Continuous monitoring of uterine contractions to control intra-amniotic administration of prostaglandin $F_2\alpha$ for therapeutic and missed abortion

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Summary

Intra-amniotic prostaglandin $F_2\alpha$ ($PGF_2\alpha$) was administered to 10 patients for midtrimester therapeutic abortion and to 20 patients for missed abortion. An epidural catheter was placed into the amniotic cavity and the other end was connected to a physiological pressure transducer to measure the uterine contractions continuously. The dosage was adjusted according to the uterine contractions, and was therefore individualized for each patient. Half the patients with therapeutic abortion required $PGF_2\alpha$ 30 mg or less, and only 20% of patients with missed abortion needed more than 30 mg. Complications such as uterine cervical lacerations could be prevented by administration of the correct dosage of prostaglandin in each case.

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Administration of prostaglandin intra-amniotically for a therapeutic abortion is not devoid of dangerous complications. Perry *et al.*[1] reported 5 cases of uterine trauma when 40 mg of prostaglandin $F_2\alpha$ ($PGF_2\alpha$) was administered intra-amniotically, followed by an oxytocin infusion of 100 mU/min. Wentz *et al.*[2] reported 2 cases of posterior rupture of the cervix in young primigravidas when prostaglandin was administered intra-amniotically for therapeutic abortion. They gave a test dose of 5 mg intra-amniotically, followed by 25 mg. Both patients received 25 mg after 8 hours; one received another 25 mg after 16 hours and the other 25 mg 10 hours later. The incidence of this complication in their series was 2%. Rupture of the uterus in 2 multigravidas was reported by Propping *et al.*,[3] who used laminaria tents to dilate the cervix overnight and then administered 40 mg $PGF_2\alpha$. Both patients required abdominal hysterectomy. An oxytocin infusion of 120 mU/min was given to both patients after the membranes had ruptured.

The American Food and Drug Administration recommended a dosage of $PGF_2\alpha$ 40 mg intra-amniotically to be followed by 10-40 mg 24 hours later unless abortion was imminent.[4] In an international multicentre study of the World Health Organization's task force on the use of prostaglandins, $PGF_2\alpha$ 25 mg was administered intra-amniotically.[5] The catheter was left in position and a second injection of 25 mg was given 6 hours later, after which the catheter was withdrawn.

The latter method for performing therapeutic abortions was examined in this hospital, but the distal end of the epidural catheter was connected to the physiological pressure transducer of a Hewlett-Packard fetal monitor. Contractions obtained after administration of 25 mg $PGF_2\alpha$ were unexpectedly high in intensity and frequency (Fig. 1). This observation encouraged the use of internal monitoring of uterine contractions to control the administration rate of prostaglandin and thereby also prevent excessive stimulation of the uterus.

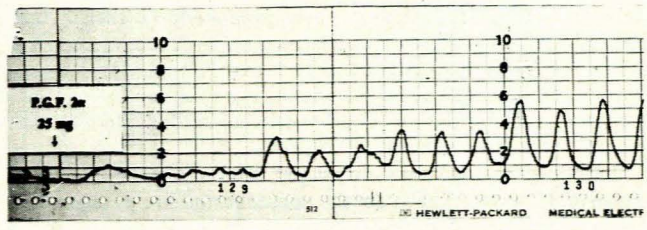

Fig. 1. Strong uterine contractions are observed after administration of $PGF_2\alpha$ 25 mg intra-amniotically (paper speed 1 cm/min; vertical scale 2-40 mmHg; 4-80 mmHg).

