Misoprostal Use for Therapeutic Abortion in Siriraj Hospital : The Year 2000

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Abstract

Objective : To evaluate the efficacy and the adverse effects of misoprostal usage for therapeutic abortion in Siriraj Hospital.

Study design : Cross-sectional, descriptive study.

Material and Method : A consecutive series of 101 therapeutic abortions was performed in the Department of Obstetrics & Gynecology, Siriraj Hospital in the year 2000. The patients were interviewed for general information and registered, as well as in-patient data. Any adverse events were recorded and collected from the inpatient record file. All data were analyzed statistically.

Results : 42 therapeutic abortions were conducted in association with misoprostal usage. Misoprostal was used for cervical ripening in 8 patients with a good outcome. 31 therapeutic abortions were induced by misoprostal alone regimen. A higher success rate (74.1%) was correlated with higher gestational age. 27 out of 31 cases were second trimester abortion. The induction to abortion interval was 18.0±10.5 hours (range 5-48). No factor, including age, weight, total dose of misoprostal use, nulliparity and viability of the fetus, could be demonstrated to affect the misoprostal activity defined by induction to abortion interval. There was no serious adverse event, except for severe abdominal cramping (26.2%) and fever (14.3%).

Conclusion : Misoprostal alone can be used with caution for abortion induction especially in second trimester abortion.

Key word : Misoprostal, Therapeutic Abortion, Second Trimester Abortion

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Misoprostal, a Prostaglandin E-1 analogue, has been taken orally for the prevention and treatment of gastric ulcers that may result from the long-term use of nonsteroidal anti-inflammatory drugs (NSAID). This drug has recently received more interest in the field of Obstetrics and Gynecology because of its uterotonic and cervical ripening actions. It has been used for many purposes other than the indication it was marketed for by Searle Pharmaceuticals under the brand name Cytotec®. These off-label uses, such as an agent for medical abortion, cervical ripening before surgical abortions, and labor induction, have become more prevalent. In spite of increased use, in some instances, there is not enough sufficient evidence available to support its efficacy (1). Recently, in 2001, the Food and Drug Administration (FDA) of Thailand allowed Misoprostal to be used only under physician prescription in the hospital. So misoprostal can no longer be bought legally over the counter (OTC).

A misoprostal-alone regimen for abortion induction has been used in Thailand, but little research on this use has been published here(2-4). However, the benefits of misoprostal for abortion induction have been well documented in many parts of the world and should not be neglected(5,6). As a result, it may be appropriate to use misoprostal under supervision of a specialist and close observation in places that have sufficient medical facilities to collect information on any serious adverse effects before any standard guidelines can be proposed. Moreover, many different misoprostal regimens are used in practice today.

In Siriraj Hospital, the use of misoprostal for therapeutic abortion has been used for a few years. Therefore, the authors decided to conduct a cross-sectional, descriptive study to evaluate the efficacy and the adverse effects of misoprostal usage for therapeutic abortion in Siriraj Hospital.

MATERIAL AND METHOD

A cross-sectional, descriptive study was established at the reproductive health research center, which belongs to the Department of Obstetrics and Gynecology, Siriraj Hospital. A consecutive series of 101 pregnant women with pregnancies less than 28 weeks of gestation underwent therapeutic abortions in the year 2000. All pregnant women who came for pregnancy termination had received authorization by the Abortion Committee of Siriraj Hospital, with medical, obstetrical or genetic indications for either the mother or the fetus.

Following appropriate counseling, informed consent forms were signed by all pregnant women before performing the pregnancy termination. All patients were admitted for care before and after the abortion under the supervision of the attending ward staff. The gynecologist, taking into the consideration the safety of the patient, determined the method for pregnancy termination individually.

After the product of conception was passed on the ward and appeared to be complete, no further interventions were undertaken. Patients, who did not pass the placenta or retained any product after 1 hour following expulsion of the fetus, would be prepared for evacuation and curettage. Abortion success was defined as complete abortion with no additional operative procedures.

All women were offered a follow-up appointment for the following week for the result of the pathological testing of the product passed, clinical assessment, and offering family planning service for women using temporary contraceptive methods.

