Termination of second trimester, complicated gestation

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إنهاء الحمل المصحوب بالمضاعفات في الأثلوث الثاني من الحمل

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الخلاصة: درس الباحث 70 حاملاً أحمالُهُنّ مصحوبة بتشوهات جنينية أو بموت الأجنَّة، لتقييم فعالية إعطاء الميسوبروستول لإفراغ الرحم في الأثلوث الثاني من الحمل. وقد تناولت المشاركات في الدراسة 200 مكروغرام من الميسوبروستول بفواصل 4 ساعات. وقد كانت فترة تحريض الإجهاض للحمل بأجنة ميتة (14.2 ساعة ± 4.3) أقصر مما في الحمل بأجنة حية، والأجنة المصابة بالتشوهات (20.2 ساعة ± 7.3). وقد كانت هذه الفروق فروقاً يُعتدُّ بها إحصائياً ($P < 0.001$). وقد كان معدل الإجهاض أعلى بنسبة يُعتدُّ بها في الأحمال بأجنة ميتة (92.1٪) من الأحمال بأجنة حية أو مشوهة (68.8٪) ($P < 0.05$). ولم تكن هناك مضاعفات كبيرة أو اختلافات هامة في معدل حدوث التأثيرات الجانبية. وقد اكتمل إجهاض جميع الحوامل خلال 48 ساعة. ويدل ذلك على أن إعطاء الميسوبروستول يُعَدَّ فعَّالاً كطريقة سريرية (إكلينيكية) لإنهاء الحمل المصحوب بمضاعفات في الأثلوث الثاني).

ABSTRACT To assess the effectiveness of intravaginal misoprostol for second trimester uterine evacuation, we studied 70 women with singleton pregnancies complicated by fetal malformation or dead fetuses. Participants received 200 µg misoprostol administered at 4-hour intervals. Gestations with dead fetuses had a shorter induction–abortion interval [14.2 hours, standard deviation (SD) 4.3] than those with live, malformed fetuses (20.2 hours, SD 7.3) (***P*** < 0.001). The abortion rate was significantly higher for gestations with dead fetuses (92.1%) than those with live, malformed fetuses (68.8%) (***P*** < 0.05). There were no major complications and no significant difference in the incidence of side-effects. All women aborted within 38 hours. Administration of misoprostol is an effective clinical method to terminate second trimester, complicated pregnancy.

Interruption d'une grossesse compliquée au deuxième trimestre

RÉSUMÉ Afin d'évaluer l'efficacité du misoprostol intravaginal pour une évacuation utérine au deuxième trimestre, nous avons examiné 70 femmes ayant une grossesse unique compliquée par une malformation ou une mort fœtale. Les participantes ont reçu 200 µg de misoprostol administré à intervalles de 4 heures. Les grossesses avec mort fœtale in utero avaient un intervalle plus court entre l'induction et l'avortement [14,2 heures, écart type (E.T.) 4,3] que celles avec malformations du foetus (20,2 heures, E.T. 7,3) ($p < 0,001$). Le taux d'avortement était significativement plus élevé pour les grossesses avec mort in utero (92,1 %) que pour celles avec malformations du foetus (68,8 %) ($p < 0,05$). Il n'y avait pas de complications majeures et pas de différence significative dans l'incidence des effets secondaires. Toutes les femmes ont avorté sous 38 heures. L'administration de misoprostol est une méthode clinique efficace pour interrompre une grossesse compliquée au deuxième trimestre.

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Introduction

Technological advances in imaging modalities to detect fetal viability and genetically abnormal fetuses have created a need for safe methods of terminating second trimester pregnancy other than surgery, which can result in serious complications such as cervical laceration, uterine perforation and bowel injury. These may occur even in experienced hands [*1,2*]. Termination of pregnancy, whether for genetic, medical or social reasons, is difficult and stressful for physician and patient alike. When second trimester termination is indicated, a variety of medical and surgical techniques have been used to effect uterine contractility or to prime the cervix.

