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EVALUATION OF TWO DOSE SCHEDULES OF INTRAMUSCULAR ADMINISTRATION OF 15-METHYL PROSTAGLANDIN F_2 a. FOR INDUCTION OF ABORTION

(Preliminary Report)

by

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Intravenous use of prostaglandin $F_{2\alpha}$ for abortion was first advocated by Karim (1970) and Wiqvist and Bygdeman (1970). Prostaglandin had proved to be reasonably effective by this route, but it soon became clear that efficient doses are associated with a high frequency of side effects. After this, many workers viz. Anderson *et al* (1972,) Bygdeman *et al* (1971) and Hingorani *et al* (1974) have utilized the intra-amniotic route of administration of $PGF_{2\alpha}$, and proved that this is an effective method of inducing abortion after 14 weeks with less side effects. However, when the pregnancy is between 10-14 weeks the puncture of the amniotic sac is not possible. Intramuscular and extra-amniotic administration of prostaglandins have the advantage that these methods are applicable in the early stage of second trimester, when amniotic sac puncture is not feasible.

The disadvantage with extra-amniotic administration of prostaglandin is the use of a catheter which increases the risk of infection. Also, sometimes there is a bloody tap and the procedure has to be abandoned.

15-methyl $PGF_{2\alpha}$ has an overall potency of approximately 10-20 times that of $PGF_{2\alpha}$ and has a longer duration of action resulting in sustained uterine stimulation (Toppozoda *et al* 1972). It was therefore,

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decided to assess the efficacy and safety of 15-me-$PGF_{2\alpha}$ as abortifacient by intramuscular route.

Material and Methods

The case material comprised of 65 healthy pregnant women between 10-20 weeks of gestation who sought Medical Termination of Pregnancy, at All India Institute of Medical Sciences Hospital. Two dose schedules were tried. The first group consisted of 30 patients who received an initial dose of 200 ugm followed 3 hourly by 400 ugms of 15-me-$PGF_{2\alpha}$ by intramuscular route. Injections were continued at 3 hourly interval till the patient aborted or for a maximum period of 30 hours.

In the second group of 35 patients an initial dose was 200 ugms of 15-me-$PGF_{2\alpha}$, but succeeding 3 hourly doses were 300 ugms each. These were continued till the time of abortion for the maximum period of 30 hours. In both dose schedules if abortion complete or incomplete did not occur within 30 hours, the trial was considered as having failed and supplimentary treatment was resorted to to complete the abortion. In both schedules 30 minutes before each of the first 3 injections, each patient received 2 tablets of Retardin* orally.

Supervision of patients and evaluation of outcome

All cases on these trials were supervised continuously and the type and frequency of side effects were noted. Temperature, pulse, blood pressure were recorded before the administration and then every three hourly.

Observations

Distributiin of patients in relation to parity and the period of gestation, in the two dose schedules are shown in Table I.

TABLE I

Induction Schedules in Relation to Parity and Gestational Period

Induction Schedules	Total No. of cases	Parity		Mean gestational period in weeks
		Nullipara	Multipara	
15-me-$PGF_{2\alpha}$. 200 ugm followed by 400 ugm 3 hrly.	30	5	25	13.8
15-me-$PGF_{2\alpha}$. 200 ugm followed by 300 ug 3 hrly.	35	4	31	11.4

Success Rate

Success rate and induction abortion interval in the two schedules is shown in Table II.

Success rate was 76.6% in the first group and 88.5% in the second group with the mean induction abortion interval of 15.8 and 16.5 hours respectively.

The cumulative abortion rate is shown in Fig. 1.

The mean total dose of 15-me-$PGF_{2\alpha}$ and mean number of injections required in the successful cases for the two schedules are shown in Table III.

*Retardin contains Diphenoxylan chloridium 2.5 mgm. Atropin 25 ugm made by Leo Halsingborg.

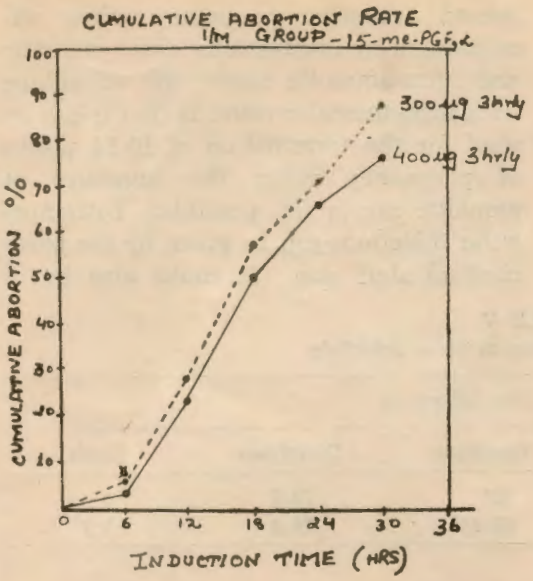

Fig. 1

Approximately 1/5 of cases had a complete abortion in both the groups.

