Termination of Second-Trimester Pregnancy with Intracervicovaginal Misoprostol

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Abstract

To evaluate the efficacy and side effects of intracervicovaginal misoprostol in termination of second-trimester pregnancy in women with live fetuses. A total of 50 pregnant women between 14 and 27 week's gestation undergoing termination of pregnancy for medical, obstetrical and genetic reasons were recruited to receive 200 ug misoprostol gel administered intracervicovaginally every 12 hours.

The rates of sucessful abortions within 24 hours and 48 hours were 54 per cent and 92 per cent respectively. The mean time from induction to abortion was 27.5 hours. The rate of complete abortion, defined as the passage of the fetus and placenta without operative assistance was 80 per cent. Side effects were fever (8%), nausea and vomitting (6%) and diarrhea (2%). Thirty one patients (62%) required meperidine as analgesia. Two patients (4%) had postpartum hemorrhage.

Intracervicovaginal misoprostol is an effective, cheap, safe and relatively convenient method for termination of second-trimester pregnancy with a live fetus.

Misoprostol, a synthetic 15-deoxy-16 hydroxy-16 methyl analogue of naturally occuring prostaglandin E1 is primarily used for prevention and treatment of gastroduodenal ulcers induced by the ingestion of nonsteriodal antiinflammatory agents. Previous studies have shown that misoprostol administered vaginally can produce cervical ripening and uterine contraction in late pregnancy and no severe adverse effects have been noted[1,2]. When given in the second trimester of pregnancy, intravaginal misoprostol in doses ranging from 800 to 1,600 ug was remarkably effective in achieving safe interruption of pregancy without any significant complications[3]. The study by Jain and Mishell indicated that vaginal administration of 200 ug of misoprostol every 12 hours was an effective and convenient way to induce abortions during the second trimester of pregnancy in women with

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either an intrauterine fetal death or a live fetus. The abortion rates were 89 per cent and 100 per cent within 24 hours and 38 hours after dosing. No severe adverse effects were reported[4].

Concerning the route of administration, it was found that in cases of highly unfavorable cervix, the intracervical application was significantly more effective than the intravaginal. But when studying the intrauterine pressure, it was confirmed that the intravaginal route could induce more myometrial activity than the intracervical. Therefore, we decided to give misoprostol concurrently by intracervical and intravaginal route to induce second-trimester abortion. Unlike the other reports, we administered misoprostol in the form of gel in which drug distribution and absorption would be better than the tablet form. Furthermore, the market price of 200 ug misoprostol (Cytotec; Searle, Illinois, U.S.A.) in our University Hospital pharmacy is equivalent to only US $ 0.5, and the drug does not require a cool temperature for storage, compared with other prostaglandin analogues.

The purpose of this study was to evaluate the efficacy and adverse effects of 200 ug misoprostol administered intracervicovaginally every 12 hours for termination of second-trimester pregnancy in women with live fetuses.

MATERIAL AND METHOD

A total of 50 pregnant women between 14 and 27 weeks' gestation with medical, obstetrical and genetic indications for pregnancy termination were enrolled to enter the study at the Department of Obstetrics & Gynaecology, Chiang Mai University Hospital, during the period July 1994 to August 1995. Criteria for exclusion from the study included previous uterine scar, cervical Bishop score >4, presence of uterine contraction or rupture of the membranes, lower genital tract infection and maternal history of hypersensitivity to prostaglandins. The study was approved by the Research Ethical Committee of the University Hospital, and informed consent was obtained from each patient.

For preparation of misoprostol gel, one tablet (200 ug) of misoprostol was crushed to powder in a sterile container and mixed with 5 ml of sterile hydroxyethyl cellulose gel (K-Y Jelly, Johnson & Johnson, New Jersey, U.S.A.). The mixture was drawn up into a sterile 10 ml syringe which was connected to a nylon feeding tube 8" 5FR. After exposure of the cervix by vaginal speculum, 2.5 ml of misoprostol gel was applied within the endocervical canal. The instillation was accomplished during the slow continuous withdrawal of the tube, starting just below the internal os. After removal of the vaginal speculum, the remaining gel was squirted into the posterior fornix and a further 2 ml of air was pushed to empty the contents in the tube.

The patient was left in supine position for 1 hour. Vital signs and side effects were monitored every 2 hours. The progression of labor was assessed by cervical examination prior to subsequent dosing. Meperidine 50-100 mg was given on demand as narcotic analgesic.