Misoprostol is a synthetic prostaglandin, structurally related to prostaglandin E1, which has been widely used for the treatment and prevention of peptic ulcer induced by the ingestion of nonsteroidal anti-inflammatory drugs [*3,4*]. It has been reported as safe and effective, administered either orally or vaginally, for terminating second trimester pregnancies [*5,6*].

The number of deliveries conducted in Queen Alia Military Hospital in Amman is approximately 3600 a year. Termination of complicated gestation comprises 7% of obstetric procedures. The incidence of missed abortion (asymptomatic non-viable pregnancy) is 9.55 per 1000 births, while the incidence of gestation complicated by fetal malformation is 0.52 per 1000 births (unpublished data, 2003).

This study was undertaken to assess the effectiveness of intravaginal misoprostol use for second trimester uterine evacuation of live, malformed and dead fetuses.

Methods

This study was conducted at Queen Alia Military Hospital between 15 September 2001 and 14 August 2002. The participants comprised 70 of 73 pregnant women who had singleton pregnancies that were complicated by either fetal malformation (n = 32) or missed abortion (n = 38). Gestational age was 15–23 weeks (2nd trimester pregnancy is defined as the period of pregnancy from the beginning of the 15th through the 28th completed week of gestation, 99–196 days). Three women were excluded from the study. Criteria for exclusion were previous uterine scar; signs and symptoms of maternal infection; history of pulmonary, hepatic, renal or cardiovascular disease; evidence of cervical dilatation or spontaneous labour; and contraindications for prostaglandin use.

On the day of admission to hospital, all women had a 5-MHz transducer sonographic examination. Gestational age was estimated by measuring the biparietal diameter or femur length and correlating this with a standard table of gestational age, calculated from the last menstrual period. Before the initiation of therapy, a full physical examination was carried out on all subjects. Blood samples were taken and baseline laboratory tests were carried out (serum electrolytes, complete blood count, blood type and screening for coagulation profile).

A 200 µg misoprostol tablet was placed in the posterior vaginal fornix every 4 hours using a vaginal speculum. No premedication was used. The assigned duty resident and the attending staff cared for the patients. Vital signs and progression of labour were assessed every 2 hours and the occurrence of adverse events was recorded.

Palliation of side-effects was considered if symptoms required: diphenoxylate plus atropine to treat diarrhoea, acetaminophen 500 µg to treat fever (temperature > 38 °C), promethazine 25 mg intramuscular injection to treat nausea and vomiting, and meperidine 50 mg to relieve uterine cramps.

Induction–abortion interval was defined as the time in hours from initiation of therapy until the expulsion of the fetus. Abortion rate was calculated for those aborted within 24 hours. This was considered complete if the placenta and membranes were expelled spontaneously within 2 hours, without heavy bleeding requiring manual removal or curettage under anaesthesia. After expulsion of the fetus, all the women received an intravenous infusion of 30 units of oxytocin administered in 1 L Ringer's solution to prevent bleeding after fetal expulsion and retained placenta. All those who aborted had bimanual, pelvic, vaginal speculum and sonographic examination to determine whether retained products of conception were present or cervical laceration had occurred. The attending physician estimated blood loss, and hematocrit level was determined 6 hours post-delivery.

For statistical analysis, the Student *t*-test was used for continuous data, while for categorical data the Fisher exact test or chi-squared was used where appropriate. $P < 0.05$ was considered significant.

Results

The characteristics of the participants are shown in Table 1. Maternal age was 18–32 years; gestational age was 15–23 weeks. Live, malformed fetuses were anencephalic.

Table 2 summarizes the effectiveness of misoprostol in inducing abortion in the 2 groups. There was a statistically significant difference in induction time, with a shorter induction–abortion interval for gestations with dead fetuses than in those with live, malformed fetuses ($P < 0.001$). The abortion rate (≤ 24 hours) also showed a statistically significant difference ($P < 0.05$) with a higher incidence among those women carrying dead fetuses (92.1%), compared to those with live, malformed fetuses (68.8%).