The data were analyzed by using SPSS 10.0 for windows program. Descriptive statistics such as percentage, mean, standard deviation, median and range were used to describe general characteristics. The correlation between the factors influenced by misoprostal effect were determined by Pearson's bivariate correlation. The comparison between the study groups was calculated by using the independent sample *t*-test. P-value < 0.05 was considered statistically significant.

RESULTS

During the study period, January 1st to December 31st, 2000, there were 101 therapeutic abortions done in Siriraj Hospital. The mean age of the patients was 29.2 years (range 14-44 years). All were Thai. 84 of 101 cases (83.2%) had finished at least primary school and 9 patients (8.9%) had graduated from a university.

Twenty-nine patients (28.7%) were primigravid but the mode of the gravid (42.6%) was second pregnancy (range 1-5), 63 patients (62.4%) had a previous delivery and 34 patients (33.7%) had a previous history of abortion. The mean gestational age was 18 weeks (range 6-27 weeks).

There was one death because of anesthetic complications in a patient with primary pulmonary hypertension.

23 patients (22.8%) had abortions in the first trimester and the other (77.2%) had abortions in the second trimester or later. Table 1 shows the general characteristics of all the patients.

The ratio of maternal and fetal indication for pregnancy terminations are shown in Fig. 1. The common maternal indications were rape, and severe maternal diseases such as cardiovascular disease and carcinoma. Severe cardiovascular diseases included primary pulmonary hypertension, atrial septal defect with Eisenmenger syndrome, ventricular septal defect with pulmonary hypertension and severe mitral valve regurgitation. Other maternal diseases included giant cell tumor, Hodgkin's Lymphoma, carcinoma of the cervix, systemic lupus erythematosus and major depressive neurosis.

Intrauterine fetal death was the leading cause of fetal indication followed by fetal anomalies, not compatible with life, such as anencephaly, cystic hygroma and bilateral renal agenesis.

When the method for termination of pregnancy was specified, some correlation with the gestational age of the pregnancy could be made as in Table 2.

For first trimester abortions, surgical techniques were most commonly used (78.3%). All were uterine curettage. 8 out of 18 cases used misoprostal

Table 1. General characteristics.

Characteristic	First trimester (n=23)	Second trimester (n=78)
Age (mean ± SD) (years)	29.26 ± 6.20	29.18 ± 6.78
Weight (mean ± SD) (kg)	53.80 ± 10.31	53.48 ± 7.16
Gestational age (mean ± SD) (weeks)	10.35 ± 2.66	20.31 ± 3.3
Gravidity (median) (range)	2 (1-5)	2 (1-5)
Parity (median) (range)	1 (0-2)	1 (0-3)
Previous abortion (median) (range)	0 (0-3)	0 (0-2)
Period of time since last pregnancy (mean ± SD) (months)	61.22 ± 55.97	39.97 ± 39.85

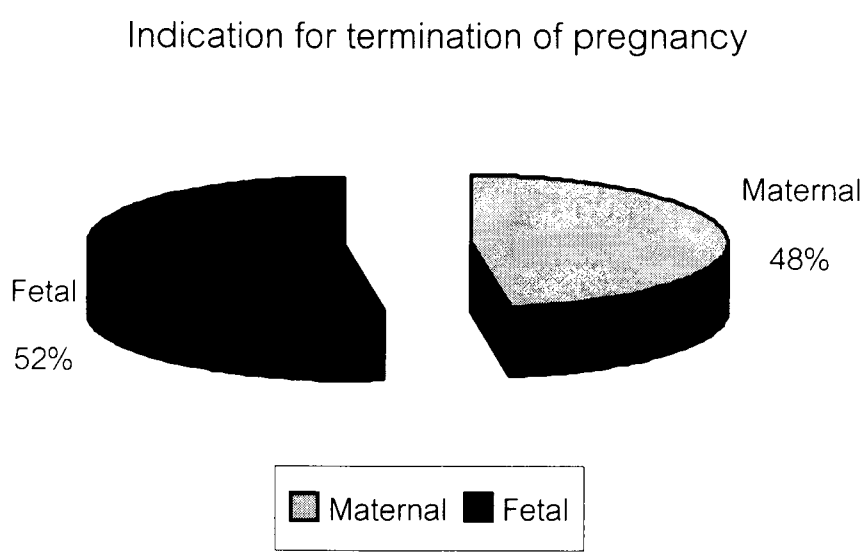

Fig. 1. Ratio for maternal and fetal indication for therapeutic abortions in the year 2000 at Siriraj Hospital.

