PAPERS AND ORIGINALS

Blood Coagulation Changes during Mid-trimester Abortion Induced by Prostaglandin $F_{2\alpha}$

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Summary

Serial studies on the coagulation system were made during second-trimester abortion induced by extra-amniotic, intra-amniotic, vaginal, and intravenous prostaglandin $F_{2\alpha}$. No significant changes were found in the prothrombin time, partial thromboplastin time, or levels of fibrin-fibrinogen degradation products. An increase in the activity of factor X occurred with all routes of administration; the activity of factor VIII increased during extra-amniotic, vaginal, and intravenous administration; factor V activity increased during extra-amniotic and vaginal administration; and the activity of factor VII-X complex increased slightly at the time of abortion with all methods.

The findings suggest that though prostaglandin induction of second-trimester abortion produces changes in the coagulation system the effects are much less than those which accompany induction of abortion by hypertonic saline or abdominal delivery in late pregnancy.

Introduction

Defective blood clotting due to intravascular coagulation may occur as a complication of induction of second-trimester abortion with intra-amniotic saline (Stander *et al.*, 1971; Brown *et al.*, 1972). Though overt coagulation failure is rare this phenomenon could account for some of the haemorrhagic complications which accompany therapeutic abortion (Halbert *et al.*, 1972). In a recent study we found an increase in coagulation factors V, VII-X complex, VIII, and X during second-trimester abortion induced by extra-amniotic administration of prostaglandin $F_{2\alpha}$ (Badraoui *et al.*, 1973).

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At present prostaglandins are being given by various routes to induce second-trimester abortion. These include intravenous intra-amniotic, extra-amniotic, and intravaginal administration (Embrey *et al.*, 1972; Hillier and Embrey, 1972; Karim *et al.*, 1972; Hale *et al.*, 1973). We therefore investigated the coagulation system changes which occur during second-trimester abortion with prostaglandin $F_{2\alpha}$ given by these different routes.

Patients and Methods

Second-trimester abortion was induced with prostaglandin $F_{2\alpha}$ given in the following ways.

Vaginal Route.—Seven patients aged 17-26 years (mean 20 years) and gravida 1-4 were studied at 14-19 weeks of gestation (mean 16 weeks). A carbowax-based pessary (Upjohn Ltd.) containing 25 mg prostaglandin $F_{2\alpha}$ was inserted at two-hourly intervals high into the posterior fornix of the vagina until abortion occurred.

Intra-amniotic Route.—Four patients aged 17-29 years (mean 22 years) and gravida 1-2 were studied at 18-22 weeks of gestation (mean 20 weeks). With full sterile precautions and under local anaesthesia a Tuohy needle was inserted trans-abdominally into the amniotic cavity. When clear liquor was obtained a thin polyethylene catheter was inserted and the needle removed. A total of 25 mg prostaglandin $F_{2\alpha}$ was injected in split doses of 5 mg at five-minute intervals. If abortion had not occurred within 24 hours a further 25 mg in split 5-mg amounts was instilled.

Intravenous Route.—Six patients aged 15-24 years (mean 19 years) and gravida 1-2 were studied at 16-20 weeks of gestation (mean 18 weeks). Prostaglandin $F_{2\alpha}$ was dissolved in sterile 5% glucose and infused at 25 μ g/min for half an hour and then at 50 μ g/min until abortion occurred.

Extra-amniotic Route.—Twelve patients aged 18-37 years (mean 23 years) and gravida 1-7 were studied at 14-20 weeks of gestation (mean 17 weeks). The method used was as described by Embrey *et al.* (1972), using an indwelling extra-amniotic Foley catheter. After an initial 250- μ g test dose prostaglandin $F_{2\alpha}$ 750 μ g was instilled two-hourly.

COAGULATION TESTS

Samples of venous blood (18 ml) were withdrawn into a plastic syringe (1) before administration of prostaglandin F₂α, (2) when uterine contractions were established (two to four hours after the initial administration of prostaglandin), (3) immediately after the expulsion of the products of conception, and (4) 24 hours after abortion.

A 9-ml sample of blood was added to 1 ml 3.8% sodium citrate for coagulation assays, and 5 ml to 0.05 ml aprotinin (5,000 units/ml) for assay of fibrin degradation products.

