MID-TRIMESTER THERAPEUTIC ABORTION BY INTRA-AMNIOTIC PROSTAGLANDIN $F_{2\alpha}$ AND CONCOMITANT OXYTOCIN

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Summary: The routine use of intra-amniotic $PGF_{2\alpha}$ and concomitant intravenous oxytocin for second trimester induced abortion is evaluated in 274 consecutive cases. Eighty-five per cent of the nullipara and 90 per cent of the parous women aborted within 24 hours and all but one within 48 hours following a single intra-amniotic dose.

Doses were 40 or 50 mg $PGF_{2\alpha}$ and the mean induction-abortion interval was not shortened by the higher dose. Neither did gestational age have any affect on abortion time. Postabortum haemorrhage occurred in 22 cases in spite of routine curettage. Parametritis was reported in eight cases. In two nullipara, cervical tears were observed, in one case forming a persisting fistula to the uterine cavity.

There were no significant toxic side effects to the administration of $PGF_{2\alpha}$ or oxytocin. It is concluded that the method has not been superseded with regard to efficacy of abortion induction and that the rate of more serious complications is not above whate can be expected from any other available method of second trimester pregnancy termination.

INTRODUCTION

The prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) was introduced as an abortifacient in 1970 and has been commercially available in Denmark since 1975.

Intra-amniotic administration of the drug soon became the most widely employed method of second trimester pregnancy termination in this country, offering fewer side effects and shorter induction-abortion interval than the hitherto preferred method of hypertonic saline instillation (Nielsen *et al.,* 1975, Lange, 1983).

In the ensuing years, new prostaglandin analogues and methods of intracervical or vaginal administration have been introduced, possibly offering less discomfort to the patient (Kajanoja *et al.,* 1975, Sørensen and Wolf, 1984).

The aim of this study has been to assess the efficacy and the safety of second trimester abortion induction by intra-amniotic $PGF_{2\alpha}$, as used routinely in a gynaecological department over a period of nine years.

MATERIAL

During the period 1.11.1975 to 31.10.1984, a total of 281 women were admitted to the Copenhagen County Hospital in Glostrup for termination of second trimester pregnancy.

Throughout the nine-year-period, the same schedule for mid-trimester therapeutic abortion war followed.

The gestational age was estimated by ultrasonic scanning. Still under ultrasonic surveillance, a needle was inserted into the amniotic cavity and about 50 ml of amniotic fluid aspirated.

Through the same needle, a solution of $PGF_{2\alpha}$ was instilled into the cavity. The dose was 40 or 50 mg, depending on which of two different commercial preparations was available at the time given.

Immediately following the instillation, an i.v. drip of 100 IU oxytocin in 1000 ml glucose was started and 10 units of oxytocin administered per hour. For analgesia, pethidine was used as needed. After the expulsion of the foetus, a suction curettage was made under general anaesthesia, irrespective of whether the abortion had been complete or not. This was done to reduce the risk of postpartum bleeding and infection; also, any cervical tears could be diagnosed and sutured without delay.

Of the 281 women referred for mid-trimester abortion, seven were excluded from the study: in six cases no amniotic fluid could be aspirated,

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Table 1. – *Mean induction-abortion time following intra-amniotic instillation of $PGF_{2\alpha}$ 40 and 50 mg in 274 consecutive cases of mid-trimester therapeutic abortion.*

	13th - 16th week	17th - 20th week	21th - 28th week	All weeks
0-para 40 mg	16.7 hours n = 17	15.4 hours n = 10	14.5 hours n = 4	19.1 hours n = 131
0-para 50 mg	19.5 hours n = 47	20.6 hours n = 44	19.3 hours n = 9	
X-para 40 mg	17.0 hours n = 25	17.2 hours n = 20	13.5 hours n = 4	15.9 hours n = 143
X-para 50 mg	14.7 hours n = 51	16.4 hours n = 30	15.7 hours n = 13	
All.:	17.0 hours	18.3 hours	16.3 hours	

and the abortion was induced by other means than $PGF_{2\alpha}$ instillation; in one case – a 34-year-old primigravida – the oxytocin drip was omitted.

Of the remaining 274 women, 131 or 48 per cent were nullipara and the remainder had a parity of 2 (range 1-6). The mean age was 25.5 years (range 14-46). Thirty-eight women were under 18 years of age. The indication for abortion was mainly psycho-social (224 or 82 per cent of the women). In 36 cases, the indication was eugenic: rubella infection during early pregnancy, chromosome anomalies, or neural tube defects. Fifteen women were referred for a late missed abortion.