for cervical priming. 400-microgram vaginal suppositories were commonly used. The minimum dosage was one 200-microgram vaginal suppository before the operation, and the maximum dosage was one 800-microgram vaginal suppository daily for 3 days. Median duration of cervical priming was 12 hours (range 10-72 hours). Concerning misoprostal use for abortion induction alone in first trimester abortion, 3 of 4 cases failed to expel the conceptive product and uterine curettage had to be done.

In contrast, medical abortion was used more often for second trimester abortions (94.9%) and misoprostal was used for 30 cases of medical abortion (38.5%). For the misoprostal alone regimen, the median of total dosage was 400 micrograms (range 100-1200 micrograms), by placing misoprostal half to two tablets (200 microgram per tablet) in the posterior fornix for a single dose or repeating a dose every 4-24 hours. The induction to abortion interval was 18.0±10.5 hours (range 5-48). 20 out of 27 (74.1%) had successful complete abortion without any surgical procedure.

No serious adverse effects were seen with misoprostal. Severe abdominal cramping and fever with chills were reported in 26.2 and 14.3 per cent of women respectively.

Overall, including both first and second trimester abortion, misoprostal alone regimen was used in 31 therapeutic abortions. 21 out of 31 (67.7%) completed the abortion process without any additional surgical procedure. When considering the success and failure of misoprostal alone regimen, it was found that only the gestational age of the pregnant women had an effect on the success rate of the misoprostal alone regimen as shown in Table 3.

There was no statistical difference between the induction to abortion time in the group of intrauterine fetal death and viable fetus by using the independent sample t test, as well as, for the group of pregnant women who came with or without a previous history of delivery as shown in Table 4.

Table 2. Method for termination of pregnancy.

Method for termination of pregnancy	First trimester (n=23)		Second trimester (n=78)	
	Number	%	Number	%
Surgical techniques				
1. Uterine curettage	18	78.26	2	2.56
2. Laparotomy (hysterotomy)	0		2	2.56
Medical techniques				
1. Intra-amniotic hyper-osmotic fluid (20% sodium chloride)	1	4.35	19	24.36
2. Oxytocin intravenously	0		11	14.10
3. Prostaglandin analogue (vaginal insertion)	4	17.39	27	34.62
Combined medical method				
1. Intra-amniotic hyper-osmotic fluid (20% sodium chloride) plus prostaglandin analogue (vaginal insertion)	0		3	3.85
2. Intra-amniotic hyper-osmotic fluid (20% sodium chloride) plus oxytocin intravenously	0		14	17.95

Table 3. Characteristics of medical abortion by misoprostal alone.

Characteristic	Success group (n=21)	Failure group (n=10)	P-value
Age (mean ± SD) (years)	28.76 ± 6.45	30.90 ± 5.11	NS
Weight (mean ± SD) (kg)	52.07 ± 5.56	54.80 ± 9.68	NS
Gestational age (mean ± SD) (weeks)	21.76 ± 3.32	16.90 ± 4.63	0.01*
Total dosage of misoprostal (mean ± SD) (microgram)	442.86 ± 289.09	780.0 ± 1,212.71	NS
Nulliparity (%)	33.33	20	NS
The viability of the fetus (% of intrauterine death)	28.57	60	NS

* The independent sample t test

Table 4. Induction to abortion interval by parity and intrauterine fetal death.

Factors	Number	Induction to abortion interval (hours)
Previous history of delivery		
Nulliparous	9	20.83 ± 13.16
Parous	22	29.86 ± 41.76
Viability of the fetus		
Intrauterine fetal death	12	17.46 ± 11.65
Viable fetus	19	33.42 ± 44.20

DISCUSSION

In a current report, it has been estimated that every year 30-40 million legally induced abortions are carried out worldwide as well as 20-25 per cent of all maternal deaths in Asia are the result of induced abortion(7). That means induced abortion still remains an unsafe procedure. In Thailand, the law has restricted induced abortion but therapeutic abortion can be performed in order to improve maternal health. However, new techniques of induced abortion have been developed in order to decrease the mortality and morbidity of pregnant women. Many medical abortion techniques including misoprostal have been developed in order to reduce an unnecessary surgical procedure.

