer disease caused by prostaglandin synthetase inhibition. Because this methyl ester of prostaglandin E1 is an effective uterine myometrium stimulant and binds selectively to EP-2/EP-3 prostanoid receptors, misoprostol was quickly recognized as a potential therapeutic alternative to other available conventional prostaglandins [2, 3].

Abortion is one of the most common surgical applications worldwide. At present most patients and physicians seem to prefer surgical pregnancy termination [4]. Medical abortion is an alternative to the surgical procedure. Perceived benefits of medical abortion are the avoidance of surgery with its discomfort and morbidity and the increased privacy [5, 6]. In developing countries medical methods of abortion hold the potential to improve women's health [7, 8]. Several medical methods for first trimester pregnancy termination have been developed by using misoprostol alone or in combination with methotrexate or mifepristone [9, 10].

The aim of this study was to certify the efficacy and safety of vaginal administration of 800 μg misoprostol as a single agent and single dose without performing post expulsion systematic curettage in first trimester pregnancy termination (7-12 weeks of gestation).

Patients and Methods

From January 2004 to December 2005, 135 women (age range 18-44 years; mean age 29 years) who requested medical termination of a pregnancy at 7-12 (mean 9) weeks of gestation were recruited for a prospective study. All of these women complied with the following inclusion criteria: ≥ 18 years of age, gestational age from 7 to 12 weeks, informed consent for medical abortion and for surgical abortion, and adequate hematological and biochemical profiles.

Twenty-two women were excluded from the study. Exclusion criteria were: hemoglobin level < 10 mg/dl, blood pressure ≥ 160/90 mmHg, poor general health for any cause, prior uterine bleeding, current genital infection and previous intolerance or allergy to prostaglandins.

The remaining 113 patients were divided into two groups depending on gestational age. The first group included participants from 7 to 9 weeks of gestation and the second more than nine weeks of gestation.

Gestational age was measured from the first day of the last menstrual period according to menstrual history and vaginal or abdominal ultrasonography. Blood samples were obtained to determine hemoglobin, hematocrit, blood group and Rhesus factor.

All women included were administered a single dose of 800 μg (four 200 μg tablets) by the vaginal route. The tablets were all placed in the left and right vaginal fornix, and were previously moistened with two to three drops of water for injection. If no abortion occurred in the next 24 hours, surgical abortion followed. An injection of 600 μg of paracetamol was given if needed to relieve pain. Patients were frequently examined for evaluation of the referred cramping, the abortion process, and the degree of bleeding. For these reasons the patients were hospitalized at least for 24 hours. Transvaginal ultrasound (TVS) was performed to confirm if abortion occurred.

Success was defined as complete evacuation of the endometrial cavity and cervix channel of the products of conception, whereas failure was considered as lack of abortion within 48 hours or as incomplete abortion. Failure led the patient to curettage.

Patients were also evaluated seven days after the expulsion or curettage by TVS and clinical examination of vaginal bleeding, and degree of pain and pelvic discomfort. Blood sample tests were also performed if considered necessary. All women were prescribed antibiotic and ergonovine treatment for three days after the abortion.

Revised manuscript accepted for publication April 23, 2007

Pearson's chi-square test was used to ascertain the independence between variables and obtained results. For comparison of hemoglobin levels before and after the application of misoprostol the t-test was used. In all cases $p < 0.05$ was considered significant. The study was approved by the Ethics Committee of the University Hospital of Alexandroupolis.

Results

The characteristics of the 113 subjects are presented in Table 1. Abortion occurred in all cases and was complete in 84 (74.3%). Suction curettage was performed in 17 women in group 1 (25.4%) and in 12 women in group 2 (26.1%). Bleeding began within 3.5 ± 0.75 hours (median 3.5 hours; range 1 to 5.5 hours) after misoprostol administration. The mean (± SD) induction-abortion time interval was 5.9 ± 1.7 hours (median 5.5 hours).

Table 1. — *Socio-demographic characteristics*.

