

TERMINATION OF MID-TRIMESTER PREGNANCY BY INTRA-AMNIOTIC INJECTION OF PROSTAGLANDINS E₂ AND F_{2α}

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SYNOPSIS

23 women whose pregnancies ranged from 12 to 24 weeks had their pregnancies terminated by intra-amniotic injection of prostaglandins. PGF₂ was used in 9 cases, PGF_{2α} in 13 cases and both PGE₂ and PGF_{2α} used in 1 case. 3 cases failed to abort with PGE₂ after the third dose of 20 mg. was given. 2 cases (12 weeks gestation) failed to abort with PGF_{2α}. Both had only 20 mg. PGF_{2α}. Larger doses could not be given as repeat amniocentesis failed. Side-effects—headaches, vomiting, diarrhoea, bronchospasm, nausea and flushing—occurred in 7 cases all of whom had PGF_{2α}. No side-effects were noted in those who had PGE₂. All the abortions except 2 were incomplete.

INTRODUCTION

Termination of mid-trimester pregnancies presents special problems. The uterus is too large for safe curettage while hysterotomy is a major operation requiring the opening of the abdominal cavity. Intra-amniotic injection of hypertonic saline or glucose is very effective^{1,2}, but side-effects have been severe in some instances and deaths were reported from hypernatraemia and intra-uterine infection^{3,4}. The use of Prostaglandins for therapeutic abortion has been reported with some success by several workers^{5,6}.

This study attempts to evaluate the effectiveness and safety of intra-amniotic injection of prostaglandins in mid-trimester abortion.

MATERIALS AND METHOD

Twenty-three women, whose pregnancies ranged from 12 to 24 weeks and whose requests for termination of pregnancy were approved by the Pregnancy Termination Board of the Ministry of Health, Singapore, were selected for the trial in the University Department of Kandang Kerbau Hospital. All the patients were fit and had no history of renal, cardiac or hepatic disease.

The patient was catheterised and a vaginal examination was performed to confirm uterine size. The abdomen was then cleansed with anti-septic solution and draped with sterile towels. The skin was then anaesthetised with 1% lignocaine.

Amniocentesis was performed with a 6" long hollow needle or a Tuohy needle. The Prostaglandins solution (dissolved in 1 ml. of absolute alcohol and diluted with 4 ml. of water) was then injected through the needle, followed by 250 mg. of Ampicillin dissolved in 5 c.c. H₂O. The needle was then withdrawn.

Any side-effects were noted. The patient was observed closely; the pulse and blood pressure were recorded hourly, the temperature 4 hourly and fluid intake and output charts kept.

Twenty-four hours after the procedure, a vaginal examination was performed and if there were no signs of abortion, the procedure was repeated with double the initial dose of Prostaglandins. After a further 24 hours, another vaginal examination was performed. If the patient had not or was not in the process of aborting the procedure was repeated a third time with a higher dose of prostaglandins. If the patient still had not aborted 24 hours after the third injection, the procedure was recorded as a failure and the pregnancy terminated by other methods.

When abortion occurred, a curettage of the uterine cavity was performed routinely and the curettings sent for histological report.

The initial dose of PGE₂ was 5 mg. and that of PGF_{2α} was 20 mg.

PGE₂ was used in 9 cases and PGF_{2α} in 13 cases. Both PGE₂ and PGF_{2α} were used in one case.

RESULTS

Efficacy

Of the 10 cases where PGE was used, 3 aborted after the 1st dose of 5 mg., 4 after the 2nd dose of 10 mg. and 3 cases failed to abort after the third dose of 20 mg. (Fig. 1).

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Of the 3 failures, one case (16 weeks gestation) was given further injections of 30 mg. PGE₂ followed by 40 mg. PGF_{2α} 24 hours later with no effect. The reason for this deviation from the regime was because we suspected the possibility of reduced potency of PGE₂ but this suspicion was not confirmed by other cases. The other 2 failures both had a 3rd dose of PGE₂ of 20 mg. One case (16 weeks gestation) was aborted with hypertonic saline and the other (18 weeks gestation) had hysterotomy and tubal ligation done. (Fig. 2).

Of the 13 cases where PGF_{2α} was used, 11 aborted successfully.

Two cases (both 14 weeks gestation) failed to abort after the initial dose of 20 mg. PGF_{2α}. Repeat amniocentesis failed and therefore larger intra-amniotic doses could not be given. However, PGF_{2α} was given into the extra-amniotic space between the fetal membranes and the uterine wall by means of a catheter inserted through the cervical os (one case had 10 mg. and the other 20 mg.) and both aborted.

Thus of the 21 cases, there were 3 failures and all three occurred in cases where PGE₂ was used (the 2 cases which aborted with extra-amniotic PGF_{2α} were not included). The success rate was 86%.