This study reviewed therapeutic abortion cases in Siriraj Hospital in the year 2000, especially in those associated with misoprostal, and 101 cases have been reported. The mean age was about 29 years, which corresponded with the general obstetric data of Siriraj Hospital.

Misoprostal should be used with caution. In our institution, the authors did not use misoprostal in patients who came with a history of previous uterine scar, history of hypersensitivity to prostagrandins patients who came with some complaints, which may mimic the side effect of misoprostal such as fever.

Normally, termination of pregnancy at a later gestational age will be more risky to the patients, because of the difficulty of the termination procedure and also more physiologic changes in the pregnant woman. The mortality case in this study was a first trimester therapeutic abortion, which used the surgical method, dilatation and curettage. This case was a high-risk patient with primary pulmonary hypertension, which has a mortality rate of nearly fifty per cent according to the American College of Obstetricians and Gynecologists(8).

The prevalence of HIV-seropositive mothers in Siriraj Hospital is about 1.13 per cent(9). This group of patient has been counseled by a specially organized counseling team. However, fortunately, the use of antiretroviral drug for the prevention of mother to child HIV-transmission has been proved its efficiency(10) and short-course zidovudine is available in our hospital. So, the policy is to give short-course zidovudine for HIV prevention which offers the mother a better chance to continue the pregnancy.

Currently, the development of technology such as ultrasonography has helped the physicians to make an earlier and more precise diagnosis of intrauterine fetal death as well as an abnormality of the fetus which is not compatible with life, so fetal death has become a common fetal indication.

Normally, important considerations in the abortion method selection include gestational age as well as medical, psychological, logistical and acceptability factors(11). In Siriraj Hospital, many abortion techniques have been used according to Paul et al (12). However, many new methods are being developed, that should be approved before being used as the standard method. In Siriraj Hospital, surgical technique plays a major role for early abortion, and medical abortion plays a major role in second trimester abortion. From this study, uterine curettage was the preferred method for first trimester therapeutic abortion and Intra-amniotic hyper-osmotic fluid (20% Sodium Chloride) was most commonly used in second trimester abortion, because of its effect of causing the death of the fetus before expul-

sion and its good success rate of 96 per cent[13], even when combined with other medical techniques. However, hypertonic saline may result in serious complications such as cardiac failure, septic shock and even death[12], Another technique such as oxytocin intravenously and hysterotomy can be used for second trimester pregnancy termination[12]. There were two cases who came with a failed abortion late in the second trimester, when the gestational age was calculated from the patient's last menstruation period, the uterine size was no bigger than twelve weeks' pregnancy, so uterine curettage was judged to be the best in these cases.

Misoprostal is used at Siriraj Hospital in first trimester abortion for two purposes, cervical ripening and single drug for induced abortion. In order to ripen the uterine cervix, the present result is fairly good as recommended by Goldberg et al[1]. Mac Isaac et al[14] reported that, 400 microgram of vaginal misoprostal is equivalent to one medium laminaria used for four hours pre-operatively but laminaria placement is more painful than misoprostal placement. In contrast, misoprostal alone for induced early abortion has a poor result. The failure rate in the present study was about 75 per cent. However, according to Blanchard et al[15], sufficient evidence is not yet available to make a judgment about the potential of misoprostal alone for early pregnancy termination.

For second trimester abortion, misoprostal alone has been used for induction of abortion in 27 cases. The success rate was about 75 per cent. When compared with another report, although the optimal regimen has not been determined, it appears that 200 to 600 microgram of misoprostal given vaginally every 12 hours or 400 microgram given vaginally every 3 hours successfully induces abortion in second trimester with a high success rate 70-90 per cent [1,16,17]. According to Wong et al[17], complete abortion would result in 48 hours. The authors found that mean induction to abortion time in the present study was 18 hours (range 5-48 hours).