Parameters studied		All cases cases	7-9 weeks group	10-13 weeks group	Significance between the 2 groups (p)
Religion-Christian		34.5%	31.3%	39.1%	0.173 (chi square test)
Religion-Muslim		65.5%	68.7%	60.9%	
History of deliveries	0	41.6%	38.8%	45.7%	
	1	26.5%	28.4%	23.9%	
	2	16.8%	16.4%	17.4%	0.618 (Chi square test)
	3	9.7%	11.9%	6.5%	
	4	3.5%	4.5%	2.2%	
	≥ 5	1.8%	0%	4.3%	
Delivery	0	41.6%	38.8%	45.7%	
VG	VG	48.7%	50.7%	45.7%	0.393 (Chi square test)
CS	CS	7.1%	9%	4.3%	
	VG+CS	2.7%	1.5%	4.3%	
Age		29.19 (SD 6.73)	28.58 (SD 6.65)	30.07 (SD 6.83)	0.252 (t-test)

VG = vaginal; CS = cesarean

No statistically significant correlation was obtained concerning success/failure rates and any patient characteristics (Table 2). Moreover there were no significant differences between the two study groups regarding the success rate ($p = 0.37$), the induction-abortion interval ($p = 0.47$), the parity ($p = 0.62$) and the intensity of bleeding ($p = 0.24$).

Table 2. — *Success-failure rate in patients*.

7-9 weeks	Incomplete abortion	17	25.4%
	Complete abortion	50	74.6%
9-12 weeks	Incomplete abortion	12	26.1%
	Complete abortion	34	73.9%
			p = 0.37

Incidence of all reported side-effects is shown in Table 3. The two groups did not differ significantly with respect to side-effects (incidence of pain, nausea, vomit, fever, headache, diarrhea and chill) ($p = 0.871$). None of the women presented severe bleeding. Only 4.4% of the patients asked for paracetamol to relieve pain. Incidence and severity of pain did not correlate with gestational age. We also did not observe significantly statistical differences concerning the amount and duration of post-expulsion vaginal bleeding. Finally there was no statistically significant correlation in decreased hemoglobin levels between the two studied groups (Table 4).

Table 3. — *Side-effects observerd*.

Side-effects	Group 1 (7-9 weeks)	Group 2 (> 9-13 weeks)	Significance between the 2 groups (p)
Total	25.4%	15.2%	0.871
Chills	13.4%	6.5%	0.448
Nausea	11.9%	2.2%	0.695
Pelvic pain - mild	83.6%	78.3%	–
Pelvic pain - moderate	10.4%	17.4%	0.911
Pelvic pain - severe	6%	4.3%	–
Elevated temperature > 38°C	4.5%	2.2%	0.789
Headache	3%	4.3%	–
Vomiting	3%	2.2%	0.829
Diarrhea	0%	2.2%	–
Mild bleeding	80.6%	89.1%	–
Severe bleeding	19.4%	10.9%	0.243

Table 4. — *Hemoglobin levels before and after abortion*.

	No.	Mean	Median	SD	
Hb (before)	113	12.648	12.800	1.034	p = 0.24
Hb (after)	113	12.256	12.400	1.049	

SD = standard deviation.

On the seventh day of examination none of the women who medically aborted had severe bleeding or pelvic distress, or any other discomfort. TVS examination showed no remains in the uterine cavity.

Discussion

Few drugs have been found to have as many potential applications in obstetric practice as misoprostol in the last 20 years [11]. For first trimester medical abortions misoprostol has been used extensively either alone or in combination with mifepristone and/or methotrexate. However, Greece is a country with no access to mifepristone and the use of methotrexate has many side-effects [12]. The main advantage of medical abortion is that it allows women to avoid the risks of surgery and anesthesia [13]. However the need for hospitalization, length of the process and time of bleeding, the multiple examinations and the potential for an after-hours intervention for bleeding or infection are perceived by many patients as negative [14]. On the contrary there are studies of women who have undergone medical pregnancy termination showing that they preferred medical over surgical termination [15, 16].

In our prospective study we found that medical termination of pregnancy using misoprostol alone was 74.6% in women with gestational age between seven and nine weeks of gestation and 73.9% in women with gestational age between nine and 12 weeks of gestation. Our results are not in contrast to those of previous studies that have shown that the efficacy of vaginally administered misoprostol is not affected by the duration of pregnancy [17].

Some authors have reported higher success rates (92% and 93.6%) with repeated dosing 48 hours apart for three vaginal doses of 800 μg [18]. In summary the studies on misoprostol alone for pregnancy termination indicate a success rate between 66% and 94% [19, 20].

In our study the overall incidence of side-effects was 25.4% lower than the respective one in other studies (34.9%-58.7%) [21, 22]. The two groups did not differ significantly with respect to side-effects, and none of the patients presented heavy bleeding – mainly due to the fact that a single dose of 800 μg of misoprostol was used. The episodes of bleeding were also shorter.

In conclusion this study showed that the abortive efficacy of a single vaginal dose of 800 μg of misoprostol is slightly lower than repeated administration of the drug but a significantly decreased incidence of observed side-effects established the safety of the method. It is clear that misoprostol alone is an inexpensive, readily available option for medical abortions as long as follow-up and a surgical termination back-up option are guaranteed. More detailed multi-center studies on the use of the method should be carried out to determine any aspects not yet clarified.

