Use of Prostaglandin E₂ in the Management of Missed Abortion, Missed Labour, and Hydatidiform Mole

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Summary: Treatment of six cases of missed abortion and one case of hydatidiform mole with intravenous infusion of prostaglandin E₂ resulted in complete abortion in all cases. Of 15 patients with missed labour, 14 were delivered successfully with similar treatment. The technique appears to be a safe, reliable, and rapid method of managing missed abortion, missed labour, and hydatidiform mole.

Introduction

Intrauterine death of the fetus is usually followed by contractions of the uterus and the expulsion of its contents within a relatively short time (Pritchard and Ratnoff, 1955; Trussell, 1962). Retention of the products of conception, including the dead fetus, may occur at any stage of pregnancy. The condition is then termed missed abortion or missed labour according to the period of gestation at which the fetus dies. Delay in the development of spontaneous labour does occur and may warrant active treatment, and circumstances may make it desirable to effect delivery at any time after the diagnosis of fetal death has been firmly established.

Medical induction of labour is usually the treatment of choice, and high concentrations of oxytocin have been infused with varying success. Surgical evacuation by the vaginal route of an early fetal death is often technically difficult, mainly owing to a tight cervix which resists dilatation. Surgical induction of labour by artificial rupture of the membranes in later pregnancies carries a very serious risk of intrauterine infection. Hysterotomy and caesarean section are undesirable, but may be the only alternative in an unsuccessful surgical induction.

Recently the use of prostaglandin E₂ (0.5 µg./minute) for the induction of labour at or near term has been reported (Karim *et al.*, 1970). The same prostaglandin in a higher concentration (5 µg./minute) is effective for therapeutic termination of pregnancy in the first and second trimesters of pregnancy (Karim and Filshie, 1970).

In this study it is shown that prostaglandin E₂ can be used in the management of missed abortion and hydatidiform mole, and for the induction of labour in cases of fetal death in the third trimester of pregnancy.

Patients and Methods

Six patients with a missed abortion (fetal death in the first and second trimesters of pregnancy), one with a hydatidiform mole, and 15 with missed labour (intrauterine death of the fetus in the third trimester) were selected for treatment. In every case the products of conception were retained in utero for at least four weeks. Except in the patient with the hydatidiform mole uterine activity was continuously measured by recording changes in the intra-amniotic pressure from a catheter inserted by the transabdominal route into the amniotic cavity. Informed consent was obtained for this procedure, and spontaneous uterine activity was recorded for at least 30 minutes before the infusion of prostaglandin E₂.

Crystalline prostaglandin E₂ (prepared biosynthetically) was dissolved in ethanol to give a 10 mg./ml. solution. This was

sterilized by ultrafiltration and diluted with sterile 5% dextrose solution just before use to give a solution containing 25 µg./ml. and 2.5 µg. of prostaglandin E₂ per ml. For the medical induction of labour in cases of missed abortion and hydatidiform mole prostaglandin E₂ was infused at the fixed rate of 5 µg./minute. For the induction of labour in cases of intrauterine death of the fetus in the third trimester of pregnancy prostaglandin E₂ was infused at the rate of 0.5 µg./minute. In the latter group the concentration of prostaglandin E₂ was increased to 1 or 2 µg./minute in some cases to obtain adequate uterine stimulation.

Results

Missed Abortion.—The results of treatment of six cases of missed abortion and one case of hydatidiform mole are shown in Table I. The patients were given an intravenous infusion of 5 µg. of prostaglandin E₂ which stimulated the uterine activity in all six women. There was a transient increase in the

TABLE I.—Results of Treatment in Six Cases of Missed Abortion and One Case of Hydatidiform Mole with Prostaglandin E₂ Infusion of 5 µg./minute

Case No.	Age	Parity	Gravida	Estimated Gestation (Weeks)		Duration of Intrauterine Death (Weeks)	Induction-Abortion Interval	Remarks
				At Death	At Delivery			
1	26	2	3	14	19	5	2½ hours	Placenta expelled after delay of one hour
2	21	1	1	18	22	4	8 hours	—
3	20	0	0	16	21	5	35 minutes	Vomiting during infusion
4	36	4	4	22	34	12	12 hours	—
5	30	3	3	15	21	6	3 hours	—
6	24	0	0	18	23	7	25 minutes	Vomiting during infusion
7	20	0	0	—	20	—	7½ hours	Hydatidiform mole

TABLE II.—Results of Treatment in 15 Cases of Missed Labour with Prostaglandin E₂ Infusion

Case No.	Age	Parity	Gravida	Estimated Gestation (Weeks)		Duration of Intrauterine Death (Weeks)	Infusion Rate (µg./min.)	Infusion Time (Hours)	Infusion-Delivery Interval (Hours)
				At Death	At Delivery				
8	30	6	8	34	44	10	0.5	9	9
9	36	4	4	30	42	12	0.5	3½	3½
10	30	5	7	36	42	6	0.5	14	14
11	24	1	1	28	36	8	1.0	18	29½*
12	24	2	2	38	42	4	0.5	7	7
13	38	6	8	40	44	4	0.5	11½	11½
14	26	2	2	34	42	8	2.0	6½	6½
15	32	9	9	38	42	4	0.5	4	5½
16	19	3	3	32	38	6	1.0	12	23
17	31	3	4	40	44	4	1.0	14	C.S.†
18	25	6	6	30	39	9	2.0	13½	14
19	20	1	1	30	36	6	1.0	8	8
20	20	1	1	38	46	8	2.0	8½	12
21	24	2	3	38	42	4	0.5	10	13½
22	22	1	1	34	40	6	0.5	13	13

*Infused over two days.

