Second trimester pregnancy termination using gemeprost

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A retrospective study of 72 second trimester pregnancy terminations using gemeprost vaginal pessary is reported. The success rate with this method of induced abortion was 93%. The mean induction to abortion interval was 12.6 hours. Minor side-effects such as fever, vomiting and diarrhoea occurred in 46%, 10%, and 18% of patients, respectively. Major complications were uncommon. One patient had blood loss of more than 500 ml and one patient had genital tract trauma. It is our experience that gemeprost is a safe and efficient method for effecting a second trimester termination.

HKMJ 1996;2:19-24

Key words: Abortion, induced; Abortion, incomplete; Pregnancy trimester, second; Prostaglandins, synthetic; Abortifacient agents

Introduction

In Hong Kong, the majority of pregnancy terminations are performed in the first trimester by surgical evacuation of the uterus. This procedure is extremely safe and effective when performed in gazetted settings.[1] Conversely, abortions carried out beyond 12 weeks of gestation are associated with a higher incidence of maternal mortality and morbidity. The maternal death rate has been quoted as being between 0.4 to 0.8 per 100 000 legal abortions between 8 to 12 weeks of gestation, increasing to 1.2 per 100 000 for gestational age between 13 to 15 weeks, and further increasing to 7.1 per 100 000 for gestational age between 16 to 20 weeks.[2] Approximately half of abortion-related maternal mortality and two thirds of major abortion-related morbidity occur in pregnancies terminated after 13 weeks of gestation.

The need for safer methods of terminating second trimester pregnancies is overwhelming. Both medical and surgical methods are available, yet none is ideal. Dilatation and evacuation is the most popular method of second trimester abortion in the United States and has been shown to be safe and effective up to 16 weeks' gestation, in experienced hands.[3] In the United Kingdom, the induction of labour using prostaglandins is the preferred method as the success of medically-induced abortion is independent of the surgical expertise of the operators.[4] The advantage of a medical method of pregnancy termination is most obvious in its use for the termination of an abnormal foetus. As the foetus is delivered intact, detailed pathological examination is possible and anomalies can be confirmed.

Since the report of using prostaglandin F2-alpha and prostaglandin E2 (PGE2) for therapeutic abortion by Karim and Filshie in 1970,[5] prostaglandins have been extensively studied for their role in the management of pregnancy termination. Various routes of administration, including intravenous, intra-amniotic, extra-amniotic, intramuscular and vaginal have been tried for the termination of pregnancies of different lengths of gestation.[6] Intravenous infusion of prostaglandin causes severe side-effects such as pyrexia, vomiting, and diarrhoea with very poor patient compliance. The intra-amniotic route requires direct injection of prostaglandin into the amniotic cavity. The extra-amniotic route involves the transcervical insertion of a catheter into the extra-amniotic space followed by the continuous administration of prostaglandin using an infusion pump. Both of these routes have an associated risk of intrauterine infection. The use of an intramuscular injection of the analogue of prostaglandin E1, sulprostone (Nalador) was quite convenient but stopped in 1992 because of the report of a sudden maternal death following its use.

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Although vaginal prostaglandin pessaries in the form of 16,16-dimethyl-trans-delta 2 PGE1 methyl ester (gemeprost, Cervagem) are reported to be a safe and acceptable method in second trimester abortion,[7] this method was only first used in our department in June 1993. No local data reviewing clinical experience with this drug in Hong Kong is available. This article reports our early experience with the use of these pessaries for the termination of second trimester pregnancies and compares our results with previous studies.

Subjects and methods

Records of all women with requests for termination of pregnancy between 14 and 24 weeks' gestation during the study period from June 1992 through October 1993 were studied.

Gestational age was assessed by menstrual history, clinical examination or with pelvic ultrasound if indicated. In all cases, pregnancy termination was indicated under the government Offences Against the Person Ordinance section 47A, Hong Kong. Written consents were obtained.

All patients were admitted to hospital for the procedures. Blood samples were taken for the determination of haemoglobin levels and for cross-matching purposes. A single pessary of gemeprost was placed in the posterior fornix of the vagina, and this procedure was repeated at three-hourly intervals until either the products of conception had been expelled, or until the severity of any side effects became so great as to warrant no further pessary insertion, or until a total of five pessaries had been given.

