

**TERMINATION OF SECOND TRIMESTER PREGNANCIES:
A BLIND STUDY USING HYPERTONIC SALINE AND
PROSTAGLANDINS F2 α . — A PRELIMINARY REPORT**

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Among all the available methods to terminate second trimester pregnancies, the intra-amniotic method is today the most popular. The ideal chemical agent to be instilled by this route has not yet been found. The 20% hypertonic saline is probably competing with the prostaglandins to take the first place amongst these agents. It is therefore imperative that these two agents are compared under controlled conditions. With this in view, a blind study comparing the effectiveness and complications of these two chemicals has been instituted at Nowrosjee Wadia Maternity Hospital.

This report submits the analysis and results of first 100 cases in this blind study.

Material and Methods

Having selected women between 15 and 20 weeks' of pregnancies for termination under Medical Termination of Pregnancy Act 1972, the patients were submitted to one of the following three methods of

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intra-amniotic instillation, done per abdomen.

- A. 20% hypertonic saline, 200 ml.
- B. Single dose; 50 mgm. Prostaglandin (PG) F2 α .
- C. Multiple doses of 25 mgm. Prostaglandin F2 α given at zero hour and six hours. Similar doses were instilled at twenty-four hours and thirty hours when necessary.

For the purpose, prepared envelopes indicating one of the methods stated above was picked up serially; the investigators being blind to what the envelopes contained till they opened them.

The report consists of 100 terminations; twenty-two of whom underwent immediate sterilisation following termination.

The distribution of the 100 cases according to the methods was 33 cases in method A (Saline series), 34 cases in method B (PG single dose) and 33 cases in method C (PG multiple dose).

The end point for a successful termination was either a complete or an incomplete abortion within 72 hours from the time of institution of the termination procedure. A complete abortion was one where the total products of conception were evacuated spontaneously. The incomplete abortion was one where placenta

and membranes were totally or partially retained in the uterine cavity after foetal expulsion. A part of the product retained in the vagina only was not considered in the incomplete group but rather in the complete one.

Results

Table I shows the distribution of these 100 cases according to the method of termination, weeks of gestation and the type of abortion obtained; whether complete, incomplete or failed. The cases have been equally divided amongst the three groups. There is no indication of relationship between the weeks of gestation and the completeness of evacuation. It could, however, be that failures are commoner in the lower weeks of gestation. The total success rate of 96% in the series is quite remarkable. The number of complete abortions was 75% and the incomplete was 25%. Though it is not shown that failure of abortion is related to a method of termination, there is no doubt that the type of abortion obtained was method dependent. The completeness of abortion with saline had been the best, followed very closely by multiple doses of Prostaglandin F_{2α}. The single dose Prostaglandin F_{2α} technique resulted in almost 50 per cent of abortions being incomplete.

Table II shows the distribution of 100 cases according to the method of termination, the parity and the type of abortion obtained. It is indicating that significantly high percentage, that is 42, is in parity zero group. The total of 19 per cent in parity IV group and above is also indicating the rejection of pregnancy in this high parity group

Out of the total abortions obtained 25 per cent were incomplete. In the individual parity groups it was seen that in parity III and IV 50 per cent of the abor-

TABLE I
Showing the Distribution of 100 Cases According to the Methods of Termination, Week of Gestation and Type of Abortion

Method	Total No. of cases	Weeks of gestation								Type of abortion		
		15	16	17	18	19	20	20	Com- plete	Incom- plete	Failure	
20% hypertonic saline	33	2	9	4* [@]	12*	1	5*		29	3	1	
PG single dose	34	6** @+	11@ ****	4	6** **	1*	6		17	15	2	
PG multiple dose	33	5@	11** *	2	10*	1	4**		26	6	1	
Total	100	13	31	10	28	3	15		72	24	4	

Each * represents an incomplete abortion.

Each @ represents a method failure.

Each @+ represents a technique failure.