Prothrombin time was measured by the method of Quick (1966), and partial thromboplastin time by using Bell and Alton's (1954) platlet substitute. Fibrin degradation products were assayed by the tanned red cell haemagglutination method (Merskey *et al.*, 1966; Bonnar *et al.*, 1969). Factor V and factor VII-X complex were assayed by the method of Stefanini and Dameshek (1962); factor VIII was assayed by the two-stage method of Biggs *et al.* (1955); factor X was assayed as described by Denson (1961). Wilcoxon's signed

ranks test and Student's *t* test were used to establish the statistical significance of the coagulation changes.

Results

As shown in the table the four routes of prostaglandin administration produced no significant changes in the prothrombin time, partial thromboplastin time, and the levels of fibrin degradation products.

Coagulation Changes during Mid-trimester Induction of Abortion with Prostaglandin F₂α, Results expressed as Mean ± 1 S.D.

Route	No. of Patients	Sample*	Prothrombin Time (sec)	Partial Thromboplastin Time (sec)	Fibrin Degradation Products (μg)
Vaginal	7	1	14.6 ± 1.2	64.8 ± 6.7	3.4 ± 0.6
		2	14.9 ± 1.2	64.5 ± 6.0	3.2 ± 1.2
		3	15.1 ± 1.7	64.3 ± 3.9	3.6 ± 1.3
		4	15.1 ± 1.9	62.6 ± 3.2	3.6 ± 2.0
Intra-amniotic	4	1	13.2 ± 0.9	74.6 ± 8.5	2.5 ± 1.8
		2	14.0 ± 0.8	66.9 ± 3.8	4.1 ± 1.9
		3	13.6 ± 0.5	68.1 ± 1.9	4.4 ± 1.2
		4	14 ± 0.3	69.9 ± 9.3	3.7 ± 1.0
Intravenous	6	1	13.9 ± 1.0	71.7 ± 11.6	—
		2	13.3 ± 0.6	68.1 ± 8.9	—
		3	13.4 ± 1.3	68.0 ± 9.7	—
		4	14.2 ± 1.4	76.7 ± 10.5	—
Extra-amniotic	12	1	13.6 ± 0.9	79.9 ± 12.5	4.5 ± 0.8
		2	13.2 ± 1.2	83.5 ± 18.8	5.0 ± 1.2
		3	12.8 ± 1.0	79.1 ± 16.8	4.7 ± 1.5
		4	13.5 ± 1.0	78 ± 12.9	5.4 ± 1.9

*For timing of samples see text.

FIG. 1—Changes in coagulation factor X during termination of pregnancy with prostaglandin F₂α. Each point is mean ± 1 S.D. For timings of sample see text.

FIG. 2—Changes in coagulation factor VIII during termination of pregnancy with prostaglandin F₂α. Each point is mean ± 1 S.D. For timings of samples see text.

During administration of prostaglandin $F_{2\alpha}$ by all routes the level of factor X increased, and the rise was significant with extra-amniotic and intravenous administration (fig. 1).

An increase of factor VIII occurred during extra-amniotic, intravenous, and vaginal administration but a decrease occurred with the intra-amniotic route (fig. 2). Factor VII-X complex showed minimal alteration; a slight increase was found at the time of abortion with all routes of administration (fig. 3). Factor V increased significantly during administration of prostaglandin $F_{2\alpha}$ by the extra-amniotic and intra-vaginal routes but a slight decrease occurred during intra-venous and intra-amniotic administration, which was not significant (fig. 4).

FIG. 3—Changes in coagulation factor VII-X complex during termination of pregnancy with prostaglandin $F_{2\alpha}$. Each point is mean $\pm$ 1 S.D. For timing of samples see text.

we found contrast with the prolonged clotting times and decreases in the levels of factors V, VIII, and IX which were found by Stander *et al.* (1971) after induction of abortion with hypertonic saline. Indeed, it is possible that the coagulation changes found in the present study were the result of the abortion process and not specifically related to prostaglandins; this could be confirmed only by investigating a group of patients having spontaneous second-trimester abortion, and opportunities for such a study are few.

FIG. 4—Changes in coagulation factor V during termination of pregnancy with prostaglandin $F_{2\alpha}$. Each point is mean $\pm$ 1 S.D. For timing of samples see text.

