MIDTRIMESTER TERMINATION OF PREGNANCY USING INTRAVAGINAL GEMEPROST (16, 16 DIMETHYL-TRANS $\triangle^2$ PGE_1 METHYL ESTER, CERVAGEM)

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SYNOPSIS

The efficacy of a new prostaglandin E_1 analogue, gemeprost (cervagem) for mid-trimester termination of pregnancy was assessed. Mid-trimester abortion was successfully induced in 32 out of 42 women with normal pregnancies within 48 hours by vaginal administration of 1 mg gemeprost pessary every 3 hours up to a maximum of five pessaries. 23 patients were nulliparous and 19 were multiparous (mean parity of 1.0). Their ages ranged from 16 to 43 years (mean of 24.7 years) and the gestation 12 to 22 weeks (mean of 16.4 weeks). 16 patients aborted within 12 hours (38.1%), 28 within 24 hours (66.7%), 31 within 36 hours (73.8%) and 32 within 48 hours (76.2%) (Total success rate). The mean induction-abortion interval was 14.4 hours and the mean dose 4.0 mg. Blood loss and side effects were minimal and the only significant complication was the occurrence of cervical tears in 2 patients which were repaired successfully at the time of currettage.

Gemeprost appears to be an effective drug that can be administered by a non-invasive route for the terminations of mid-trimester pregnancy.

PATIENTS AND METHODS

The study was carried out at the B Unit, Kandang Kerbau Hospital on 42 patients with normal mid-trimester pregnancy during the period between 1st September 1982 and 30th April 1983. All patients had requested for termination of their unwanted pregnancies. Patients with known hypersensitivity to prostaglandins, obstructive airways disease, elevated intraocular pressure, previous uterine surgery, cardiovascular disorders, thyrotoxicosis, cervicitis or vaginitis were excluded from the study. The ages of the subjects ranged from 16 to 43 years (mean 24.7 years), parity was 0 to 6 (mean 1.0) and the gestation 12 to 22 weeks (mean 16.4 weeks). The patients were admitted to hospital on the morning when induction was scheduled. Haemoglobin estimation was performed and two pints of matched blood were made available in reserve. The subjects were allowed a normal diet until strong uterine contractions and/or abortion occurred where upon they were prepared for uterine evacuation and curettage under caudal anaesthesia.

The gemeprost pessaries were kept refrigerated and allowed to warm to room temperature in the unopened foil sachet prior to use. Each pessary contained 1 milligram of 16, 16-dimethyl transΔ^2 PGE^1 methyl ester. One pessary was placed high in the posterior vaginal fornix every 3 hours until the foetus was expelled or five pessaries had been inserted. The state and dilatation of the cervix was noted prior to insertion of each pessary. Blood pressure, pulse and temperature were noted hourly and all side effects recorded. Antiemetic (prochlorperazine) and antidiarrhoel (kaolin with tincture of opium) agents were administered as necessary for appropriate symptoms. Pain was relieved by intramuscular injections of 50 mg or 75 mg pethidine hydrochloride. Intramuscular ergometrine maleate 0.5 mg was given immediately after the patient had aborted. In all cases, a curettage was performed to ensure that there were no retained products of conception.

The technique was considered successful if the products of conception (POC) were expelled within 48 hours after cervagem application. It was considered a failure if none of the POC was expelled 48 hours after cervagem application. In those cases which failed to abort with cervagem, abortion was achieved either by suction aspiration, intra-amniotic 15 (S) 15-methyl $PGF_{2\alpha}$ or by intramuscular 16-16-dimethyl PGE_2 para-benzaldehyde semicarbazone ester (CD_4).

The patients were discharged 24 hours after the evacuation and curettage. A follow-up examination was conducted 4 weeks and 8 weeks after discharge from the hospital.

TABLE 1

AGE DISTRIBUTION

AGE	NO OF SUBJECTS	PERCENTAGE
15-19	10	23.8
20-24	16	38.1
25-29	5	11.9
30-34	7	16.7
35-39	3	7.1
40 +	1	2.4
TOTAL	42	100

TABLE II

RACIAL DISTRIBUTION

ETHNIC GROUP	NO OF SUBJECTS	PERCENTAGE
CHINESE	23	54.8
MALAYS	18	42.8
INDIANS	1	2.4
TOTAL	42	100

TABLE III

NUMBER OF ABORTIONS BY PARITY AND GESTATIONAL SIZE

UTERINE SIZE (WEEKS)	NULLIPAROUS		MULTIPAROUS	
	NO OF SUBJECTS	NO ABORTED	NO OF SUBJECTS	NO ABORTED
12-14	0	0	10	8
15-17	13	10	4	3
18-20	9	6	5	4
21-23	1	1	0	0
TOTAL	23	17	19	15

RESULTS

32 successful abortions were achieved with cervagem pessaries. The time required for the products of conception to be expelled ranged from as early as 6 hours 5 minutes to 38 hours 20 minutes, giving a mean induction-abortion interval of 14.4 hours. 16 patients aborted by 12 hours (38.1%), 28 by 24 hours (66.7%), 31 by 36 hours (73.8%) and 32 by 48 hours (76.2%). The effective total dose of gemeprost ranged from 1 mg to 5 mg with a mean dose of 4.0 mg. In these 32 patients, abortion was complete in 7 cases (21.9%) and incomplete in 25 cases (78.1%). 73.9% of nulliparous patients had a successful abortion compared with 78.4% of multiparous patients.