Higher doses of misoprostal are associated with higher rates of adverse effects, including a temperature above 38 degree Celsius (0-28%), nausea and vomiting (4-20%) and diarrhea (0-22%)[3]. In the present series, only severe abdominal cramping and fever with chill were, reported in 26.2 and 14.3 per cent respectively, and there was no uterine rupture. The risk of uterine rupture associated with induction of abortion with misoprostal in second trimester is as yet unknown[1].

The success of medical abortion induced by misoprostal might be influenced by many factors such as the patient's age and weight, gestational age, total dosage of misoprostal usage, history of previous delivery and viability of the fetus, but statistical significance could only be demonstrated from gestational age. There is more probability to complete the therapeutic abortion process in pregnant women who come with later gestational age.

As well as misoprostal activity, these factors may influence the efficacy of misoprostal, defined by induction to abortion time, and were studied in the present study. None had correlation with induction to abortion time. However, the present study is a retrospective study in a small group of the population, so further study should be established.

In summary, misoprostal can be used with caution for abortion induction in second trimester abortion in the form of vaginal administration without any serious adverse effect. But misoprostal alone for first trimester therapeutic abortion still has an unacceptable outcome. Further research should be conducted to find an appropriate method for optimum use of misoprostal.

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การใช้ยาไมโซพรอสทอลสำหรับการทำแท้งเพื่อการรักษาในโรงพยาบาลศิริราช : พ.ศ. 2543

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วัตถุประสงค์ : เพื่อศึกษาถึงประสิทธิภาพและผลข้างเคียงของการใช้ยาไมโซพรอสทอลสำหรับการทำแท้งเพื่อการรักษา

รูปแบบการศึกษา : การศึกษาเชิงพรรณนา แบบตัดขวาง

วิธีการศึกษา : สตรีตั้งครรภ์จำนวน 101 ราย ได้เข้ามารับการทำแท้งเพื่อการรักษาในโรงพยาบาลศิริราชระหว่างปี พ.ศ. 2543 ข้อมูลของผู้ป่วยเป็นข้อมูลที่ได้จากการสัมภาษณ์ สำหรับข้อมูลการรักษาพยาบาลเป็นข้อมูลที่ได้จากบัตรบันทึกผู้ป่วยใน จากนั้นจึงนำมาวิเคราะห์ทางสถิติ

ผลการศึกษา : มีการใช้ใช้ยาไมโซพรอสทอลในการทำแท้งเพื่อการรักษาจำนวน 42 ราย ทั้งนี้ 8 ราย เป็นการใช้ยาไมโซพรอสทอลเพื่อเตรียมความพร้อมของปากมดลูกก่อนการทำหัตถการขูดมดลูกซึ่งได้ผลเป็นที่น่าพอใจ ผู้ป่วยจำนวน 31 ราย ได้รับการกระตุ้นการแท้งด้วยยาไมโซพรอสทอลเพียงอย่างเดียว โดย 27 รายเป็นการแท้งในไตรมาสที่ 2 ทั้งนี้โอกาศสำเร็จ (ร้อยละ 74.1) จะมีมากขึ้นถ้าอายุครรภ์ของผู้ป่วยมากขึ้น และเวลาเฉลี่ยที่ใช้ในการทำแท้งเท่ากับ 18.0±10.5 ชั่วโมง จากการศึกษาไม่พบปัจจัยอื่นเช่น อายุ น้ำหนัก ขนาดยาไมโซพรอสทอล ประวัติการคลอด การมีชีวิตของทารกในครรภ์ ที่มีผลต่อประสิทธิภาพการใช้ยาไมโซพรอสทอล และไม่พบผลข้างเคียงที่มีอันตราย พบว่ามีอาการปวดท้องน้อยร้อยละ 26.2 และมีไข้ร้อยละ 14.3

สรุป : ยาไมโซพรอสทอลสามารถกระตุ้นให้เกิดการแท้งได้โดยเฉพาะการแท้งในไตรมาสที่ 2 อย่างไรก็ตามควรมีการใช้อย่างมีความระมัดระวังถึงผลข้างเคียงที่อาจจะพบได้

คำสำคัญ : ไมโซพรอสทอล, การทำแท้งเพื่อการรักษา, การแท้งในไตรมาสที่ 2

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