†Caesarean Section (see text for details).

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tone of the uterus which was followed by regular and rhythmic contractions (Fig. 1). The uterine contractions were over 100 mm. Hg strong with a frequency of five to seven contractions every 10 minutes. The contractions were effective in dilating the cervix, and abortion was successful and complete in all seven cases. The induction-abortion interval in the six cases of missed abortion varied between 2½ and 14 hours, with a mean of 8 hours. Ergometrine 0.5 mg. was given intramuscularly after the expulsion of the fetus. Blood loss was minimal in all cases.

Missed Labour: Intrauterine Fetal Death in the Third Trimester.—The 15 patients with intrauterine death of the fetus in the third trimester of pregnancy were treated in the same manner as the series of cases of induction of labour at or near term previously reported (Karim *et al.*, 1970). Prostaglandin E₂ was infused at the rate of 0.5 to 2 µg./minute. This produced uterine activity similar to that of normal labour, with an increase in frequency and amplitude of contractions without an increase in resting tone. Eight women in this group responded to 0.5 µg./minute infusion. Four women required 1 µg./minute infusion, and in three the infusion rate had to be increased to 2 µg./minute before sufficiently strong contractions were produced to effect dilatation of the cervix. In 14 women prostaglandin infusion was effective in producing a delivery. The average induction-delivery interval was 12 hours and 10 minutes. There was one case of failed induction. Prostaglandin E₂ 1 µg./minute infused for 14 hours produced strong contractions which lasted for at least 12 hours after stopping the infusion. The cervix, however, remained undilated. Pregnancy was terminated by caesarean section. All patients were given 0.5 mg. of ergometrine intramuscularly after the expulsion of the fetus. The third stage of labour was normal and blood loss was minimal.

The only side-effects in this series were in the missed abortion cases receiving 5 µg./minute. Two out of the six women vomited during the prostaglandin E₂ infusion.

FIG. 1.—Case 6. Record of prostaglandin-E₂-induced uterine activity in a case of missed abortion at 18 weeks. Infusion rate 5 µg./minute.

FIG. 2.—Case 14. Continuous record of prostaglandin-E₂-induced uterine activity in a case of missed labour (intrauterine fetal death at 34 weeks).

Discussion

Controversy has always existed about the treatment recommended for missed abortion and missed labour. Supporters of active intervention are aligned against those who advocate waiting for spontaneous termination of the condition. The disadvantages of watchful expectancy are said to include inconvenience, mental distress, continued abeyance of reproductive function, and restriction of full activity (Corbett, 1958). Another major disadvantage is that of coagulation defects associated with missed abortion and missed labour. A deficiency of circulating fibrinogen associated with prolonged retention of the dead fetus has been reported by many workers (Hodgkinson *et al.*, 1954; Barry *et al.*, 1955; Pritchard and Ratnoff, 1955; Quinn and Harper, 1955). O'Driscoll and Lavelle (1955) suggested that such a disorder was more likely to develop when the dead fetus had been retained for more than four weeks. These authors questioned the wisdom of the belief held by some conservative obstetricians that the standard treatment of missed abortion and missed labour should be one of expectancy, and stated their belief that labour should be induced at the earliest possible moment after confirmation of fetal death.

Once the diagnosis of fetal death is confirmed the treatment at present available is medical induction or surgical intervention. The advantages of a medical method of treating missed abortion and missed labour are considerable. Surgical intervention, in the presence of macerated products of conception, is always attended by risk of infection, haemorrhage, and trauma. Many drugs and hormones have been used to stimulate uterine contractility in missed abortion and missed labour. Of these, oestrogen treatment has enjoyed the widest popularity since its introduction by Robinson *et al.* (1935). In a critical revaluation of the role of oestrogen therapy, however, Martin and Menzies (1955) showed that oestrogen therapy had no merit when used in the treatment of missed abortion and missed labour, and that where such therapy was successful the induction delivery interval was on an average 7.7 days.

A high concentration of oxytocin infusion has been shown to be effective in medical induction in cases of missed abortion and missed labour, and is preferable to surgical intervention. Instances of severe cutaneous vasoconstriction and hypertension during oxytocin therapy have been reported. In some cases the induction-abortion interval has been several days (Loudon, 1959; Toaff and Ayalon, 1962). Medical induction with prostaglandin E₂ in cases of missed abortion, hydatidiform mole, and missed labour gives promise of being safe, reliable, and rapid.

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