Blood loss was minimal in all cases, averaging 50 to 100 mls. There were two cases of cervical tears. The tears occurred posterolaterally at 7 o'clock and 4 o'clock position in the respective women and were diagnosed at the time of evacuation of the uterus. These tears, approximately 2 cm and 3 cm respectively were repaired with interrupted chromic O catgut sutures. There was no excessive bleeding in either case and follow-up examinations showed no residual cervical abnormality.

The side effects were mild and consisted of lower abdominal cramps, mild pyrexia, nausea, vomiting and diarrhoea (Table IV). 36 patients (85.7%) had mild lower abdominal pain of which only two required pethidine for pain relief. 18 patients (42.8%) had pyrexia with one or more reading of 38°C. 8 patients (19%) had one episode of vomiting each which required no treatment. Nausea alone was experienced by 9 other patients (21.4%). 7 patients (16.7%) had mild diarrhoea (averaging 1.4 episodes per patient).

DISCUSSION

For second trimester pregnancy termination, the search continues for a simple, safe and more effective procedure and agent. The aim is to avoid invading the uterus with any form of instrumentation, thereby reducing the risk of infection and haemorrhage. The ideal abortifacient should cause the patient very little side effects, practically no complications and a reasonably short induction-abortion interval.

At present, local administration of prostaglandins shows great promise. Gemeprost (a PGE_1 analogue) is effective by the vaginal route, and can produce strong uterine contractions which are long lasting. The uterine stimulant potency of gemeprost in rats on day 20 of pregnancy after intravenous injection is ten times greater than that of PGE_1 and PGE_2 and one hundred times greater than $PGF_{2\alpha}$ (5). As confirmed by the present study, this preparation produces significant clinical effects, achieving a 66% expulsion rate at 24 hours and 76% at 48 hours and a satisfactory induction-abortion interval of 14.4 hours. The potential hazards associated with intra-amniotic administration of prostaglandins are avoided with the use of cervagem vaginal pessaries. Its administration is simple and can be performed by nursing staff.

Most of the side effects seen are relatively mild and the blood loss during abortion minimal. Although nearly 86% of the patients in this study experienced lower abdominal pain, only about 5% required pethidine for pain relief. It was felt that many of the patients may have actually deemed uterine contractions as lower abdominal pain. Moreover, pain, being a complex experience influenced by multiple factors such as culture, patient's expectation, personal attitude, stress and physical factors is difficult to quantify.

TABLE IV

COMMON SIDE EFFECTS

LOWER ABDOMINAL CRAMPS			VOMITING AND DIARRHOEA				
				VOMITING		DIARRHOEA	
SEVERITY	NO. OF SUBJECTS	%	EPISODES	NO	%	NO	%
NONE	6	14.3	0	34	81	35	83.3
MILD	35	83.3	1	8	19	5	11.9
MODERATE	1	2.4	2	0	0	1	2.4
SEVERE	0	0	2	0	0	1	2.4
TOTAL	42	100	TOTAL	42	100	42	100

All 32 patients who aborted with cervagem pessaries had resumed normal menstruation by the second follow-up examination. The 10 patients who failed to abort with cervagem were grouped as failures. One of them aborted 49 hours 45 minutes after the start of cervagem treatment. Three others aborted after a single intra-amniotic injection of 1.5 mg 15 (S) 15 methyl prostaglandin $F_{2\alpha}$ and one after two intramuscular injections of 150 mcg CD4. In the remaining five patients, the uterus was sufficiently reduced in size to permit safe and successful evacuation of uterus by suction curettage.

The majority of abortions achieved with cervagem vaginal pessaries are however incomplete abortions and therefore routine post abortion curettage is necessary.

In this study, significant cervical softening and dilatation caused by the cervagem was also noted. This effect of cervagem is a mechanism in its own right and is not directly related to the uterine contractions produced by the drug (6).

Recognised complications of mid-trimester abortion using prostaglandins includes cervico-vaginal fistulae (7) and uterine rupture (8,9,10). One serious complications is transverse rupture of the posterior uterine wall at the level

of the cervico-isthmic junction (11,12). Cervical injury is probably the result of unusual cervical resistance in the face of strong uterine contractions and is therefore more likely to occur in young nulliparae in the late second trimester of pregnancy (13). To prevent this complication, administration of cervagem pessary should be stopped as soon as any ballooning of the lower uterine segment above the cervix is detected.

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