Patients and methods

Thirty patients, 20 with missed midtrimester abortion and 10 undergoing therapeutic abortion, were included in the series. Patients were informed what the procedure entailed. After the patient had emptied her bladder the condition of the cervix was assessed. The abdomen was cleansed and draped, using a strict aseptic and antiseptic technique. Using 1% lignocaine, local infiltration of the skin was performed in the midline halfway between the fundus of the uterus and the pubis. An amniocentesis was then performed using a 7 mm 18-gauge Tuohy needle. Once the position of the amniotic cavity had been confirmed by aspiration of amniotic fluid, a 90 cm long epidural catheter (Portex) was partly threaded through the Tuohy needle into the amniotic cavity. The needle was then removed and the puncture wound was covered with a sterile gauze swab. The catheter was tightly secured to the abdominal wall with Elastoplast. The other end of the epidural catheter was then connected to a sterile physiological pressure transducer and a Hewlett-Packard cardiotocograph for pressure recordings. Correct calibration of the transducer was always ensured. A recording speed of 1 cm/min was used. Basal uterine pressures were observed for 10 minutes. An initial dose of 5 mg $PGF_2\alpha$ was then injected into the amniotic cavity with the aid of a three-way tap and was repeated every 30 minutes, depending on the amplitude and frequency of uterine contractions. After 1 patient had developed severe adverse effects from the prostaglandins,

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probably owing to quick systemic absorption, this policy was changed. $PGF_2\alpha$ 5 mg was diluted with 10 ml saline; 1 ml (0,5 mg) of this solution was given slowly intra-amniotically and when no adverse effects were observed the other 9 ml was given. The $PG_2\alpha$ in subsequent administrations, however, was still undiluted.

All patients were given antibiotic prophylaxis in the form of ampicillin 500 mg intravenously every 6 hours. Once the contractions started, adequate pain relief was ensured. Membranes were kept intact as long as possible, but when spontaneous rupture occurred no further $PGF_2\alpha$ was administered intra-amniotically. If necessary, contractions were augmented with an oxytocin or prostaglandin infusion. Once strong contractions were established, aseptically performed vaginal examinations were used to assess progress. After abortion the fetus was weighed and the placenta and membranes examined for completeness. The patient was observed for vaginal haemorrhage. An evacuation of the uterus was performed when the abortion was incomplete.

Results

Patients undergoing therapeutic abortion

In 10 patients the indication for prostaglandin administration was therapeutic abortion. Indications for therapeutic abortion were sexual assault (5 patients), eclampsia and fulminating pre-eclampsia (2 patients), Down syndrome, anencephaly and excessive pelvic radiation in early pregnancy (1 each). Ages ranged from 14 to 39 years and duration of pregnancy from 16 to 26 weeks. In all the patients except 1 (case 7, Table 1) the cervix was long and undilated prior to the $PGF_2\alpha$ injection. All except 3 patients were nulliparous. Uterine contractions usually followed quickly upon the injection of $PGF_2\alpha$.

Induction-to-delivery time ranged from 6 to 60 hours, with a mean of 33 hours. $PGF_2\alpha$ dosage ranged from 15 to 95 mg, with a mean of 38,5 mg. Vomiting occurred in 7 patients and diarrhoea in 3. In 1 patient (case 5) severe bronchospasm occurred immediately aftr the injection of $PGF_2\alpha$. She also had severe vomiting and diarrhoea. The bronchospasm responded well to the intravenous administration of hexoprenaline and the nausea was well controlled by prochlorperazine. On removal of the catheter it was found that blood was present in the distal 2 cm, which led to the assumption that the $PGF_2\alpha$ had been injected into the intervillous space or the myometrium. A repeat amniocentesis was performed and a new catheter was inserted. No further problems were encountered in this patient.

One failure occurred in a 14-year-old primigravida who was 26 weeks pregnant (case 1). Strong uterine contractions were established after 20 mg $PGF_2\alpha$ had been injected. Initially the cervix started dilating, but when it was 1 cm dilated and well effaced, further dilatation failed to occur in spite of strong and frequent contractions. Oxytocin was also administered, as well as intravenous $PGF_2\alpha$. Although the contractions were strong and regular throughout, the cervix failed to dilate. Fifty-four hours after the initial injection the induction was abandoned and a hysterotomy was performed.

It was not necessary to administer supplementary oxytocin or intravenous $PGF_2\alpha$ to 4 of the patients. In a further 4 patients (cases 5, 6, 7 and 10) oxytocin was only administered after spontaneous rupture of the membranes as intra-amniotic $PGF_2\alpha$ was discontinued at this stage. In 1 patient the catheter became obstructed but adequate contractions were obtained with intravenous oxytocin. The remaining patient (case 1) had oxytocin and intravenous prostaglandin before rupture of the membranes.