TABLE II
Showing the Distribution of 100 Cases According to the Method of Termination, the Parity and the Type of Abortion Obtained

Method	Total No. of cases	Parity					Type of abortion			
		0	I	II	III	IV	V & +	Complete	Incomplete	Failure
Hypertonic Saline	33	13	7	4	3**	3@*	3	29	3	1
PG Single Dose	34	14** ***	6@ ***	4**	5**	3**	2@*	17	15	2
PG Multiple Dose	33	15** **	4@	6	0	3*	5*	26	6	1
Type of abortion										
Complete	72	33	12	12	4	4	7	—	—	—
Incomplete	24	9	3	2	4	4	2	—	—	—
Total abortion	96	42	15	14	8	8	9	—	—	—
Failure	4	—	2	—	—	1	1	—	—	—

* Represents an incomplete abortion.
Each @ represents a failure.

tions were incomplete and in the other parity groups it varied from 14 to 22 per cent. The higher rate of incomplete abortions in the former parity groups were not exactly method related but seemed parity dependent.

Table III shows the frequency distribution by age and parity. The number of patients in the parity zero group seeking mid-trimester abortion is at least 10 per cent higher than those reaching third trimester for delivery in the same parity group.

Amongst the 42 patients in parity zero group, as many as 33 were unmarried, which also meant that nine married women wanted their first pregnancy to be terminated.

The age range of unmarried women varied from 15 years to 29 years, the large majority being under 24 years. As the age of the patients advanced to beyond 24 years, their parities were higher than one, except in five patients.

Table IV shows the distribution of cases according to community, marital status, residence and education.

When compared with the community distribution of a general population of Bombay, amongst the second trimester termination group, there is a preponderance of the Catholic community by at least four times. This may be due to greater awareness amongst the Catholics of the new facilities provided in the Medical Termination of Pregnancy Act 1972.

TABLE III
Showing Frequency Distribution — Age and Parity

Parity	Total No. of cases	Age in years						
		15-19	20-24	25-29	30-34	35-39	40-44	45 +
0	42	19	20	3	0	0	0	0
I	17	2	13	1	1	0	0	0
II	14	0	5	7	1	1	0	0
III	8	0	1	2	3	2	0	0
IV	9	0	0	2	2	4	1	0
V +	10	0	0	3	2	5	0	0
Total	100	21	39	18	9	12	1	0

TABLE IV
Showing Distribution According to Community, Marital Status, Education and Residence

1. Community	Hindu 68	Catholic 21	Muslim 9	Protestants 2
2. Marital status	Unmarried 33	Previously Married 11	Currently Married 56	
3. Education in years	Nil 32	1-4 15	5-8 34	9-11 18 12 & + 1
4. Residence	Urban Local 80	Urban Outside 8	Rural Outside 12	

Forty-four per cent of the cases had pregnancies from extra-marital relationship, thirty-three being unmarried and the remaining eleven were separated or widowed.

Thirty-two per cent were not educated; 15 were poorly educated and 34 per cent had done primary schooling, while only 19 per cent were better educated. These figures are encouraging to the extent that uneducated and poorly educated women did seek terminations in large number.

Primarily, Nowrosjee Wadia Maternity Hospital served the local population, but 20 per cent were from outside. The latter were mainly those poor unmarried or those who wanted simultaneous sterilisation; the motivation in both the groups being strong.

Table V shows the distribution of 100 cases according to the method of termination and the initiation expulsion of the foetus time. There were three failures, one in each group, which took longer than 72 hours for expulsion. It is noted that PG single dose technique started the abortion process early, as many as 14 aborted within 18 hours. The hypertonic-saline was the slowest to start and only about 45% aborted by 24 hours time. The PG multiple dose was between the above two in the onset of expulsion but by 24 hours time had the maximum number of expulsions. In the saline and PG multiple dose groups almost all the patients had aborted by 48 hours, indicating that the saline technique caught up with the latter in the second 24 hours time. The single dose PG technique had 5 cases left after 48 hours compared to two cases in saline and one case in PG multiple doses, demonstrating the waning effect of the single dose PG.