RESULTS

At amniocentesis, 140 (51 per cent) of the women were in the 13th - 16th gestational week, 104 or 38 per cent in 17th - 20th week, and 30 women or 11 per cent in week 21 - 28. Ten women had a twin pregnancy, one carried triplets.

Following the intra-amniotic installation of $PGF_{2\alpha}$, abortion occurred within 2 - 71 hours; 90 per cent of the parous women and 85 per cent of the nullipara had aborted within 24 hours (fig. 1).

In two cases, both nullipara, a laminar tent was inserted after 30 hours, and the abortion completed after 45 and 71 hours, respectively. In no case was the instillation repeated.

The 11 plurigravida all aborted within 24 hours.

Eigthy women had a $PGF_{2\alpha}$ dose of 40 mg instilled and 194 had 50 mg.

The two groups were evenly distributed with regard to parity and gestational age. The higher dose had no effect on the mean induction-abortion time: 16.4 hours in the 50 mg group and 16.0 hours in the women who only received 40 mg. Neither was the induction-abortion interval influenced by gestational age (table 1).

Complications

There were no serious immediate reactions to the instillation.

Three patients complained of severe nausea, prickling skin sensation, vomiting and diarrhoea; they recovered within an hour.

In ten cases the blood loss was extensive, necessitating transfusion of 2 or 3 units of blood.

Cervical lacerations were seen in two cases, both nullipara in the 18th gestational week: one had a posterior cervical tear. After suture, healing was complete, and at delivery three years later the cervix seemed normal. The other patient presented a classic "boucket handle tear", an eight cm long tear in the posterior fornix, communicating into the uterine cavity. The cervical os was closed, and the foetus had

obviously been expelled through the tear. At examination one year later, a persisting small fistula was seen. Abortion time in these two cases had been 17 and 19 hours, respectively.

The most frequent complication was postabortum hemorrhage within the first week, which in 22 cases necessitated a repeat curettage.

Within the first month following the abortion, eight patients presented the symptoms of a slow parametritis: slight fever lasting for more than one day, pains and recurrent bleeding. Three of these patients had had a silent gonococcal infection diagnosed and treated on admittance.

Fourteen of the 15 patients with a missed abortion had the pregnancy terminated without complications. One patient, a primipara 34-year-old with one earlier spontaneous abortion, evolved a deep venous thrombosis with phlebitis. She was in the 25th gestational week at the abortion induction, and the intrauterine death had probably occurred two or three weeks earlier. She recovered, but was hospitalized for a total of 40 days, her case exhibiting the most serious complication of this study.

There were no reports of fetuses delivered alive.

DISCUSSION

In this study, 88 per cent of the abortions took place within 24 hours of the induction and all but one within 48 hours.

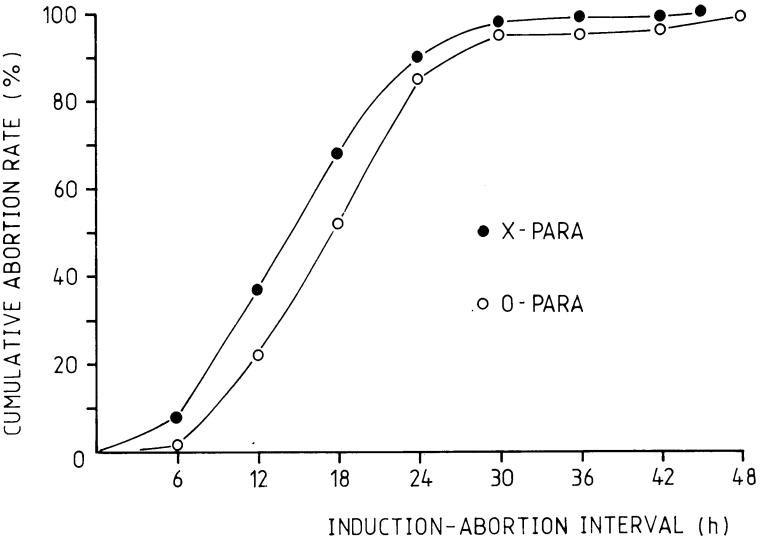

Fig. 1. — Cumulative abortion rates after intra-amniotic instillation of $PGF_{2\alpha}$ in 274 consecutive cases.

The results are similar to what has been reported from other series using intra-amniotic prostaglandins, the most efficient method of second trimester abortion induction to date (Kajanoja *et al.*, 1975, Lange, 1983, Cameron and Baird, 1987).