Complete abortion was defined as the expulsion of both the fetus and placenta without any additional operative procedure. If the products of conception were not completely expelled or had to be instrumentally or manually evacuated, the condition was considered to be an incomplete abortion. Treatment success was defined as abortion which occurred within 48 hours after the initial gel insertion and no serious adverse effect was noted.

The baseline date and outcome variable were installed in the microcomputer program SPSS PC+ for analysis. Statistical tests were conducted by using the chi square and the Student's *t* test as appropriate to examine the difference and were regarded as significant at $P<0.05$.

RESULTS

The characteristics of the patients are presented in Table 1. Twenty four and 20 patients were nulliparous and primiparous respectively. The indications for termination of pregnancy are shown in Table 2. Congenital anomalies included 13 fetuses with homozygous alpha thalassemia 1 (hydrops fetalis), 3 fetuses with beta thalassemia major and 1 fetus with bata thalassemia E which were prenatally diagnosed by fetal blood hemoglobin typing from cordocentesis. Six patients had fetuses with severe anomalies of the central nervous system detected by ultrasonographic examination. Abnormal chromosome obtained by amniocentesis were found in 3 fetuses which were trisomy 18, trisomy 21 and triple x syndrome. The remaining one patient had a fetus with large omphalocele.

Forty two patients (84%) were delivered within the first 36 hours, 46 (92%) within the first 48 hours. Only 4 patients (8%) required more than

Table 1. Characteristics of the 50 patients.

Characteristics	Mean value	SD*	Range
Age (years)	28.0	6.6	16-40
Parity	0.6	0.7	0-2
Gestational age (weeks)	20.5	3.8	14-27

*SD = standard deviation

Table 2. Indications for pregnancy termination.

Indications	Number	%
Congenital amonalies	27	54
Uncontrolled severe hypertension	1	2
HIV infection*	19	38
Others*	3	6

HIV = Human immunodeficiency virus
Others = Mental retardation, radiation exposure, first-trimester rubella infection

Table 3. Interval from gel insertion to abortion.

Interval (Hours)	Number	%
≤ 12	8	16
> 12-24	19	38
> 24-36	15	30
> 36-48	4	8
> 48	4	8

Table 4. Interval from gel insertion to abortion by parity and gestational age.

Factors	Number	Interval (Mean±SD) (h)
Parity		
Nulliparous	24	36.7 ± 25.9
Parous	26	22.0 ± 10.2
Gestational age		
14-20	27	25.5 ± 17.4
21-27	23	29.8 ± 23.5

48 hours in which 2 were HIV patients (18 and 20 weeks' gestation) the other two were patients with hydropic fetus and anencephalic fetus (22 and 27 week's gestation respectively) (Table 3). No other abortion techniques were employed in these patients. The mean time from induction to abortion was 27.5 hours. A comparison between nulliparous and parous women demonstrated a significantly shorter abortion time in the parous group compared to the nulliparous (P = 0.03). The interval from gel insertion to delivery was shorter in women with earlier than those with later gestational age, but the difference was not of statistical significance (P = 0.6) as shown in Table 4.

The rate of complete abortion was 80 per cent. The remaining patients underwent endometrial curettage if attempt to manually remove the placenta failed. An estimated blood loss of more than 500 ml was observed in 2 patients each caused by uterine atony and retained placenta. No severe side effects were seen, 4 patients (8%) had fever (temperature ≥ 38°C) resolved by paracetamol ingestion. Nausea and vomiting were noted in 3 patients, who responded to metoclopramide injection. Diarrhea was found in one patient which could be treated by diphenoxylate. Uterine pain necessitating meperidine as analgesia occurred in 31 patients (62%). Eighteen of 24 nulliparous women (75%) needed narcotic analgesia when compared with 13 of 26 parous women (50%). However, the difference did not reach statistical significance (P = 0.06). Requirement for meperidine was noted in 16 of 27 women (59.3%) and 15 of 23 women (65.2%) with earlier (14-20 weeks) and later (21-27 weeks) gestational age respectively (P = 0.92).

DISCUSSION

Abortion techniques in the second trimester of gestation can be generally divided into medical and surgical. The former is associated with a high incidence of gastrointestinal side effects and the latter with serious complications of uterine perforation, hemorrhage and infection. Currently, medical abortion with various forms of synthetic prostaglandins is preferable to dilatation and evacuation of the uterine cavity or intra-amniotic infusion of hypertonic solution. Local administration of either PGE1 or PGE2 in the endocervical canal or the vaginal canal is the most widely used to produce both cervical ripening and uterine contraction. Such treatment has been accepted as an effective, safe and non-invasive method to induce second-trimester abortion in women with either intrauterine fetal death or a live fetus[3-6].