Patients with missed abortion or intra-uterine death

In 20 patients $PGF_2\alpha$ was administered for missed abortion or intra-uterine death. Ages ranged from 17 to 42 years and duration of pregnancy from 18 to 41 weeks. In many patients, however, the fundal height was much lower than the corresponding duration of pregnancy (Table II). Parity varied between 0 and 12. The cervix was long and undilated in 14 patients. Induction-to-delivery time ranged from 3,9 to 46,1 hours, with a mean of 15 hours. The total dosage of $PGF_2\alpha$ administered varied from 5 to 100 mg, with a mean of 18,75 mg. Only 5 mg was necessary in 6 patients. The uterus usually started contracting very soon after the injection (Fig. 2). Supplementary oxytocin or $PGF_2\alpha$ was given to only 3 patients. Vomiting occurred in 6 patients. In 1 patient the catheter became obstructed and had to be replaced (case 15).

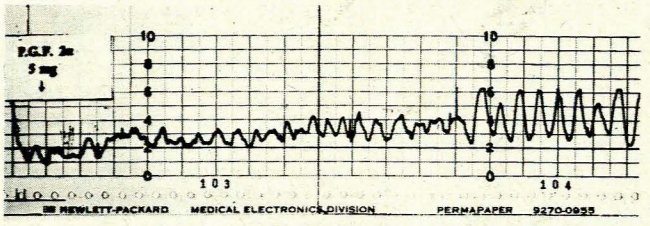

Fig. 2. Case 26. Strong uterine contractions immediately followed the injection of $PGF_2\alpha$ (paper speed 1 cm/min; vertical scale 2-40 mmHg; 4-80 mmHg).

TABLE I. CLINICAL DETAILS OF PATIENTS UNDERGOING THERAPEUTIC ABORTION

No.	Age	Duration of pregnancy	Parity	Indication	Condition of cervix	Induction-delivery time (hrs)	Total $PGF_2\alpha$ dosage (mg)	Complications
1	14	26	0	Sexual assault	Long and closed	54,0	20*	Vomiting and diarrhoea. Delivered by hysterotomy
2	37	16	3	Anencephaly	Long and closed	7,6	35	Vomiting and diarrhoea
3	22	16	0	Excessive radiation in early pregnancy	Long and closed	60,0	95*	Catheter blocked. Vomiting
4	37	18	0	Sexual assault	Long and closed	32,6	55	Vomiting
5	39	20	3	Down syndrome	Long and closed	23,3	30*	Intra-arterial injection, bronchospasm, vomiting, diarrhoea
6	18	26	0	Eclampsia	Long and closed	37,0	15*	Nil
7	20	24	1	Fulminating pre-eclampsia	1 cm dilated, poorly effaced	51,5	60*	Nil
8	15	23	0	Sexual assault	Long and closed	6,6	20	Vomiting
9	21	18	0	Sexual assault	Long and closed	16,9	20	Vomiting
10	16	18	0	Sexual assault	Long and closed	37,0	35*	Nil

* Also received intravenous oxytocin or prostaglandin.