An intravenous infusion was started when uterine contractions were noted by the patient. They were then kept nil by mouth during the procedure; blood pressure, pulse and body temperature were monitored. Patients were given analgesia (pethidine hydrochloride, 75 mg intramuscularly every 4 hours) if required, and antipyretics (paracetamol, 500 mg) if indicated.

Successful abortion was defined as abortion being achieved by gemeprost without the addition of supplementary methods such as oxytocin infusion. If abortion did not occur after five pessaries, patients were allowed to rest. Another course of treatment was repeated 24 hours later.

The induction to abortion interval was calculated from the time when the first vaginal pessary was inserted to the time when the abortus was delivered. If a second course was required, the induction to abortion interval was also calculated from the time when the first vaginal pessary was inserted in the first course.

Intramuscular Ergometrine (ergometrine maleate, 0.5 mg) was injected at abortion to reduce blood loss. The foetus and placenta were examined and sent for histology. Uterine evacuation under general anaesthetic was performed if the placenta was retained or incomplete. Blood loss at abortion was recorded.

Before discharge, all patients were given appropriate contraceptive advice. They were asked to attend for follow up six weeks later.

Statistical analysis was performed by student's *t*-test and Chi-square test. Values were expressed as the mean ± standard deviation.

Results

During the study period, 605 pregnancy terminations were performed, of which 77 (12.7%) were second tri-

Table 1. Patient characteristics (n = 72)

Age group (y)	No. of patients (%)
15 - 20	15 (20.8)
21 - 30	26 (36.1)
31 - 35	11 (15.3)
35 - 40	11 (15.3)
> 40	9 (12.5)
Marital status	
Single	22 (30.6)
Married	49 (68.1)
Divorced	1 (1.3)
Parity	
0	32 (44.4)
1 - 2	33 (45.8)
3 - 4	5 (6.9)
> 4	2 (2.9)
Gestation (wk)	
12 - 14	17 (23.6)
15 - 18	26 (36.1)
19 - 21	16 (22.2)
22 - 24	13 (18.1)

mester pregnancy terminations. One patient was excluded from data analysis because she had rupture of membranes before insertion of the vaginal pessary. The medical records of four patients were not available for the final analysis.

Various characteristics of the remaining patients are shown in Table 1. The average age was 29.1 years (range, 14-47 y). Forty-four percent of patients were nulliparous and the average duration of gestation was 17.7 weeks.

Table 2. Indications for termination of pregnancy (n = 72)

Indications	No. of patients (%)
Anxiety state	40 (55.5)
Rubella infection	2 (2.8)
Abnormal foetus	30 (41.7)
- Down's syndrome (5)	
- Anencephaly (4)	
- Alpha thalassaemia hydrops (6)	
- Other chromosomal anomalies (4)	
- Miscellaneous (11)	

Table 3. Patient characteristics according to their indications for termination

	Anxiety state (n = 40)	Abnormal foetus (n = 30)
Age (y)*	25.8	33.5
Marital status (Single)*	21	1
Parity (Nulliparous)†	21	9
Gestation (wk)*	16.2	19.7

* $P < 0.001$
† $P < 0.05$

The indications for termination of pregnancy are shown in Table 2. Thirty pregnancies (41.7%) were terminated because of abnormal foetuses; thalassaemia hydrops accounted for six cases. There were statistically significant differences ($P < 0.05$) in terms of age, marital status, parity, and length of gestation between those who requested termination of pregnancy for anxiety state (under the category of condition number 2 in the Offences Against the Person Ordinance) and those who had terminations because of foetal abnormalities as shown in Table 3. Patients who had termination of pregnancy for anxiety state were relatively younger (mean age, 25.8 y) than those who had an abnormal foetus (mean age, 33.5 y) [$P < 0.05$].

Sixty-seven patients (93%) had successful abortions with gemeprost alone. The mean induction to abortion interval was 12.6 ± 6.1 hours. Five patients required oxytocin infusion in addition to gemeprost to achieve abortion and further vaginal pessaries were withheld because they had had spontaneous rupture of the membranes following the gemeprost insertion. Sixty-eight patients (94%) had successful abortions within 24 hours. All 72 patients had successful induced abortions when supplementary treatment such as oxytocin was given. The cumulative abortion rate is shown in Fig 1.

