INDUCTION OF MIDTRIMESTER ABORTION WITH PROSTAGLANDINS (PGF2a)

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Prostaglandin is the generic name for a family of biologically active lipids. Von Euler in 1935 reported the smooth muscle stimulating effect of fresh human seminal fluid and attributed this biological activity to a lipid which he named "Prostaglandin". The history of prostaglandin (PG) is very closely linked with the reproductive system. In human semen there are at least 13 different prostaglandins. Human menstrual fluid and endometrium contain PGE2a. It has been demonstrated in amniotic fluid, umbilical cord, decidua and in maternal circulation at term, spontaneous labour and abortions (Speroff and Ramwell, 1970; Karim and Hillier, 1970). All these point out to the physiological role of prostaglandins in human parturition and spontaneous abortions.

Pickles and co-workers (1966) reported that intrauterine application of very small dose of PGF2, stimulated the motility of the non-pregnant human uterus. The first clinical trials on the use of prostaglandins were carried out by the intravenous route by Bygdeman and Wiqvist in 1969. They emphasised the contrast between oxytocin and prostaglandins in that, the early pregnant uterus (6-8 weeks) is very sensitive to the stimulating effect of the latter. Since then numerous reports have been published regarding the use of prostaglandin as abortifacient (Karim, 1970; Hillier, 1971; Wiqvist and Bygdeman, 1971, soon after Wiqvist and Bygdeman, 1969). Karim (1971) attempted termination of pregnancy with prostaglandins by intravenous and vaginal routes. It soon became clear that the doses needed for termination of pregnancy by these routes were associated with high incidence of side-effects like nausea, vomiting, diarrhoea, pyrexia and local erythema at the site of venipuncture (Karim and Filshie, 1970; Karim and Sharma, 1971; Wiqvist and Bygdeman, 1971).

The intrauterine route of administration seemed to be preferable for induction of second trimester abortion since the incidence of side effects was significantly reduced by this approach. The total dose needed for induction of abortion by the extra amniotic method was about 10-20 times lower than the intravenous dose. The major drawbacks of the method were the need for repeated instillation and the inconvenience of an indwelling catheter with a potential risk of inducing intrauterine infection (Embrey, Hillier and Mahendran, 1972). Injection of PGE2a or PGF2a into the amniotic sac in the midtrimester pregnancy induces a rapid in-

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crease in uterine tonus with subsequent development of forceful uterine contractions. Different dose schedules have been used to achieve a high success rate, a short injection-abortion interval and a low incidence of side effects.

The effectiveness of intra-amniotic administration of PGF2a (Tham Salt*) for induction of midtrimester abortion was studied in 15 patients admitted for therapeutic abortion in Governmtnt Erskine Hospital, Madurai, between 1st November 1972 to 31st January, 1973.

Material and Method

Choice of cases: Fifteen healthy women with confirmed pregnancy of 14-20 weeks by pelvic examination were chosen for this study. The mothers were less than 40 years of age, had not more than four previous pregnancies and no previous attempts at interruption of pregnancy. Excluded from the study were patients with history of spontaneous abortion in the previous nine months, two or more spontaneous abortions, uterine anomalies, previous uterine surgery, pelvic inflammatory disease or systemic disease. Out of 15, nine were primigravidae and six multiparous women.

Method

After voiding and preparation of the abdominal wall with antiseptic solution, the amniotic cavity was punctured transabdominally by a 18 gauge 6" thin walled needle and local anaesthesia (1% xylocaine). A fine polyethylene catheter of 1 mm diameter was passed into amniotic sac though the needle which was then withdrawn. Amniotic fluid withdrawal or replacement was not necessary, but a free flow of clear liquor was confirmed before injecting the drug. Through the catheter PGF2a (Tham salt) 1 ml. (5 mgm) was administered over the first five minutes and the remaining 4 ml (20 mgm) over the next 5 minutes. The patient was kept under close observation for 24 hours following initial therapy and all the vital signs were recorded every hour. At the end of 24 hours, if abortion was not imminent a second dose of 25 mgm PGF2a was repeated through the polythelene catheter. Treatment was considered a failure if abortion did not occur after 36 hours of initiation of therapy. In such cases of failure, pregnancies had to be terminated by alternate methods.

Clinical outcome: In this group of 15 patients, 12 (80%) were successfully terminated within 36 hours. Ten were complete abortions and two were incomplete as the placenta had to be digitally removed from the cervical canal. The mean abortion time in these cases was 20.1 hours with a wide range from 9-36 hours. Sixty per cent of patients aborted within 24 hours thus requiring only a single injection of 25 mgm PGF2a. In one case as the first ml. (5 mg) of drug was injected through the polythelene catheter, the patient complained of intense nausea and acute pain in the lower abdomen. Hence further administration of PGF2a was withheld. Patient continued to have abdominal pain and had vaginal bleeding 2 hours after injection, and aborted at the end of 23 hours.

In primigravidae, termination of pregnancy within 36 hours was successful in 66% of cases with the mean abortion induction interval of 23.2 hours. By comparison the success rate in multigravidae was 100% and the mean abortion time 17.3 hours. In the 3 cases of failure pregnancy was terminated successfully by high titre pitocin drip.

* Manufactured by Upjohn Company, Kalamazoo, Michigan, U.S.A.

The incidence of side effects in our series was minimal. Only two patients had slight nausea and vomiting and none had diarrhoea or pyrexia. No appreciable changes were noted in the vital signs in the cases studied.

Nine patients after abortion with PGF2a had an intrauterine device (copper T device) inserted and five underwent transvaginal tubectomy 72 hours after the abortion. There was no endometritis in this series.