TABLE II. CLINICAL DETAILS OF PATIENTS WITH MISSED ABORTION AND INTRA-UTERINE DEATH

No.	Age	Duration of pregnancy (wks)	Fundus height (wks)	Parity	Condition of cervix	Induction-delivery time (hrs)	Total $PGF_{2\alpha}$ dosage (mg)	Complications
11	37	?	26	5	Closed	6,5	5	Nil
12	21	18	18	2	Closed	12,0	15*	Vomiting
13	23	38	27	0	Closed	46,1	100*	Nausea, vomiting
14	18	41	38	0	2 cm dilated, 60% effaced	8,0	10	Vomiting
15	30	34	22	8	1 cm dilated, uneffaced	23,1	20	Catheter blocked, replaced
16	24	25	24	2	1 cm dilated, poorly effaced	6,3	10	Vomiting
17	22	26	26	2	Closed	14,4	10	Nil
18	17	30	28	0	Closed	21,5	10	Nil
19	22	28	22	2	Closed	21,8	35	Nil
20	19	32	32	0	Closed	34,4	45*	Allergic to iodine
21	20	29	28	0	2 cm dilated, 60% effaced	5,5	5	Nil
22	28	32	24	2	Closed	6,3	5	Nil
23	42	20	28	12	Closed	20,9	35	Nil
24	19	27	22	0	Closed	5,1	5	Nil
25	18	26	20	0	Closed, 50% effaced	9,6	15	Nil
26	24	33	24	1	Closed	14,5	5	Nil
27	17	28	24	0	Closed	4,4	10	Nil
28	29	25	24	4	Closed	11,6	20	Vomiting
29	23	32	26	1	Closed, 50% effaced	3,9	5	Vomiting
30	17	28	16	0	Closed	17,5	10	Nil

* Received intravenous oxytocin or prostaglandin.

Discussion

Intra-amniotic injection of 20% saline and 50% glucose was for a long time the most popular method of terminating midtrimester pregnancy. However, the administration of 50% glucose was associated with fatal anaerobic infection of the uterine cavity and 20% saline with maternal mortality due to intravascular administration of the hypertonic solution. In recent years they have largely been replaced by intra-amniotic prostaglandin, since the latter is associated with a higher success rate and fewer harmful side-effects.[5]

Apart from the usual minor side-effects such as vomiting and diarrhoea, only a few serious complications have been reported. These were mostly rupture of the uterus, laceration of the cervix and cervicovaginal fistulae and cervical incompetence.[6-8] Many of these complications could have been caused by strong uterine contractions when a high cervical resistance was encountered. During labour, sensitivity to intravenous oxytocin or prostaglandin varies from patient to patient. For this reason a fixed dose is never administered, but the administration rate is adjusted to uterine contractions and progress of labour. Difference in response could therefore also be expected when intra-amniotic prostaglandins are given for midtrimester abortions and especially for missed abortions. This difference in response is reflected in the variation in the dose of prostaglandin injected. For therapeutic abortion the dosage varied from 15 to 95 mg and for missed abortion it varied from 5 to 100 mg. The fact that midtrimester abortions were induced with dosages as low as 15 mg, which is much lower than the recommended dosage,[4,5] also suggests that there is a difference in patient response. Although doses lower than those recommended were used in some patients, the induction-delivery interval compared favourably with that in other series.[9-13]

In the patient in whom termination of pregnancy by prostaglandin could not be achieved, strong and frequent uterine contractions lasted for several hours. Although the uterus could be stimulated, the cervix failed to dilate. More intra-amniotic prostaglandin in this case could have caused excessive contractions without adequate relaxation of the uterus. These events might have led to rupture of the uterus or laceration of the cervix, a complication strictly to be avoided in the primigravida.

No infection occurred during this series, but antibiotics had been given prophylactically. As an invasive technique is used, the possibility of infection should always be considered, especially when the catheter remains in the uterine cavity for long periods. Bringing the catheter out in a relatively sterile area on the anterior abdominal wall instead of through the cervix may cause less infection. A similar situation exists when the bladder is drained by a suprapubic catheter rather than an indwelling urethral catheter. The latter was found to cause a higher frequency of urinary tract infection.[14]

Another disadvantage of the method is that the patient's mobility is severely hampered. Owing to the shortness of the catheter the patient lies on her back or on her side, facing the transducer all the time. Changes in position were always handled very carefully to prevent strain on the thin catheter. A long catheter, however, would be more convenient for the patient. As this technique requires facilities for internal monitoring of uterine contractions, it can be applied at selected units only.

Use of prostaglandin suppositories applied vaginally to induce labour in missed abortion or intra-uterine death[15] may eventually replace intra-amniotic prostaglandin injections. Until such time, however, there is still a place for the use of intra-amniotic prostaglandin, but it should be administered with care to prevent harmful effects. Monitoring of intra-uterine contractions is of great help in deciding upon the exact dosage for the individual patient.

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