Table 1 **Characteristics of the women in the study group**

Characteristic	Participants (n = 70) No.	%
Maternal		
Nulliparous	44	62.9
Parous	26	37.1
Fetus		
Live, malformed	32	45.7
Dead	38	54.3

Maternal age range 18–32 years; mean 27.4 years, standard deviation 3.2.
Gestational age range 15–23 weeks, mean 18.7 weeks, standard deviation 3.4.

The complete abortion rate showed no statistically significant difference between the 2 groups (Table 2). The most interesting finding was that the majority of cases (63.2%) were aborted within 16 hours of initiation of treatment in those with dead fetuses in comparison to the group with live, malformed fetuses (28.1%) ($P < 0.01$). Complete abortion within 24 hours was achieved after 3 doses of misoprostol in 82.3% (22/27) of the group with dead fetuses, and in 17.7% (5/27) after 4 doses. In the group with live, malformed fetuses, complete abortion within 24 hours was achieved in 84.6% (11/13) of cases after 5 administrations of misoprostol.

Placental removal, either manually or under general anaesthesia, was needed only in 29.8% of cases.

Table 3 shows the incidence of side-effects for both groups. Severe cramps were the most obvious finding in both groups. There was no statistically significant difference between the 2 groups for any of the side-effects.

Table 2 **Effectiveness of misoprostol in inducing abortion in 2 groups of women with complicated second semester gestation**

Measure	Fetus: Live, malformed, (*n* = 32) No.	%	Fetus: Dead, (*n* = 38) No.	%	Significance, *P* < 0.05
Abortion[a]	22	68.8	35	92.1	
Complete abortion[b]	13	59.1	27	77.1	NS
Induction–abortion interval (hours)					
< 8	2	6.3	6	15.8	NS
8–16	7	21.8	18	47.4	
> 16–24	13	40.6	11	28.9	NS
> 24	10	31.3	3	7.9	NS
Mean (SD)	20.2 (7.3)		14.2 (4.3)		*P* < 0.001

[a]Aborted in ≤ 24 hours of induction.
[b]Placenta and membranes expelled spontaneously in ≤ 2 hours, without heavy bleeding (expressed as percentage of those aborted in ≤ 24 hours).
NS = not significant.
SD = standard deviation.

Discussion

Cervical priming and absence of spontaneous uterine contraction are the major difficulties which can face the gynaecologist in attempting to evacuate second trimester pregnancy, especially in cases where complication of pregnancy (missed abortion or fatal fetal malformation) mandate termination.

Table 3 **Incidence of side-effects in 2 groups of women given misoprostol to terminate second trimester, complicated gestation**

Side-effect	Fetus: Live, malformed, (*n* = 32) No.	%	Fetus: Dead, (*n* = 38) No.	%
Nausea	6	18.8	5	13.2
Vomiting	3	9.4	3	7.9
Diarrhoea	1	3.1	1	2.6
Fever	4	12.5	2	5.3
Bleeding[a]	0	–	0	–
Severe cramps[b]	8	25.0	10	26.3

[a]Defined by haematocrit level necessitating blood transfusion.
[b]Necessitating the administration of analgesia more than once.

Currently, prostaglandins are the most widely used clinical method of termination. It has been reported that misoprostol administered vaginally has a prolonged myometrial stimulation and a direct cervical effect leading to long lasting and continuously increasing uterine stimulation [*7*]. Recent studies have reported the safety and efficacy of intravaginal misoprostol for cervical priming and even induction of labour at term [*3,4,8*].

In our study, using 200 µg misoprostol every 4 hours, the induction–abortion interval was significantly shorter, with fewer doses of misoprostol in the missed abortion group than in the group with live, malformed fetuses. All the women in both groups had their pregnancies terminated

within 38 hours of initiation of treatment. Our findings were comparable with those reported by Ho et al., who used the same dose but at 3-hour intervals, up to 5 doses, after pretreatment with mifepristone [*9*]. Other studies had a lower abortion rate (40%–62%) with a longer mean induction–abortion interval (27.8 hours) [*4,10*]. This could be explained by the longer interval for misoprostol administration (6 hours or 12 hours).