The results of the present study show that intracervicovaginal administration of 200 ug of misoprostol every 12 hours is a relatively effective

and safe method for termination of second-trimester pregnancy. Ninety two per cent of patients achieved abortion within 48 hours after gel application. The success rate was less than that reported by Jain and Mishell using the same dose and interval of misoprostol but applied in the form of tablets in the posterior vaginal fornix[4]. The abortion rates in their series were 100 per cent within 38 hours after dosing[4]. The difference between the results of the two studies can be explained by a difference in the study population. Our study included only patients with live fetuses and unfavorable cervix while the other recruited cases with either a dead or a live fetus and no cervical status was mentioned. It was found that patients with an intrauterine fetal death usually aborted earlier than those with a live fetus[4]. The abortion time in parous women, in this study was significantly shorter than in the nulliparous. This may be due to the fact that the cervix of parous woman is more favorable and easy to efface and dilate than that of the nulliparous.

In this study, the complete abortion rate was 80 per cent. Other investigators have reported a similar success[7]. We did not routinely perform endometrial curettage after all second-trimester abortions as suggested by some authors[3,4].

The side effects of intravaginal misoprostol at this dosage were neither frequent nor severe, accordingly we did not premedicate the patients with antiemetic, antidiarrheal and antipyretic agents before induction of abortion. Such pretreatment was considered necessary for patients receiving larger doses of PGE2 because of the high frequency of gastrointestinal and pyrogenic side effects associated with PGE2. High incidences of fever (63%), vomiting (33%) and diarrhea (30%) in association with PGE2 (20 mg intravaginally) were reported despite such premedication[4].

Analgesic requirement for uterine pain in this study was somewhat high, similar to the other study[4]. No difference was observed in demand for analgesic between parous and nulliparous women or women with earlier and later gestational ages.

Thus far, no data on pharmacodynamics of intracervical and intravaginal misoprostol are available. Clinical data on oral misoprostol show that it is well tolerated and has few systemic side effects, mainly gastrointestinal[8]. At present, the dosage and frequency of misoprostol administration are still varied in each report, which need further investigation. This study presents our experience in giving misoprostol at a dosage of 200 ug in the form of gel administered intracervicovaginally every 12 hours to terminate second-trimester pregnancy in women with live fetuses.

In summary, intracervicovaginal administration of misoprostol is an effective, cheap, safe and relatively convenient method for induction of abortion in second-trimester pregnancy with a live fetus.

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การยุติการตั้งครรภ์ในไตรมาสที่สองโดยการสอดยามิโสโปรตอล ทางปากมดลูกและช่องคลอด

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เพื่อประเมินประสิทธิภาพและผลข้างเคียงของการสอดยา misoprostol ทางปากมดลูกและช่องคลอดในการยุติการตั้งครรภ์ในไตรมาสที่สองที่ทารกยังมีชีวิต ได้สอดยา misoprostol gel 200 ไมโครกรัม เข้าทางปากมดลูกและช่องคลอดทุก 12 ชั่วโมง เพื่อยุติการตั้งครรภ์ในสตรี 50 ราย อายุครรภ์ระหว่าง 14-27 สัปดาห์ ที่มีข้อบ่งชี้ทางอายุรศาสตร์ สูติศาสตร์ และพันธุศาสตร์ ในการยุติการตั้งครรภ์ อัตราการแท้งสำเร็จภายใน 24 ชม. และ 48 ชม. คิดเป็นร้อยละ 54 และ 92 ตามลำดับ ระยะเวลาเฉลี่ยตั้งแต่สอดยาจนกระทั่งแท้ง = 27.5 ชม. อัตราการแท้งครบ ซึ่งหมายถึง ทารกและรกคลอดออกมาโดยไม่ต้องใช้หัตถการเพิ่มเติม ร้อยละ 80 ผลข้างเคียงได้แก่ ไข้ (ร้อยละ 8) คลื่นไส้อาเจียน (ร้อยละ 6) และท้องเสีย (ร้อยละ 2) ต้องให้ยาแก้ปวด meperidine ร้อยละ 62 มีผู้ป่วยตกเลือดหลังคลอด 2 ราย (ร้อยละ 4) การสอดยา misoprostol ทางปากมดลูกและช่องคลอดเป็นวิธีที่มีประสิทธิภาพ ราคาถูก ปลอดภัย และค่อนข้างสะดวกในการยุติการตั้งครรภ์ในไตรมาสที่สองที่ทารกยังมีชีวิต

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