Use of Prostaglandin E₂ for Therapeutic Abortion

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Summary: Termination of pregnancy was attempted with intravenous infusion of prostaglandin E₂ (5 µg./minute) in 52 consecutive cases. Abortion was successful in 50 of these and complete in 43. There were no serious side-effects.

Introduction

The stimulant action of different prostaglandins on the intact pregnant human uterus has been shown by several investigators (Bygdeman *et al.*, 1968; Embrey, 1969). Prostaglandins E₂ and F_{2α} have been successfully used for the induction of labour in women at or near term (Karim, 1969a, 1969b; Karim *et al.*, 1969, 1970a). Prostaglandin F_{2α} in higher concentrations (50 µg./minute) has also been used to stimulate the uterus in the first and second trimesters of pregnancy to induce therapeutic abortion (Karim and Filshie, 1970). In this paper we describe the effects of an intravenous infusion of 5 µg. of prostaglandin E₂ per minute on the early and mid-pregnant uterus in 52 women and its usefulness for therapeutic termination of pregnancy in the first and second trimesters.

Patients and Methods

Fifty-two patients recommended for therapeutic abortion were treated with prostaglandin E₂ infusion at Mulago Hospital, Kampala, Uganda, and at King's College Hospital, London. Their ages ranged from 13 to 40 years. Twenty-three (44%) were nulliparous. The gestation varied from 9 to 22 weeks. In 30 cases (all over 14 weeks' gestation) uterine activity was continuously monitored, and these patients were prepared as follows. The patient was given 100 mg. of pethidine and 50 mg. of promazine (Sparine). One hour later the bladder was catheterized and emptied. The vagina was examined to assess the size of the uterus and to exclude any abnormality. The abdominal skin was prepared with full sterile precautions and a 16 gauge Tuohy needle, with stylet, was inserted into the amniotic sac under local anaesthetic (1% lignocaine). When free reflux of liquor was obtained an 18 gauge epidural catheter (Portex) was inserted into the amniotic cavity through the Tuohy needle. The needle was then withdrawn. The epidural catheter was connected to a Devices pressure transducer attached to a Devices M2 recorder. The transducer dome and the catheter were filled with isotonic saline solution containing 1 mg. of ampicillin or 1 mg. of tetracycline per ml. Informed consent was obtained for these procedures, and spontaneous uterine activity was recorded for 30 minutes before the infusion of prostaglandin E₂. A solution of prostaglandin E₂ 10 mg./ml. in absolute ethanol was sterilized by ultrafiltration and diluted with 5% dextrose solution to give a concentration of 5 µg./ml. This was infused intravenously at the rate of 5 µg./minute until the abortion was complete. The patient remained under close observation throughout this time. Maternal blood pressure, pulse, and temperature were measured at regular intervals.

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Results

Abortion was attempted in 52 women with an infusion of 5 µg. prostaglandin E₂ per ml. and was successful in 50 cases. The average induction-abortion interval was 14 hours 50 minutes. In 37 women the fetus and the placenta were expelled simultaneously and in eight further cases the placenta was expelled after a delay which varied from 30 minutes to 10 hours. In 43 women abortion was eventually complete and no further treatment was found necessary. In the remaining seven patients in whom abortion was successfully induced it was necessary to evacuate the uterus of small retained products of conception. The two cases of failed abortion are discussed later. Detailed results are shown in Tables I and II.

Uterine Activity.—With intravenous infusion of 5 µg. of prostaglandin E₂ per minute used in this study stimulation of uterine activity was observed in all 52 women. Usually two types of activity were noted. The uterine response which appeared after a latent period of one to five minutes was characterized by an increase in tone which varied between 10 and 40 mm. Hg. In some cases this hypertonus disappeared within 15 to 30 minutes and the uterus began to contract regularly and rhythmically with an increase in frequency and amplitude of contractions (Fig. 1). In a few cases the tone of the uterus remained raised by 10-25 mm. Hg throughout the infusion period. In these cases uterine contractions were superimposed on the hypertonus (Fig. 2). With continuing infusion the contractions became stronger and abortion followed.