References

[1] Oi Shan Tang, Pak Chung Ho: "The pharmacokinetics and different regimens of misoprostol in early first trimester medical abortion". *Contraception,* 2006, *74*, 26.
[2] Broekhuizen F.F.: "Misoprostol, its use in obstetrics and gynecology". *Curr. Probl. Obstet. Gynecol. Fertil.,* 2000, *23,* 193.
[3] Templeton A.: "Misoprostol for all?". *Br. J. Obstet. Gynecol.,* 1998, *105,* 937.
[4] Baird D.T., Grimes D.A., Van Look P.F.A. (eds.). Modern Methods of Inducing Abortion. London, Blackwell, 1995.
[5] Creinin M.D., Park M.: "Acceptability of medical abortion with methotrexate and misoprostol". *Contraception*, 1995, *52,* 41.
[6] Wiebe E.R.: "Choosing between surgical abortions and medical abortions induced with methotrexate and misoprostol". *Contraception,* 1997, *55*, 67.
[7] The Population Council: "Medical methods of early abortion in developing countries. Consensus statement". *Contraception*, 1998, *58,* 257.
[8] Cheng L.: "Medical abortion in early pregnancy: experience in China". *Contraception*, 2006, *74*, 61.
[9] Creinin M.D., Carbonell J.L., Schwartz J.L., Varela L., Tanda R.: "A randomized trial of the effect of moistening misoprostol before vaginal administration when used with methotrexate for abortion". *Contraception,* 1999, *59,* 11.
[10] Bartley J., Brown A., Elton R., Baird D.T.: "A double blind randomized control trial between vaginal gemeprost and misoprostol in combination with mifepristone for induction of abortion in early pregnancy". *Hum. Reprod.*, 2001, *16,* 2098.
[11] Hofmeyr G.J.: "Misoprostol in obstetrics and gynecology-unregistered, dangerous and essential". *S. Afr. Med. J.,* 1998, *88*, 535.
[12] Zikopoulos K.A., Papanickolaou E.G., Kalantaridou S.N.: "Early pregnancy termination with vaginal misoprostol before and after 42 days gestation". *Hum. Reprod.,* 2002, *17,* 3079.
[13] Grimes D.A.: "Medical abortion in early pregnancy: a review of evidence". *Obstet. Gynecol.,* 1997, *89,* 790.
[14] Harvey S.M., Beckman L.J., Castle M.A., Coeytaux F.: "Knowledge and perceptions of medical abortion among potential users". *Fam. Plann. Perspect.,* 1995, *27,* 203.
[15] Winikoff B.: "Acceptability of medical abortion in early pregnancy". *Fam. Plann. Perspect.,* 1995, *27,* 142.
[16] Jain J.K., Harwood B., Mecksroth K.R., Mishell D.R. Jr: "Early pregnancy termination with vaginal misoprostol combined with loperamide and acetaminophen prophylaxis". *Contraception,* 2001, *63,* 217.
[17] Grimes D.A., Singh S., Romero M., Ganatra B., Okonofoua F.E., Iqbal H.S.: "Unsafe abortion the preventable pandemic". *Lancet,* 2006, *368*, 1908.
[18] Carbonell J.L.,Varela L.,Velazco A., Fernandez C.: "The use of misoprostol for termination of early pregnancy". *Contraception,* 1997, *55,* 165.
[19] Carbonell J.L., Varela L.,Velazco A., Fernandez C., Sanchez C.: "The use of misoprostol for abortion at less than 9 weeks gestation". *Eur. J. Contr. Rep. Health Care*, 1997, *2,* 181.
[20] Bugalho A., Faundes A., Jamisse L., Usfa M., Maria E., Bique C.: "Evaluation of the effectiveness of vaginal misoprostol to induce first trimester abortion". *Contraception*, 1996, *53,* 244.
[21] Ho P.C., Ngai S.W., Liu K.L. *et al.*: "Vaginal misoprostol compared with oral misoprostol in termination of second trimester pregnancy". *Obstet. Gynecol.,* 1997, *90,* 735.
[22] Carbonell J.L., Varela L., Velazco A., Cabezas E., Tanda R., Sanchez C.: "Vaginal misoprostol for late first trimester abortion". *Contraception,* 1998, *57,* 329.

Address reprint requests to:
P. TSIKOURAS, M.D.
Lysimachou/Petrina
6 Km Alexandroupolis/Makri
Box 16
68100 Alexandroupolis (Greece)
e-mail: ptsikour@med.duth.gr