Discussion

Recent reports have highlighted the risk of haemorrhagic complications accompanied by changes consistent with disseminated intravascular coagulation which may occur when second-trimester abortion is induced with hypertonic saline (Wagatsuma, 1965; Halbert *et al.*, 1972; Stander *et al.*, 1972). It has been estimated that severe defibrination will occur with saline-induced abortion in one in 1,500 patients (Brown *et al.*, 1972). Though we have investigated only a small number of patients the findings, while indicating some activation of the coagulation system, do not suggest that prostaglandin-induced abortion results in disseminated intravascular coagulation. The minimal changes in the prothrombin time, partial thromboplastin time, and levels of fibrin degradation products which

The coagulation differences observed between the various routes of administration were not marked but the slight decrease of factors V and VIII which occurred after intra-amniotic administration, in contrast to the increase found with extra-amniotic and vaginal administration, suggests that the route of administration may be relevant. The number of patients we investigated with intra-amniotic prostaglandin was too few to draw any firm conclusions, but it is of interest that the changes were in the same direction as those reported in patients having mid-trimester abortion induced with hypertonic saline. At present there is a trend towards using larger doses of intra-amniotic prostaglandins (Craft, 1973), and further studies should clarify this point.

The actions and effects of vaginally administered prostaglandins would be expected to be similar to those of intravenous therapy, as the effect is considered to be via systemic absorption from the vagina. At present the plasma levels of prostaglandin $F_{2\alpha}$ obtained after vaginal administration are uncertain. The pattern of coagulation changes found in the present study showed no obvious difference between the intravenous and vaginal route.

The present study suggests that when second-trimester abortion is induced by prostaglandins the effect on the coagulation system is considerably less than that which accompanies induction of second-trimester abortion with hypertonic saline or occurs with abdominal delivery in late pregnancy (Bonnar *et al.*, 1970).

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Electroencephalographic Changes in Epileptics while Viewing Television

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Summary

Ten consecutive epileptic patients who showed abnormal electroencephalographic (E.E.G.) responses to intermittent photic stimulation have been studied while watching television. Though only two gave a history of television epilepsy nine exhibited spike-wave discharges in the E.E.G. during viewing. This effect occurred when the set was functioning normally but was increased in five subjects when the screen was deliberately caused to flicker.

Introduction

It is well established that watching television may precipitate seizures ("television epilepsy") both in some patients with known epilepsy and in others who do not apparently suffer fits except when viewing (Karlson, 1959; Klapatek, 1959; Lange, 1961; Charlton and Hoefer, 1964). Photic stimulation by a stroboscope also produces seizures in a significant proportion of people with epilepsy and elicits paroxysmal electroencephalographic (E.E.G.) discharges in many more (Gastaut *et al.*, 1958). Abnormal photic responses can usually be demonstrated in patients with television epilepsy (Gastaut and Tassinari, 1966; Jeavons and Harding, 1970) but there have been few E.E.G.

studies of epileptics viewing television. Gastaut *et al.* (1962) investigated 35 people thought to have television epilepsy and recorded their E.E.G.s during viewing, but in none was any significant response observed. Other authors have elicited paroxysmal activity by using television as a stimulus, but only by putting the controls grossly out of adjustment to produce slow flicker or by changing channels (Ritcher, 1960; Dumermuth, 1961; Andermann, 1971). We report a similar study with very different results.

Material and Methods

The study is based on 10 consecutive patients who exhibited photoconvulsive responses (as defined by Bickford *et al.*, 1952) to stroboscopic stimulation during routine E.E.G. investigation in a recording suite where a television set was installed. Their ages ranged from 7 to 29 years (mean 15.7 years); two gave a history of television epilepsy and one reported strange sensations when using a stroboscope to tune a motor car engine. Nine patients showed spontaneous paroxysmal activity in the resting record. The photic stimulator used (Specialised Laboratory Equipment, Type C.P.S.1) had a fine grid placed over the cover glass as recommended by Jeavons *et al.* (1972) and was placed at a distance of 25 cm from the nasion. When photosensitivity was detected bursts of flashes were delivered at various frequencies to determine the range of flicker rates over which abnormal responses could be elicited with the eyes open or closed.

The patient was then asked to view, under conditions of normal room lighting, a 24 in. (61 cm) 405-line black and white television set from a distance of roughly 0.5 m. If paroxysmal activity occurred or showed an appreciable increase above the resting level the patient was then progressively moved away from the set until this effect ceased. When no E.E.G. response was apparent the set was deliberately put out of adjustment.

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