Complete abortion rates for missed abortion (77.1%) and the group with live, malformed fetuses (59.1%) were higher for our groups than those reported by Jain and Mishell in 1996 (43.8% and 33.3% respectively) [*3*]. This could be explained by the shorter dosing interval to maintain a higher misoprostol concentration specifically for cases of live, malformed fetuses which was used in our study. The overall rate of placental removal was only 29.8% compared with ≥ 80% reported in other studies [*11,12*].

Furthermore, in contrast to other studies, there were no major complications in either group [*10,13,14*]; severe cramps were the most prominent side-effect.

To sum up, misoprostol used vaginally in 200 μg doses is safe, and is more effective when a shorter dosing interval is used. This resulted in a shorter induction–abortion interval and a higher abortion rate, especially for gestations complicated by intrauterine fetal death. It is, therefore, a suitable clinical method for second trimester pregnancies requiring termination, and could be carried out by persons who had little skill or expertise in the large majority of cases.

References

1. Grimes DA, Cates W. Complications from legally-induced abortion: a review. ***Obstetrical and gynecological survey***, 1979, 34(3):177–91.
2. Peterson WF et al. Second trimester abortion by dilatation and evacuation: analysis of 11 747 cases. ***Obstetrics & gynecology***, 1983, 62(2):185–90.
3. Collins PW, Pappo R, Dajani EZ. Chemistry and synthetic development of misoprostol. ***Digestive diseases and sciences***, 1985, 30(11 suppl.):114–7S.
4. Collins PW. Misoprostol: discovery, development and clinical application. ***Medicinal research reviews***, 1990, 10(2): 149–72.
5. Jain JK, Mishell DR Jr. A comparison of misoprostol with or without laminaria tents for induction of second trimester abortion. ***American journal of obstetrics and gynecology***, 1996, 175(1):173–7.
6. Herabutya Y, O-Prasertsawat P. Second trimester abortion using intravaginal misoprostol. ***International journal of gynecology and obstetrics***, 1998, 60(2): 161–5.
7. Danielsson KG et al. Comparison between oral and vaginal administration of misoprostol on uterine contractility. ***Obstetrics & gynecology***, 1999, 93(2):275–80.
8. Sanchez-Ramos L et al. Misoprostol for cervical ripening and labour induction: a meta-analysis. ***Obstetrics & gynecology***, 1997, 89:633–42.
9. Ho PO et al. Vaginal misoprostol compared with oral misoprostol in termination of second trimester pregnancy. ***Obstetrics & gynecology***, 1997, 90(5): 735–8.
10. Nuutila M et al. A comparison between two doses of intravaginal misoprostol

and gemeprost for induction of second trimester abortion. ***Obstetrics & gynecology***, 1997, 90(6):896–900.

11. Rodger MW, Baird DT. Pretreatment with mifepristone (RU 486) reduces interval between prostaglandin administration and expulsion in second trimester abortion. ***British journal of obstetrics and gynaecology***, 1990, 97(1):41–5.

12. Thong KJ, Baird DT. Induction of second trimester abortion with mifepristone and gemeprost. ***British journal of obstetrics and gynaecology***, 1993, 100(8):758–61.

13. Perry KG Jr et al. Second-trimester uterine evacuation: A comparison of intraamniotic (15S)-15-methyl-prostaglandin F2alpha and intravaginal misoprostol. ***American journal of obstetrics and gynecology***, 1999, 181(5 pt 1):1057–61.

14. Jain JK, Kuo J, Mishell DR Jr. A comparison of two dosing regimens of intravaginal misoprostol for second-trimester pregnancy termination. ***Obstetrics & gynecology***, 1999, 93(4):571–5.

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