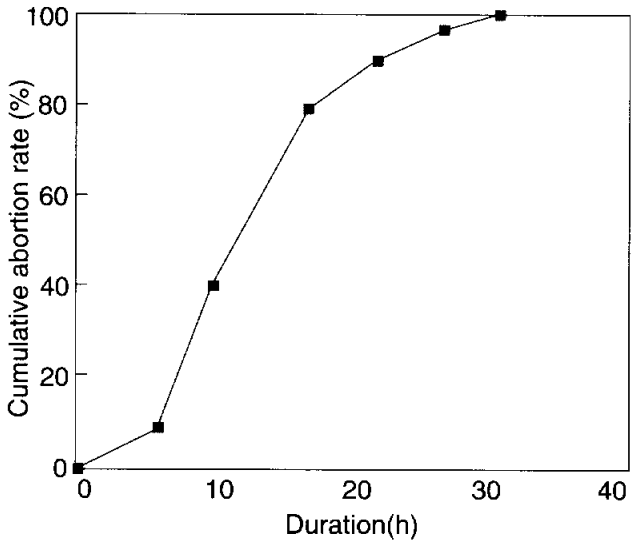

Fig 1. Cumulative abortion rate with gemeprost (Cervagem)

As shown in Table 4, there was no relationship between the number of gemeprost pessaries used and the induction to abortion interval achieved ($P > 0.05$) for the very early second trimester (12-14 wk), the early second trimester (15-18 wk), the mid second trimester (19-21 wk) or the late second trimester (19-24 wk) when terminations were carried out.

Table 4. Induction to abortion interval and number of vaginal pessaries used per treatment according to gestation length (n = 72)

	Gestation (wk)			
	12 - 14	15 - 18	19 - 21	22 - 24
Induction-abortion interval (h)*	13.9 ± 6.8	11.3 ± 5.3	11.1 ± 5.6	14.2 ± 6.2
Number of vaginal pessaries used*	3.9 ± 0.9	3.8 ± 1.4	4.4 ± 1.8	5.2 ± 1.9

* $P > 0.05$

Table 5. Frequency of side-effects and complications (n = 72)

	No. of patients (%)
Side-effects	
Temperature > 37.5°C	33 (45.8)
Vomiting	7 (9.7)
Diarrhoea	13 (18.0)
Complications	
Blood loss > 500 ml	1 (1.4)
Blood transfusion	2 (2.8)
Pelvic infection	2 (2.8)
Genital tract trauma	1 (1.4)
Uterine evacuation	32 (44.0)

The mean number of gemeprost pessaries required was 4.3 ± 1.7 (range, 1-10). Sixty-five patients (90%) required no more than five pessaries to successfully achieve the abortion.

Thirty patients (42%) underwent treatment without requesting any analgesics. Only one dose of pethidine was required in thirty patients for pain relief.

The side effects and complications of second trimester pregnancy termination using gemeprost are listed in Table 5. Thirty-three patients (46%) had a temperature higher than 37.5°C which returned to normal within eight hours of the last dose of gemeprost being given. Two patients had high temperatures of 39°C. In one patient, further gemeprost application was withheld because her fever did not respond to paracetamol. The results of a sepsis work up in this patient were negative.

Diarrhoea and vomiting developed in seven (9.7%) and thirteen patients (18%), respectively, but these symptoms were self-limiting and disappeared within 24 hours of the last gemeprost pessary being inserted.

The amount of blood loss was not recorded in 25 patients. The mean estimated blood loss was 140 ml (range, 20-500 ml). Only one patient had a recorded blood loss of more than 500 ml and another patient had a cervical tear which required suturing under general anaesthesia; both patients required blood transfusion.

Retained placenta or incomplete abortion occurred in 32 patients (44%). All required suction evacuation of the uterus under general anaesthesia. All histology reports confirmed retained products of gestation. Two patients (2.8%) had pelvic infection following abortion and both recovered uneventfully after antibiotic treatment.

Sixty-three patients (87%) were discharged from hospital within 48 hours of the abortion. Six patients had hospital stays of more than three days because they requested tubal sterilisation. Four patients had unplanned readmission because of pelvic infection or incomplete abortion.

Discussion

Natural prostaglandins, PGE2 and PGF2-alpha, with their stimulatory effects on the uterine myometrium were first tested as abortifacients in 1970.[6] In order to be effective, high doses of these natural prostaglandins were infused intravenously which resulted in severe gastrointestinal side-effects, high rates of incomplete abortions and irritation at the infusion sites. As natural prostaglandins are rapidly degraded in the lungs, kidneys and liver once they are introduced into the systemic circulation, their biological activity is much reduced. The development of prostaglandin analogues created compounds which can resist enzymatic degradation. These prostaglandin analogues have increased selectivity for uterine muscle and a stronger stimulatory action on myometrial contractility. The effective dose required can therefore be lowered with an associated reduction in the dose-related gastrointestinal side-effects. The introduction of local methods of administration using the intra-amniotic, extra-amniotic or vaginal routes has helped to reduce the dose and side-effects of prostaglandins.