TABLE V
Showing the Cumulative Distribution of 100 Cases According to the Method of Termination and the Initiation Expulsion of the Foetus Time

Method	Total No. of cases	Initiation — expulsion of foetus time in hours									
		6	8	12	18	24	30	36	48	72	> 72
Hypertonic Saline	33	0	0	0	5*	15*	20	23	31*	32	33@
PG Single Dose	34	1*	2	6	14	19** ***	26** **	27*	28*	32***	34@@+
PG Multiple Dose	33	0	2*	8	20*	26**	29	30*	32*	32	33@

Each * represents an incomplete abortion.
Each @ represents a failure.
Each @@+ represent technique failure.

The completeness or otherwise of an abortion was not dependent on the initiation expulsion of the foetus time, but was method related, the incomplete being many more in PG single dose method. Though a policy of waiting for two hours after the expulsion of foetus for placenta and membranes to come out spontaneously was generally applied, it was not possible to follow it in every case. In few cases more than two hours were allowed for spontaneous expulsion of the placenta, while in a few surgical evacuation of the placenta had to be done earlier than two hours. Moreover, in a number of cases the placenta must have been lying expelled in the vagina for quite sometime, but it was removed from the vagina much later. These facts would further alter the interval between the foetal and the placental expulsion. Due to the above discrepancies it was thought inadvisable to compare the total initiation—abortion time among the different method groups.

The incomplete abortions were finally evacuated by ring forceps application on the placenta and/or by blunt curettage under analgesic-sedatives only, in all cases.

The technique of any of the methods gave no problem, all being simple procedures. There were 15 blood taps prior to successfully getting into the amniotic sac with the needle, eight being at 15 to 16 weeks' of pregnancy, when a total of 43 were terminated at those weeks of gestation. Amongst the remaining 57 cases terminated at 17 to 20 weeks, there were seven blood taps. The more frequent blood taps at earlier, gestational weeks were accounted for by the smaller uteri. Blood taps were more frequent with inexperienced operators. None of the taps was serious and no morbidity occurred in these cases. In each of the three method

group there was one case with blood-stained liquor. The drugs were instilled in spite of blood-stained liquor with no ill effect. All the three cases had complete abortion within 18 hours.

Table VI shows the immediate side-effects and complications by the three methods. The total number of side-effects in the hypertonic saline methods was 9, the reactionary fever accounting for 5 of them. The total number in the PG single dose method and PG multiple dose method were 32 and 30, respectively, in each of them vomiting accounted for 14 cases. The other side effects found almost equally distributed in both the PG groups were fever and diarrhoea. Bleeding of amounts of more than 100 ml. was significantly noted with PG single dose technique. This high incidence of haemorrhage was essentially due to incompleteness of abortion (six out of seven) and not method related. It is interesting to observe that a patient receiving PG multiple dose had severe bronchospasm by the time she received 15 mgm of PGF_{2α}, there being no history of associated respiratory disease or other allergic manifestation in the patient. This patient in addition to bronchospasm had vomiting, rigor with fever and momentary collapse. She had immediate uterine contractions too. She recovered from these side effects soon after 0.5 ml. of 1:1000 subcutaneous injection of adrenaline and intravenous injection of 10 mg. of chlorpheniramine maleate. She also received about 100 ml. of 5% dextrose intravenously. After six hours when PG was repeated slowly she vomited after 15 mg. of PG, no further dose being administered. The patient aborted at 24 hours time and the placenta had to be surgically removed. She had tubal ligation immediately after abortion

TABLE VI
Showing the Distribution of Side Effects and Complications According to the Method Used

Method	Total No. of cases	Fever (More than 98.6°F)	Infection	Vomiting	Diarrhoea	Bleeding PV 100 ml+	Bronchial spasm	Other complications
Hypertonic saline	33	5	-	1	2	1	-	-
PG single dose	34	5	2*	14	4	7@	nil	Giddiness 1 Blood Transfusion 1
PG multiple dose	33	7	1*	14	7	nil	1	-

* Received antibiotics.

