MANAGEMENT OF FOETAL DEATH IN UTERO BY 15 METHYL PROSTAGLANDIN F_2 ALPHA

by

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Introduction

Prostaglandins being potent myometrial stimulants and having a priming effect on the cervix have been employed by several authors for the management of missed abortion and intrauterine foetal death (Karim 1970; Filshie 1971; Embrey *et al* 1974). The present study reports the use of 15(S) 15 methyl prostaglandin $F_{2\alpha}$ (15 me $PGF_{2\alpha}$) administered intramuscularly (i.m.) and intravenously (i.v.) for the termination of pregnancy in subjects with intrauterine foetal death.

Material and Methods

Eleven subjects between 23 to 35 years of age with parity from zero to 3 and who had no contraindications for prostaglandin administration were included in this study. Each patient had a complete physical and gynaecological examination. In addition to haemoglobin estimation, urinalysis, the serum fibrinogen level and platelet counts were estimated. The size of uterus at the time of induction varied from 22 to 36 weeks of gestational age. In 2 patients attempted induction of labour with syntocinon infusion had failed. In others no attempt for induction was made before 15 methyl $PGF_{2\alpha}$ administration. Seven subjects received the drug by the intramuscular route and in 4 it was administered by the intravenous infusion. Patients received two tablets of lomotil (Diphenoxylate 2.5 mg. + atropine sulphate 0.25 mg.) and one of stemetil (Prochlorperazine 5 mg.) half an hour prior to the administration of the drug and this was repeated at the end of three hours.

The dose schedule for the intramuscular and intravenous routes of administration of 15 methyl $PGF_{2\alpha}$ was as follows:

Intramuscular route:

0 hours 200 μg. I.M.
3 hours 300 μg. IM. and this was repeated 3 hourly till the patient delivered.

Intravenous route:

0.25 μg (0.25 ml.)/minute for 30 minutes (0-30 minutes)
0.50 μg. (0.50 ml.)/minute for 30 minutes (31-60 minutes)
1.0 μg. (1.0 ml.)/minute from 61 minutes till the patient delivered. For intravenous

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administration the solution was prepared by adding 2 ml. (500 μg.) of 15 methyl PGF_{α_2} to 500 ml. of 5% dextrose solution having a concentration of 1.0 μg./ml.

Subjects were continously supervised during therapy and the following parameters were monitored two horly, the pulse rate, temperature, blood pressure and respiration. The onset of uterine pain, vaginal bleeding as well as any episodes of nausea, vomiting or diarrhoea were recorded. The induction delivery interval was recorded in every patient. In subjeet No. 11, the infusion of 15 me $PGF_{2\alpha}$ was started in the same regime but till one hour she had no uterine pain so the dose was increased to 1.5 μg. (1.5 ml.) per minute during the second hour and 2.0 μg. (2.0 ml.) per minute for the next two and half hours. However, she did not have appreciable uterine contractions. Then 15 me $PGF_{2\alpha}$ was administered intramuscularly 200 μg. initial dose and 300 μg. after 3 hours to which she responded and delivered at the end of eight hours and five minutes.

Results

Eleven subjects were studied and in all the treatment was successful. The clinical details, induction delivery interval, total dose of prostaglandin required and side effects are presented in Table I. In 7 patients who received 15 methyl $PGF_{2\alpha}$ by intramuscular route, the size of uterus varied from 22 to 34 weeks and induction delivery interval ranged from 3 hours 30 minutes to 11 hours (mean 8 hours 15 minutes) and mean dose required was 890 μg with a range of 500 μg to 1100 μg. Six subjects had complete expulsion of products of conception, only 1 patient needed assistance for the delivery of placenta. Four subjects were treated with intraven-

TABLE I

Prostaglandin in Intrauterine Death Cases

Sr. No.	Route of administration	Age in years	Parity	Uterine Fundal Height	Total Dose (μg.)	Induction abortion interval	Procedure Complete/ Incomplete	Side Effects (No. of Episodes)	
								Vomiting	Diarrhoea
1.	I.M.	26	1+1+0+1	24 wks.	500	3 hrs. 30 mins.	Complete	—	—
2.	I.M.	30	3+0+0+3	28 wks.	800	8 hrs.	Complete	2	—
3.	I.M.	20	1+2+3+0	20 wks.	1100	9 hrs. 15 mins.	Complete	—	—
4.	I.M.	35	2+0+2+1	34 wks.	800	7 hrs.	Complete	4	1
5.	I.M.	20	1+0+0+1	22 wks.	1100	11 hrs.	Incomplete	—	—
6.	I.M.	30	2+0+1+1	22 wks.	800	8 hrs.	Complete	—	—
7.	I.M.	30	2+0+0+2	28 wks.	1100	11 hrs.	Complete	4	—
8.*	I.V.	20	2+0+0+2	30 wks.	565	10 hrs.	Complete	—	—
9.	I.V.	23	Primi	22 wks.	640	11 hrs. 15 mins.	Complete	—	—
10.	I.V.	30	3+0+1+3	22 wks.	950	16 hrs. 15 mins.	Complete	—	1
11.*	I.V.	24	Primi	36 wks.	1000 (500 I.M. 500 I.V.)	8 hrs. 5 mins.	Complete	2	—