Although not directly comparable, the 24-hour rate of success of this series – where oxytocin was given in every case and without delay – seems slighly better than the rates reported from other studies, using oxytocin only in the case of insufficient labour, i.e. with a delay of six

to eight hours. Although no sufficiently conclusive study has been made, it seems probable that the addition of oxytocin shortens the induction-abortion interval. It must be of great psychological importance to the patient that the whole operation can be finished within 24 hours; also, a more effective labour frees the patient of a possible second $PGF_{2\alpha}$ injection, and whatever risk this may carry.

However, the oxytocin drip itself has its drawbacks: "water intoxication", due to the antidiuretic effect of oxytocin, has been described in a number of cases, where the electrolyte derangement – mostly in connexion with rather high dose rates and fluid overload – has led to grand mal-like seizures (Sederberg-Olsen and Olsen, 1983 and Lange, 1983).

Some authors consider that the – probably – faster induction caused by oxytocin may lead to an increased risk of cervico-vaginal injuries. Thus, Kajanoja *et al.* (1975) in their series of 626 induced abortions reported a cervical tear in nine cases, eight of which had received additional oxytocin. All cases were primipara, the frequency of cervical tears in this group being 4%, in the whole series 1.4%. In a study of 796 women who had mid-trimester abortion induced by intra- or extra-amniotic administration of different PG-analogues as well as saline, Purandare *et al.* (1977) described seven cases of cervico-vaginal injuries, all occurring in young nullipara. Oxytocin was not applied.

Perry *et al.*, in 1977, reported five cases of cervical laceration in a series of 80 nullipara (6.2%), who had mid-trimester abortion induced by $PGF_{2\alpha}$ and concomitant oxytocin; in one case the tear was associated with uterine necrosis, probably caused by cornual sacculation and ischaemia. Based on this series and a Literature review, he suggests that the use of concomitant oxytocin in nullipara is associated with a higher risk of cervical rupture.

The two cases of this series represent 1.5% of the primigravida, thus not contributing to the theory of an increased risk of tears by the use of oxytocin.

$PGF_{2\alpha}$ itself has a number of side effects: most frequently the well-known gastro-intestinal effects of prostaglandins; but also more serious complications like anaphylactic reactions, broncho-constriction, epileptiform cramps (Lyneham *et al.* 1973); and hemodynamic effects like bradycardia, low blood pressure, even cardiac arrest have been attributed to $PGF_{2\alpha}$ accidentially entering the circulation of the patient. The rapid break-down of $PGF_{2\alpha}$, especially in lung tissue, may explain the short duration and benign outcome of these attacks.

Most authors consider that other methods of pregnancy termination should be employed in the case of intrauterine death, due to the possibly altered diffusion of prostaglandins over the membranes.

In this small series of 15 cases of missed abortion, no unexpected adverse effects were seen. Although it cannot be completely excluded as a prostaglandin complication, the case of severe deep venous thrombosis and phlebitis seen in this group is a well-known complication of delivery as well as spontaneous late abortion. In another series of 30 cases of death in utero, intra-amniotic $PGF_{2\alpha}$ was used for abortion without complications (Antsaklis *et al.*, 1979).

In the present study, 50 mg of $PGF_{2\alpha}$ was not more efficient than 40 mg, a finding of other authors, e.g. Kajanoja *et al.* (1975). The many – partially dose-related – side effects of $PGF_{2\alpha}$ make it mandatory to use as low a dose as possible; 40 mg of $PGF_{2\alpha}$ would seem sufficient, whereas 25 mg doses lead to significantly more failures of induction (Kajanoja *et al.*, 1975, Lange, 1983).

It may be concluded from this and other studies that mid-trimester abortion induction by $PGF_{2\alpha}$ with or without con-

comint oxytocin is a relatively simple and safe method.

Statistical analyses on large but unrandomized series from the USA would seem to indicate that at least until the 17th gestational week, dilatation and evacuation offer advantages over the induced abortion with regard to side effects like bleeding, infection, incomplete abortion and cervical tears. Also, the mortality rates were half those of the instillation method. However, these figures regard the combined instillation of $PGF_{2\alpha}$ *and* hyperosmolar urea (Kafrissen *et al.,* 1984, Grimes *et al.,* 1985). The dilatation and evacuation method calls for significantly fewer days of hospital confinement, an aspect of particular importance to the paying patient in the USA. Apart from this method's alleviating much of the patient's discomfort and stress of the late abortion, so far no study has answered the question of possible damage caused by instrumental dilatation of the cervix for second trimester abortion, and its consequences for the outcome of later pregnancies.

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