The gemeprost vaginal pessary has been shown to be safe and reasonably effective in the termination of early pregnancy.[8] The use of gemeprost also compares favourably with the more conventional extra-amniotic infusion of PGE2 for second trimester abortion.[9] The success rate has been reported at 77%. In our study, 93% of women successfully aborted without additional methods.

In the present series, 12.7% of pregnancy terminations were in the second trimester. This figure is similar to the 10% to 15% reported in the United Kingdom.[10] In the first trimester, nearly all terminations were performed because of anxiety state in the mother. In the second trimester, more therapeutic abortions were performed because of foetal abnormality. In our study, 42% of the second trimester abortions were related to foetal anomalies found as a result of prenatal diagnosis using amniocentesis and high-resolution obstetric ultrasound.

An earlier study reported that 82% of women aborted within 24 hours.[11] The number of pessaries used ranged from two to five. The mean induction to abortion interval was 14 hours, 41 minutes. The abortion success rate increased to 96.5% following further treatment. Comparable figures were obtained by us.

In our study, 46% of patients had pyrexic episodes with temperatures greater than 37.5°C after vaginal prostaglandin insertion. The thermogenic effect of prostaglandin is a well-known intrinsic property that is self-limiting. The incidence of gastrointestinal-associated problems encountered was similar to findings of previous studies.[9,12] This is also a dose-related transient symptom. Further reduction of these intrinsic, unpleasant side-effects of prostaglandin would enhance patient tolerance and compliance.

The induction of labour for abortion is an extremely unpleasant and painful experience for patients. Forty-two per cent of our patients did not require any pain relief. The acceptability of gemeprost was not assessed in this review. However, it was reported that women in the extra-amniotic prostaglandin group required twice the number of pethidine injections as did those in the pessary group.

The risk of haemorrhage at abortion is low and no patients have needed a blood transfusion after gemeprost termination of pregnancy.[13] However, in our study, two women required blood transfusion (2.8%). Blood loss of more than 500 ml occurred in one woman who had pre-existing α-thalassaemia anaemia with a haemoglobin level of 89 g/L before abortion and transfusion was therefore given. The second patient had a cervical tear which required suturing. The incidence of genital tract injury following gemeprost treatment has been reported as 0.1%[13]—a much lower figure than the 1.4% in our series. This may be due to statistical bias because of our small sample size. In our study, two patients (2.8%) had pelvic infections. The risk of pelvic infection varies with the route of administration of prostaglandin and increases with the induction to abortion interval. Although the induction to abortion intervals are comparable with other series, our rate of pelvic infection is high. Without knowledge of the background pelvic infection rate in the general population, it is difficult to explain the higher infection rate.

Approximately 44% of women required uterine evacuation for retained products of gestation. Cameron reported that complete abortion occurred in only 20% of women.[11] The frequency of incomplete abortion with extra-amniotic PGE 2 was 35%.[14] Despite such a high rate of incomplete abortion, it must be noted that the level of expertise required and the severity of intra-operative complications in surgical evacuation of retained products of gestation are far less than those in which a forceful dilatation of an unripe cervix and surgical extraction of an intact 16-week pregnancy is performed.

Vaginal administration of prostaglandin has been shown to be an effective and safe method for second trimester pregnancy termination. However, the duration of the induction to abortion interval is unpredictable. Prolonged hospitalisation and high doses of vaginal pessaries may be required if the cervix is not ripe. Recent studies have demonstrated that a combination treatment using mifepristone, a progesterone receptor blocker, and prostaglandin can shorten the induction to abortion interval and reduce the dosage of prostaglandin required.[15-17] Moreover, misoprostol, a prostaglandin E1 analogue used in the treatment of peptic ulcers, has been investigated as a cervical ripening agent in pregnancy at term.[18] This cervical ripening property of misoprostol may be employed as a pre-treatment to improve the efficacy of intravaginal gemeprost pessaries in the termination of second trimester pregnancy. With further development of the various regimes, more medically-induced second trimester terminations could be managed as day cases—welcome news to health providers and consumers alike.

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