Failed Abortions.—In two women (Cases 6 and 25) infusion of 5 µg. of prostaglandin E₂ per minute failed to produce an abortion. One was nulliparous and the other a primigravida. Both were in the first trimester of pregnancy (10 and 12 weeks' gestation, respectively). Prostaglandin infused for 42 and 48 hours, respectively, failed to dilate the cervix and produce an abortion despite strong contractions throughout the infusion period. Pregnancy in these two cases was terminated by the suction method.

FIG. 1.—Case 37. Continuous record of prostaglandin-E₂-induced uterine activity at 15 weeks.

TABLE I.—Detailed Results of Therapeutic Abortion Induced by Infusion of 5 µg. Prostaglandin E₂ per Minute

Case No.	Age	Nationality	Parity	Gravida	Gestation-weeks	Induction Abortion Interval	Interval Between Delivery of Fetus and Placenta	Remarks
1	20	West Indian	0	0	10	7 hr. 30 min.	0	—
2	18	British	0	0	14	43 hr.	0	Pyrexia of 38°C. after abortion. Responded to antibiotic
3	17	South American	0	0	14	44 hr.	0	E.R.P.C. after retained placenta
4	20	Indian	0	0	16	14 hr.	0	—
5	28	German	0	0	17	20 hr.	0	—
6	17	British	0	0	10	Failed Induction after 42 hr.	0	Vomiting, blurring of vision. Suction termination
7	38	Italian	0	0	15	11 hr. 30 min.	0	—
8	22	British	0	0	15	38 hr.	0	—
9	32	West Indian	0	0	22	54 hr. 25 min.	0	—
10	19	British	0	0	18	29 hr. 45 min.	0	Nausea. Twins. Failed saline termination
11	15	British	0	0	13	14 hr. 45 min.	0	E.R.P.C. after retained placenta
12	24	British	0	0	20	17 hr. 35 min.	0	Vomiting
13	16	British	0	0	18	20 hr.	0	—
14	24	British	0	0	16	11 hr. 30 min.	0	—
15	13	Indian	0	0	16	9 hr. 45 min.	0	Vomiting
16	16	Indian	0	0	16	11 hr.	0	—
17	18	East African	0	0	10	18 hr.	0	Nausea
18	25	British	0	0	17	10 hr.	30 min.	Vomiting and Diarrhoea
19	20	British	0	0	16	12 hr. 15 min.	0	—
20	18	Indian	0	0	16	16 hr.	0	—
21	21	East African	0	0	15	7 hr.	0	Nausea
22	23	British	0	0	15	4 hr. 30 min.	0	E.R.P.C. after retained placenta
23	20	East African	0	1	12	8 hr. 20 min.	30 min.	Failed saline termination
24	25	British	1	1	13	13 hr.	0	E.R.P.C. after retained placenta
25	30	British	1	1	12	Failed Induction After 48 hr.	0	Nausea and Vomiting. Suction termination
26	22	German	1	1	14	24 hr.	30 min.	—
27	23	British	2	2	18	32 hr.	0	—
28	24	British	2	2	14	9 hr. 15 min.	0	Nausea
29	24	British	2	2	15	5 hr. 15 min.	0	—
30	28	British	2	2	12	24 hr. 45 min.	30 min.	—
31	34	British	2	2	12	16 hr. 45 min.	0	—
32	23	British	2	2	12	16 hr.	6 hr.	Vomiting and diarrhoea. Vomiting prior to infusion
33	18	West Indian	2	2	16	9 hr. 15 min.	0	Vomiting and diarrhoea
34	26	British	2	2	12	11 hr. 45 min.	0	E.R.P.C. after retained placenta
35	40	British	2	2	14	9 hr. 30 min.	0	—
36	24	British	2	2	14	15 hr. 35 min.	0	—
37	28	West Indian	3	3	15	8 hr.	0	—
38	27	British	1	3	9	15 hr. 25 min.	0	—
39	28	British	3	3	12	12 hr.	0	—
40	31	West Indian	2	3	16	15 hr.	0	Nausea
41	30	West Indian	4	4	15	30 hr.	0	E.R.P.C. after retained placenta. 250 ml. blood loss
42	31	West African	3	4	11	7 hr. 45 min.	60 min.	—
43	25	British	4	4	14	12 hr. 30 min.	0	—
44	28	West Indian	4	4	15	12 hr. 45 min.	0	—
45	24	Indian	4	4	20	6 hr. 30 min.	0	—
46	29	British	2	4	16	13 hr. 45 min.	0	Vomiting and diarrhoea
47	28	British	4	5	17	9 hr. 30 min.	10 hr.	Vomiting. Tubal ligation after abortion
48	26	British	5	5	20	1 hr. 30 min.	0	Missed abortion?
49	36	British	4	5	12	9 hr. 30 min.	0	E.R.P.C. after retained placenta
50	38	Italian	5	5	18	13 hr.	60 min.	—
51	34	West African	7	7	18	7 hr. 20 min.	0	Failed saline termination
52	34	British	10	10	16	27 hr.	0	Blood loss 700 ml 2 pints blood transfusion