@ Received I.V. 5% glucose.

and was discharged uneventfully from the hospital.

Out of 17 patients with fever, in 3 there was infection; 2 of them needed antibiotics. Among the 29 patients who had vomiting, in none it was serious to require intravenous therapy; except for 2 patients antiemetic drugs were avoided. Diarrhoea too was not a serious problem in any patient. Nine women required sedatives and or analgesics in the PG group, while these drugs were not necessary in the saline group.

Out of the 100 cases, request for tubal ligation came from 22 multiparous women; 6 were in saline group, 8 were in PG single dose group and 8 were in PG multiple dose group. Six of the 22 sterilised patients had surgical evacuation of the placenta while others were cases of complete abortion. Operation of tubal ligation was done as early as within one hour of abortion to as late as 48 hours depending on the time and day of abortion and convenience of doctor performing the same. All ligations were done under spinal anaesthesia and no antibiotic was given to any of the patients. Each patient was kept in the hospital for a minimum of 96 hours after the tubal ligation; no complication of sterilisation operation was noted till the time of discharge.

Discussion

As far as is known to the authors, there has been no similar blind study reported from anywhere in India. In absence of an ideal abortifacient for second trimester pregnancy termination, a constant search for better and safer agent is being undertaken. The validity of this blind comparative study stems from these facts.

The results of this preliminary presentation of a report of 100 cases have indicated that the success rates of each of the

three methods were nearly equal. When however, among the successful cases the completeness and incompleteness of abortions were compared, the hypertonic saline gave the best results. (29 complete out of 33), followed by PG multiple dose (26 complete out of 33). The PG single dose gave only 17 complete abortions out of 34.

With the PG multiple doses method, the abortion rates at the end of 12, 18, 24 and 48 hours were 24, 60, 78, and 96 per cents. The abortion rates at similar time intervals for the PG single dose and the saline methods were, 18, 42, 57, 84 and 0, 15, 45, 93 per cents, respectively. The remaining successfully induced cases aborted by the end of 72 hours in each of the three groups. Prostaglandin by both the methods brought about significantly greater number of abortions within 24 hours period. However, the saline and the prostaglandin methods had almost the same number of abortions by 48 hours time.

The results of 110 cases of hypertonic saline instillation done at N. Wadia Maternity Hospital earlier (1972) had indicated almost the same rates of abortion in the given periods of time as is shown in the present series with hypertonic saline group.

The ideal dosage schedule for PG administration has not yet been finalised. The one with the highest efficacy and the least number of complications would be considered ideal.

The schedule of 50 mgm. single dose has not yet been reported, though reports with 40 mgm. single dose with minor modifications are known (Anderson, 1972). The schedule of 25 mgm. given at zero hour, and repeated at 6 hours, 24 hours, and 30 hours has been reported only by Brenner *et al* (1972) when they were

trying to establish "Ideal" dosage schedule. In a preliminary report of 10 cases, Brenner *et al* obtained 70 per cent abortions in 24 hours and 100 per cent in 48 hours.

The other report of multiple doses of PGF_{2α} comes from Ballard *et al*, (1972) who instilled an initial 25 mgm. of PGF_{2α} followed six hours later by 15 mgm. of PGF_{2α}; at the end of 30 hours, 17 out of 20 aborted giving a success rate of 85 per cent. In the present study the PG multiple dose at the end of 30 hours had a success rate of 87 per cent. Though not quite comparable, the rates of incomplete abortions were 17.6 per cent (3 out of 17) in Ballard's series and 13.7 per cent (4 out of 29) in the present series, which are not significantly different.