Of the 18 cases which aborted with intra-amniotic prostaglandins only 2 cases were complete (one was 16 weeks gestation and the other 20). Products of conception were found in all cases except 2 at curettage of the uterine cavity.

It appears from Table I that with increasing gestation, larger doses of intra-amniotic prostaglandins are necessary to effect abortion.

The average time taken was 14.6 hours, the shortest being 6 hours and the longest 35 hours.

Side-Effects and Complications

Of the 23 cases, 7 experienced side-effects and all had PGF_{2α}. No side-effects were noted in those who had PGE₂.

Four patients experienced severe side-effects almost immediately after the intra-amniotic injection of prostaglandins. These consisted of severe throbbing headaches, vomiting and diarrhoea. One patient, who was rather anxious, complained of dizziness, moderate chest pain, generalised body aches, breathlessness and carpopedal spasms within one minute of the injection. All the above side-effects except the diarrhoea and the headache passed off spontaneously within 8 minutes of the injection. Two cases had diarrhoea which persisted for 5 hours and one case had a throbbing headache which lasted 9 hours.

Milder side-effects occurred in 3 cases and consisted of nausea, vomiting and flushing. There were no cases of pelvic sepsis or excessive haemorrhage requiring blood transfusion. No other complications were noted.

The average age of the patients was 29, the youngest being 16 and the oldest 41.

Eight were nulliparous and single; one had 2 children while all the remainder (14) had 3 or more children.

DISCUSSION

Prostaglandins was first described as a physiological constituent of semen some 35 years ago by Von Euler⁹. Since then, at least 13 different types of prostaglandins have been isolated from human seminal fluid.

Prostaglandins is a hydrocarboxylic acid which has a myometrial spasmogenic action and has been used for the induction of labour and for therapeutic abortion by several workers⁵⁻⁸.

Prostaglandins has been administered by various routes to effect abortion—intravenous, intra-amniotic, extra-amniotic and vaginal. The intravenous route, however, is associated with a high incidence of side-effects e.g. vomiting, diarrhoea, local erythema and phlebitis at the site of venepuncture¹¹⁻¹² while the intra-uterine transcervical extra-amniotic route is associated with immediate severe side-effects such as severe headache, flushing, vomiting and diarrhoea^{13,14}. The intra-vaginal route requires large repeated doses and the incidence of side-effects is also high. Intra-amniotic injection of PGE₂ and PGF_{2α} has been used to terminate mid-trimester pregnancies effectively and with few side-effects^{9,10}.

In this study, 18 of 21 cases aborted with intra-amniotic prostaglandins. Two other cases received a second dose by the extra-amniotic route because amniocentesis failed the second time. The main disadvantage was that most of the abortions were incomplete. Bygdeman *et al*⁶ likewise found that the majority of their abortions were incomplete. However, Karim *et al*⁵ using slightly larger doses of PGF₂ reported that most of their abortions were complete.

About half of the cases which aborted required a second larger dose of prostaglandins (Figs. 1 and 2). It appears that a larger initial dose (10 mg. PGE₂ and 40 mg. PGF_{2α}) would be more effective and therefore reduce the number of cases requiring further injections. From Table III, it appears that with more advanced gestation larger doses of prostaglandins were necessary to effect abortion in this trial.

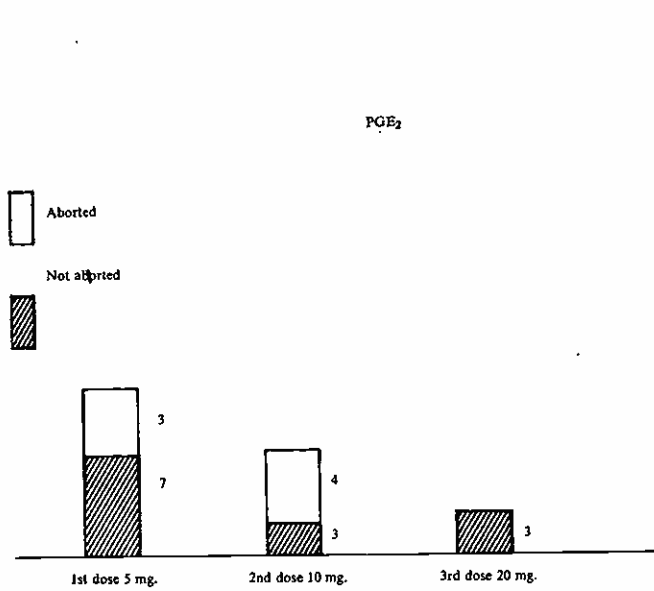


Fig. 1.