E.R.P.C.=Evacuation of retained products of conception.

TABLE II.—Summary of Therapeutic Abortion with Prostaglandin E₂ in 52 Women

Gravida	No. of Cases	Maturity (Weeks)	Average Induction-Abortion Intervals
0	22 (21 successful)	10-22	19 hours 30 minutes
1	4 (3 successful)	12-14	15 hours 7 minutes
2	10	12-18	15 hours
3	4	9-16	12 hours 36 minutes
4	6	11-20	13 hours 52 minutes
5	4	12-20	8 hours 22 minutes
7	1	18	7 hours 20 minutes
10	1	16	27 hours
Average for 50 successful cases			14 hours 50 minutes

Failed Saline Terminations.—In three patients (Cases 10, 23, and 51) abortion had been previously attempted by instilling hypertonic saline without success. Prostaglandin infusion was given 72 hours later. All three aborted satisfactorily.

Side-effects.—There were a few side-effects in this series, but none has been serious. The most common were nausea and vomiting, which occurred in 10 of the 52 cases and were found to be worse in patients already suffering from hyperemesis gravidarum. Diarrhoea occurred in four patients. The nausea and vomiting responded to perphenazine (5 mg. intramuscularly) and the diarrhoea to kaolin and morphine mixture. A transient pyrexia of less than 1° C. was observed in two cases following prostaglandin-induced abortion. In one case a genital tract infection resulting in a pyrexia of 38° C. was treated with an antibiotic, but no pathogens were isolated from the high vaginal swab. One patient had blurring of vision which subsided with temporary discontinuance of prostaglandin infusion. Examination of the eyes and central nervous system showed no abnormality.

Blood Loss.—Ergometrine 0.5 mg. was given by the intramuscular route to all women after the abortion. Blood loss

was minimal in 48 cases. In one patient (Case 41) the estimated blood loss was 250 ml., and in a gravida-10 patient (Case 52) 2 pints (1,140 ml.) of blood was transfused following a blood loss of 700 ml.

Discussion

Several methods for the therapeutic termination of pregnancy are in use. Early pregnancy is best terminated by dilatation and curettage or by dilatation followed by vacuum suc-

FIG. 2.—Case 21. Continuous record of prostaglandin-E₂-induced uterine activity at 15 weeks.

tion. The vaginal operation of therapeutic abortion is fraught with several hazards, including perforation of the uterus, haemorrhage, infection, and cervical incompetence as a result of stretching of muscles of the cervix. The likelihood of these complications increases sharply after the twelfth week, and the procedure is not usually employed after this. After 12 weeks pregnancy is usually terminated by abdominal hysterotomy. This is not an ideal solution and is associated with an operative and postoperative risk (Diggory *et al.*, 1970). Further, the presence of a scar in the uterus may in future pregnancies render caesarean section the only safe way of delivery.