* Failed induction of labour with syntocinon infusion.

ous administration but in 1 the intramuscular route of administration was used in addition. The size of uterus varied from 22 to 36 weeks and induction delivery interval ranged from 8 hours 5 minutes to 16 hours 15 minutes (mean 11 hours 25 minutes). The mean dose of 15 methyl $PGF_{2\alpha}$ required in 3 subjects was 718 μg. with a range of 565 μg. to 950 μg. In the patients where both intravenous and intramuscular regime were used the total dose required was 1000 μg. In this group all patients had complete expulsion of products of conception. During therapy the only side effects observed were that of vomiting/diarrhoea. With the intramuscular route 3 subjects had vomiting (two episodes in one and four episodes in two patients) and one patient had one episode of diarrhoea. While with the intravenous route only one subject had one episode of diarrhoea and the patient who had both intravenous and intramuscular route of administration had two episodes of vomiting during intramuscular administration. The mean no. of episodes of vomiting and diarrhoea per patient observed were 1.1 and 0.16 respectively. No patient had any excessive blood loss, excessive uterine pain or any cervicovaginal injury.

Discussion

A delay of four weeks or more in spontaneous expulsion of the dead foetus is associated with the increased risk of disturbances of blood coagulation (Hodgkinson *et al* 1954; O'Dris Coll and Lavelle 1955) and psychological trauma to the mother. Prostaglandins and its analogues have been successfully used by several authors for the management of missed abortion, intrauterine foetal death, anencephaly and molar pregnancy (Filshie 1971; Ylikokala *et al* 1976; Sharma *et al* 1975; Lippent and Luthi 1978). Ylikokala *et al* (1976) have successfully induced labour in 11 mothers with intrauterine foetal death and 2 with anencephaly by intramuscular 15 me $PGF_{2\alpha}$. In this series all but 2 subjects had gastrointestinal side effects. Lippent and Luthi (1978) used PGF_2 gel extra-amniotically and compared their results with other available methods of treatment. The average induction delivery interval with PGE_2 gel was 12 hours, while for the other group it was about 30 hours. But the extra-amniotic method is an invasive procedure and has the potential risk of intrauterine infection. The studies with PGE_2 vaginal suppositories for treatment of foetal intrauterine death, El'Demarawy *et al* (1977) Southern *et al* (1978) achieved a success rate of 97%. With this the incidence of gastrointestinal side effects were very high and other side effects like shivering, headache, flushing and rise of temperature were also observed. In the present study, 15 methyl $PGF_{2\alpha}$ was used by the intramuscular and intravenous route and in all cases the treatment succeded. With intramuscular administration the induction delivery interval was shorter but the mean dose used was more than that by the intravenous route, as with this method the concentration of 15 methyl $PGF_{2\alpha}$ in the infusion fluid was very low (1.0 μg/ml.). This may explain the longer induction delivery interval and low incidence of gastrointestinal side effects. Only 1 subject had one episode of diarrhoea during intravenous infusion. 15 methyl Prostaglandin $F_{2\alpha}$ is effective in inducing labour in intrauterine foetal death cases when administered either by the intramuscular or the intravenous route. With both dose schedules the side effects were minimal and easily managable.

Summary and Conclusion

Eleven patients with foetal death in utero were induced with 15 me $PGF_{2\alpha}$, 7 by the intramuscular route and 4 by the intravenous route of administration. The fundal height was between 22 to 36 weeks of gestation. The induction was successful in all cases, only 1 patient required assistance for the removal of the placenta. The mean induction abortion interval was less with the intramuscular route of administration, 8 hours 15 minutes as compared to 11 hours 25 minutes with the intravenous route of administration. The mean dose of the drug administered by the intramuscular route was 890 μgm. and that by the intravenous route 718 μgm. One patient who was on the intravenous drip required the intramuscular route of administration in addition. The only side effects noted were gastrointestinal, the mean episodes of vomiting being 1.1 and that of diarrhoea 0.16 per patient in all the patients. No major untoward reaction or side effects were noted.

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