Table IV shows the relationship of period of gestation to induction abortion interval in the two groups. In the first group, the mean induction-abortion interval was sifinificantly higher, in cases, where the gestation period was more than 14 weeks ($P < .05$). While in the second group, even though induction-abortion interval was slightly longer when the period of gestation was more than 14 weeks, this difference was not statistically significant.

Side effects

The side effects seen in the 2 schedules are shown in Table V. The most frequent side effect observed was vomiting

TABLE II

Success Rate and Induction Abortion Interval in Relation to Dose Schedule

Dose Schedule	Total No. of cases	No. of cases aborted	Success rate %	Induction abortion interval in hours Mean	Range
15-me-$PGF_{2\alpha}$. 400 ug 3 hrly.	30	23	76.6	15.8	6-30
15-me-$PGF_{2\alpha}$. 300 ugm 3 hrly.	35	31	88.5	16.5	6-30

TABLE III

Number of Injections and Mean Dose in the Two Schedules

Induction Schedule	No. of Injections Mean	Range	Mean Total Dose (Mg)
15-me-$PGF_{2\alpha}$, 200 ugm followed by 400 ugm 3 hrly.	5.2	2-11	1.9 mg
15-me-$PGF_{2\alpha}$, 200 ugm followed by 300 ugm 3 hrly.	5.3	2-10	1.8 mg

TABLE IV

Induction Abortion Interval in Relation to Gestation Age in the Two Schedules

Induction Schedule	Gestational age less than 14 weeks	Gestational age more than 14 weeks
15-me-$PGF_{2\alpha}$ 400 ugm 3 hrly.	12.7 hrs.*	18.3 hrs*
15-me-$PGF_{2\alpha}$ 300 ugm 3 hrly.	16.3 hrs.	17.6 hrs.

*$P < 0.05$.

and this was seen in 70% of the cases in the first schedule. However, this was reduced to 45.7% ($P < 0.05$) in the second schedule in which smaller dose was used. The incidence of diarrhoea was the same in the two groups. Flush was observed in 2 patients (5.7%) in the second group. No evidence of local reaction or pain was noted at the injection site.

TABLE V
Side Effects in Relation to Dose Schedule

	Side effects %		
	Vomiting	Diarrhoea	Flush
15-me-$PGF_2\alpha$ 400 ugm 3 hrly.	70*	76.6	0
15-me-$PGF_2\alpha$ 300 ugm 3 hrly.	45.7*	74.3	5.7

* $P<0.05$.

In group I the mean frequency of vomiting and diarrhoea analysed as episodes per patient was 1 and 2 respectively, while in group II, it was 0.9 and 1.7. Troublesome frequency of gastrointestinal side effects, requiring intravenous replacement therapy, was encountered in 1 patient in the first group.

Management of failed trial cases

Table VI shows the management and outcome of failed trials.

Discussion

Although natural prostaglandins and its analogues can successfully terminate the second trimester pregnancy when administered by intravenous, extra-amniotic and intra-amniotic route, the advantage with intramuscular route is that it can be used for the termination of 10-14 weeks of pregnancy when the puncture of amniotic sac is not possible. Intramuscular injections can be given by the paramedical staff also. It could also be of value for completing second trimester abortion when the same is unsuccessfully initiated by other methods. From the present observations it is seen that an initial dose of 200 ugm followed by 300 or 400 ugm at 3 hours interval is quite effective. The frequency of side effects associated with intramuscular injection is some what high but in the 300 ug schedule it is not very troublesome. The method has been found to be acceptable to our patients.

Summary

Feasibility, acceptability, effectiveness as abortifacient and side effects of 15-me-

TABLE VI
Management of Failed Trials

Subsequent Method	Initial Induction Method	
	15-meth. $PGF_2\alpha$	I.M.
	400 ug 3 hrly.	300 ug 3 hrly.
Syntocinon and evacuation	1	0
Hysterotomy and ligation	1	0
15-me-$PGF_2\alpha$ 750 ugm extra-amniotically	3	4
Delayed abortion	1	0

$PGF_{2\alpha}$ administered by two different intramuscular dose schedules, have been evaluated in 65 women with pregnancies ranging between 10-12 weeks. In one group 30 women received 400 ugm 3 hourly and a second group of 35 women received 300 ugm 3 hourly. Both groups received the injections intramuscularly until the time of abortion or for a maximum period of 30 hours. The trial was considered as failure, if complete or incomplete abortion did not occur by 30 hours. The success rate was 76.6% and 88.5% and the induction-abortion interval was 15.8 and 16.5 hours respectively in the two groups. The incidence of vomiting was 70% and 45.7% respectively in the two groups. Significant reduction in vomiting was achieved by reducing the dose.

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