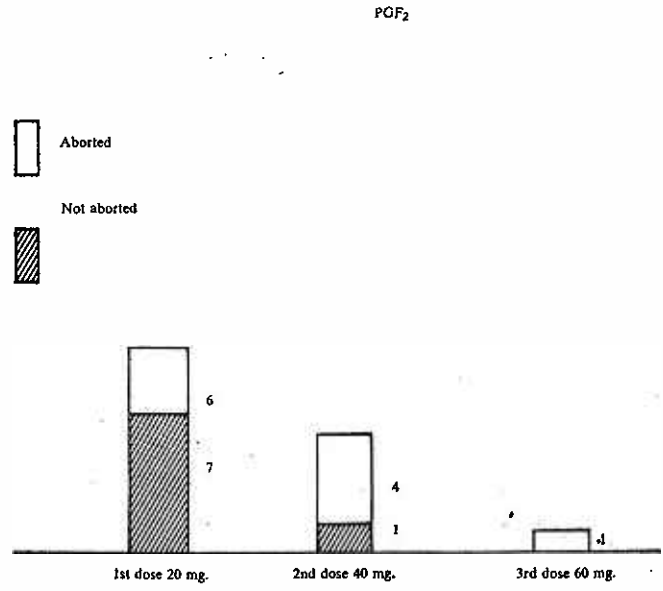


Fig. 2.

TABLE I

PGE ₂		PGF ₂ α	
Dose given	Gestation of Cases successfully aborted	Dose given	Gestation of Cases Successfully aborted
5 mg.	14, 16, 14 weeks Average = 14.7 weeks	20 mg.	12, 12, 18, 16, 16, 14 Average = 14.6 weeks
10 mg.	14, 16, 24, 20 weeks Average = 18.5 weeks	40 mg.	16, 14, 14, 20 Average = 16 weeks
20 mg.	—	60 mg.	18 weeks

AGE AND PARITY

TABLE II

Age	
<15	0
15 - 19	2
20 - 24	4
25 - 29	4
30 - 34	9
35 - 39	2
40 or more	2

PARITY

TABLE III

Age	
0	8
1 - 2	1
3 - 4	4
5 or more	10

Side-effects occurred in 7 out of 23 cases and all 7 had PGF_{2α}. Other series also show higher incidence of side-effects with PGF_{2α}. No side-effects were noted when PGE₂ was used. Although there were more failures with PGE₂, the number of cases were too small to compare its efficacy with PGF_{2α}. It is possible that some of the initial severe side-effects could have been due to the inadvertent intravenous injection of prostaglandins caused by the needle point slipping into the uterine myometrium.

CONCLUSION

This small study shows that PGE₂ and PGF_{2α} were effective in terminating mid-trimester pregnancies; the success rate was 86%. The main disadvantage of intra-amniotic prostaglandins was that most of the abortions were incomplete. Consequently, in our opinion it is advisable to perform curettage routinely soon after abortion. PGE₂ appears to have much fewer side-effects than PGF_{2α}.

REFERENCES

1. Bengtsson, L. P.: Fifth World Congress of Obstetrics and Gynaecology, Sidney, 1967, pp. 774-780, 1967.
2. Bengtsson, L. P.: Med. Gynec. and Sociology, Vol. 3, No. 1, pp. 6-14, 1968.
3. Cameron, J. M. and Dayan, A. D.: Brit. Med. Journal, 1, 1010-1013, 1966.
4. Avar, Z.: Magy Noorv Lap. 26, 72-4, (Hun), March 1963.
5. Karim, S. M. M. and Sharma, S. D.: Lancet, pg. 47, 3.7.1971.
6. Bygdeman, M., Topozada, M. and Wiquist, N.: Acta Physiolog. Scand., 82, pp. 415-416, 1971.
7. Beazley, J. M. and Gillespie, A.: Lancet, pg. 152, 23.1.1971.
8. Croft, I. L. and Cullum, A. R. *et al*: British Med. Journal Vol. 3, p. 276-279, 1971.
9. Von Euler: U.S. Klin. Wschr., 14: 1182, 1935.
10. Hillier, K. and Embrey, M. P.: Journal of Obst. and Gynec. Brit. Commonwealth, Vol. 79, p. 14-22, Jan. 1972.
11. Bygdeman, M. and Wiquist, N.: Transaction of the New York Academy of Science Meeting on Prostaglandins, 180: 473-482, 1971.
12. Karim, S. M. M. and Filshie, G. M.: Lancet, 1: 157-159, 1970.
13. Allan Ng, Cheng, M. and Ratnam, S. S.: Termination of pregnancy by Injection of Prostaglandins into the Extra-Amniotic Space (in press).
14. Wiquist, N. and Bygdeman, M.: Lancet, 3: 716, 1970.