Discussion

Bygdeman *et al*, (1971) found a single intra-amniotic injection of 25 mgm of PGF2a produced an increase in the tone and frequency of uterine contractions leading to midtrimester abortions in all 9 cases (100%) studied between 14-20 weeks of gestation. They beleived that PGF2a acts locally on the myometerium after diffusion through the foetal membrances. In the same year, Karim and Sharma (1971) tried single injection of PGE2 2.5 to 5 mgm or PGF2a 25 mg intra-amniotic, in 10 women 13-22 weeks pregnant. All of them aborted and the mean injection-abortion interval was 11.4 hours. At the Third Conference of Prostaglandins in Fertility Control held at Stockholm in 1972, out of 52 cases presented with 15 mgm of PGF2a there was 61% success compared to 96% success rate using 25 mgm in 28 cases of midtrimester abortion. Toppozada *et al*, (1971) used 5-25 mgm of PGF2a as a single shot in 35 midtrimester pregnancies and claimed success rate of 89 per cent, with mean induction abortion interval of 28 hours. Anderson *et al*, (1972) instilled 40 mg. of PGF2a as a single dose in 35 midtrimester pregnancies and reported 100 per cent success. In our series of 15 cases, the success rate was 80% and the mean induction abortion interval 20.1 hours which is comparable with results obtained by other workers. Sixty per cent of patients aborted within 24 hours requiring only a single injection of 25 mgm PGF2a.

Perhaps, as the intra-amniotic instillation of PGF2a does not result in appreciable amount in the blood, the side effects were minimal when compared to systemic administration (Green *et al*, (1972). The incidence of side effects with our dose schedule was found to be minimal. Only two patients had nausea with vomiting but did not require any concomitent antiemetic therapy or rehydration. None had diarrhoea or pyrexia during therapy. Embrey (1972) noted vomiting in 50% of his cases. However, in other series, side effects were minimal. In 80 cases of intra-amniotic PGF2a presented at the Stockholm Conference (1972) the mean frequency of vomiting and diarrhoea with 15 mgm dose was 0.9 episode per patient compared to 1.8 per patient with 25 mgm doses.

When compared with intra-uterine administration of hypertonic saline, prostaglandins PGF2a offers an alternative method which probably has advantages regarding simplicity, safety and abortion time. In a series of 15 cases of intra-amniotic saline tried during the same period, the mean induction abortion interval was 34 hours compared to 20.1 hours with PGF2a. The 15 methyl anologue of PGF2a was found to be 5-10 times more potent in stimulating uterine contractions and response was more prolonged. A single injection of 5 mgm of 15-me-PGF2a resulted in abortion in all 14 cases with a mean injection abortion interval of 22 hours (Bygdeman *et al*, (1972).

The intra-amniotic method of administration of prostaglandins appears to be one of choice in midtrimester abortions

as it is simpler and safer than other intra-uterine instillations. It gives rise to a high success rate with minimal side effects.

Summary

Intra-amniotic injection of PGF2a with an initial dose of 25 mg and repeated if necessary after 24 hours was tried for the induction of midtrimester abortion in 15 cases. It was successful in 80% with the mean induction abortion interval of 20.1 hours. Except for slight nausea and vomiting in 2 cases, no other side effects were noticed. The place of prostaglandins in induction of mid-trimester abortion is discussed.

References

1. Anderson, G. G., Hobbins, J. C., Rajkovik, V., Speroff, L. and Caldwell, B. V.: Prostaglandins, **1**: 147, 1972.
2. Bygdeman, M., Toppozada, M. and Wiqvist, N.: Acta Physiol, Scqndinav. **82** 415, 1971.
3. Bygdeman, M., Beguin, F., Toppozada, M., Wiqvist, N. and Bergstrom, S.: Lancet, **1**: 1336, 1972.
4. Embrey, M. P.: in Prostaglandins in Fertility Control Report of the Third Conference, Stockholm, W.H.O., 1972, 137.
5. Embrey, M. P., Hillier, K. and Mahendran, P. Brit. Med. J., **3**: 146, 1972.
6. Green, K., Beguin, F., Bygdeman, M., Toppozada, M. and Wiqvist, N.: in Prostaglandins in Fertility Control, Report of the Third Conference, Stockholm, W.H.O., 1972, 189.
7. Hillier, K.: Prostaglandins in Fertility Control Reports from 2 conferences in 1971, MHO Research & Training Centre, Stockholm., 1971.
8. Karim, S. M. M.: Brit. Med. J., **2**: 196, 1970.
9. Karim, S. M. M.: Annals of N.Y. Acad-Sciences, **180**: 1/568, 1971.
10. Karim, S. M. M. and Hillier, K.: J. Obst. Gynec. Br. C'wlth., **77**: 837, 1970.
11. Karim, S. M. M. and Filshie, G. M.: Brit. Med. J., **3**: 198, 1970.
12. Karim, S. M. M. and Sharma, S. D.: J. Obst Gynec. Br. C'wlth., **78**: 294, 1971.
13. Pickles, V. R., Hall, W. J., Clegg, P. C. and Sullivan, T. J.: Mem. Soc. Endocr., **14**: 89, 1966.
14. Speroff, L. and Ramwell, P. W.: Am. J. Obst. Gynec., **107**: 111, 1970.
15. Third Conference on Prostaglandins in Fertility Control, Jan. 17-20, 1972, Eds. Bergstrom, S., Green, K. and Samuelson, B., WHO, Research and Training Centre, Stockholm, 1972, p. 154.
16. Toppozada, M., Bygdeman, M. and Wiqvist, N.: Contraception, **4**: 293, 1971.
17. Van Euler, U. S.: J. Physiol., **84**: 21, 1935.
18. Wiqvist, N. and Bygdeman, M.: Excerpta Medica, International Congress Series, **234**, B: 117, 1971.