Other methods used for therapeutic termination of pregnancy include the intra-amniotic injections of hypertonic saline or the instillation of abortifacient paste between membranes and the uterine wall. The former technique is usually employed after 14 weeks and, though usually successful, needs skill and experience. Recently, however, there have been disquieting reports of several deaths following the intra-amniotic injections of hypertonic saline (Wagatsuma, 1965; Cameron and Dayan, 1966; Sabeti and de Watterville, 1967; Frost, 1968; Diggory *et al.*, 1970). The abortifacient paste can be used in early and mid-pregnancy (Lachelin and Burgess, 1968), but is not free from risk, and sudden death from embolism or vagal inhibition has been reported (Dutra *et al.*, 1950; Williams *et al.*, 1955; Karim and Filshie, 1970). Hence therapeutic abortion is not a simple operation, and no method of terminating pregnancy before term is entirely devoid of risk. A simple, safe, and effective method for the management of therapeutic abortion is highly desirable.

Medical induction seems to be a more desirable approach to the problem. In this paper we report the use of prostaglandin E₂ infusion for therapeutic termination of pregnancy. The safety of the infusion and the optimum concentration required for therapeutic abortion have been determined (Karim *et al.*, 1970b). According to these authors, a concentration of less than 1 µg./minute can stimulate the uterus in the middle trimester of pregnancy. Nevertheless 5 µg./minute is the optimum concentration needed to produce contractions of sufficient strength and frequency to dilate the cervix and produce abortion. An infusion of up to 40 µg./minute in normal male volunteers has been shown to have no effect on the cardiovascular system, nor does it produce any subjective side-effects (Karim *et al.*, 1970b).

We have previously reported the use of prostaglandin F_{2α} (50 µg./minute) for therapeutic termination of pregnancy in the first and second trimester of pregnancy (Karim *et al.*, 1970a). Prostaglandin E₂ is also effective over the same gestational period at one-tenth of the concentration. In the prostaglandin E series only four patients out of 52 had diarrhoea compared with about 50% incidence in the prostaglandin F_{2α} group. This suggests a more selective action of prostaglandin E₂ on the uterus and less effect on the smooth muscle of the gastrointestinal tract compared with prostaglandin F_{2α}. The reduced incidence of diarrhoea, apart from adding to the comfort of the patient, reduces contamination of the perineum during abortion.

The uterine activity produced by prostaglandin E₂ in the

first and second trimesters of pregnancy is different from the prostaglandin-induced activity at or near term. On the uterus at or near term prostaglandin E₂ in a concentration of 0.5–6 µg./minute produces normal labour-like contractions with increase in frequency and amplitude (Embrey, 1969; Karim, 1969b, Karim *et al.*, 1970a). The tone of the uterus does not increase. In the first and second trimesters of pregnancy prostaglandin E₂ 5 µg./minute produces in the uterus an increase in tone as well as frequency and amplitude.

Apart from vomiting and diarrhoea, the only other side-effect was blurring of vision during prostaglandin E₂ infusion reported by one patient. Whether this was caused by the drug is difficult to assess. No such effect has been reported with an infusion of up to 40 µg. of prostaglandin E₂ per minute in non-pregnant volunteers (Karim *et al.*, 1970b).

The results of the present series are encouraging. Medical induction of abortion with prostaglandin E₂ appears to be effective even in the first trimester of pregnancy. It is simple and safe, eliminating many of the hazards encountered with other methods used. A large proportion of abortions were complete, needing no further surgical intervention.

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