The other reports of multiple doses of PGF_{2α} come from (1) Brenner *et al*, (1972) who used two schedules, one of 15 mgm. and the other of 25 mgm. given at zero and 24 hours respectively, (2) Wentz (1972) who used 10, 15 or 25 mgm., repeating the dose when necessary, (3) Bygdeman *et al*, (1972) who used 25 mgm. repeated after 24 hours and (4) Karim *et al*, (1972) who employed 25 mgm. every 10 hours for four doses. None of these are strictly comparable with the multiple dose regime of the present work. In general, one could therefore conclude that the results at the end of 48 hours, with any of the dosage schedules have not been significantly variant from each other.

The only report for comparison with the single dose schedule is that of Anderson *et al*, (1972) who administered 40 mgm. as a single dose with minor modifications. They reported a 65 per cent abortion rate after the end of first 24 hours which is slightly better than the present series which was 57 per cent in first 24 hours. At the end of 48 hours they

had 92.5 per cent abortion rate against ours of 84 per cent. They had, however, injected a smaller second dose after 24 hours.

Naftolin *et al*, (1972) working with different dose schedule of PGF_{2x} given intra-amniotically noted a distinct shortening of the abortion time with increasing doses. The latter however increased the side effects in dose related fashion. Anderson *et al*, (1972) using 40 mgm. dosage schedule noted the nausea and vomiting in 62.5 per cent of cases and diarrhoea in 17 per cent; which is substantially greater than the rates of the same complications in the present study. The side effects in the present series were expected to be more in the single dose technique compared to the multiple dose technique due to larger single dose. The three side effects compared were vomiting, diarrhoea and fever. Table VII gives

chospasm has been reported both *in vivo* and *in vitro* experiments following administration of PGF_{2α}. Brenner *et al* (1972) have reported a case following intra-amniotic 50 mgm. PGF_{2α} and Carter *et al*, (1972) have reported a case following intra-venous PGF_{2α}. In the series of N. Wadia Maternity Hospital one case was present where bronchospasm occurred after 25 mgm. of PGF_{2α}; but the patient recovered enough to allow the administration of second dose of 25 mgm. PGF_{2α} six hours later when no further side effects occurred. Bronchospasm was not related to the rate of drug administration or to the dosage employed.

Conclusions

The following conclusions can be drawn from the present work—

(i) All the three methods employed intra-amniotically to terminate the second

TABLE VII

Showing Side Effects in Relation to PG Method and Induction—Abortion of Foetus Time

Side effects	PG single dose			PG multiple dose		
	Total No. of cases	Duration		Total No. of cases	Duration	
		18 Hrs.	18 Hrs.+		18 Hrs.	18 Hrs.+
Vomiting	14	4	10	14	7	7
Diarrhoea	4	1	3	7	3	4
Fever						
More than 98.5°F	nil	5	5	7	2	5

the detail of the side effects by both these methods and by abortion time. The figures in the Table do not substantiate the observation of Naftolin *et al*, (1972) that the side effects could be greater by increasing the initial dose administered. Even the number of abortions by 18 hours is not more in the single dose technique compared to the multiple dose method.

A special mention of the complication of 'Bronchospasm' may be made. Bron-

trimester pregnancies have similar results at the end of 72 hours of initiation of therapy.

(ii) When one compares the results at the end of 24 and 36 hours, the number of abortions with the PGF_{2α} methods were greater. These patients aborting earlier had consequently gone home earlier too. There is no doubt therefore that when one aims at quicker abortions, prostaglandin is superior to hypertonic saline.

The PG single dose method did not prove superior to PG multiple dose method.

(iii) The hypertonic saline method resulted in the maximum number of complete abortions (29 out of 32) followed closely by the PG multiple dose method (26 out of 32). Only a little more than 50% of the cases receiving PG single dose, aborted completely (17 out of 32). The latter technique therefore required the maximum number of surgical interferences.

(iv) The study did not reveal significant relationship between parity and weeks of gestation on the one hand and the method employed on the other hand, as far as the success of the terminations is concerned.

(v) The main side effects of nausea, vomiting, diarrhoea and fever were undoubtedly greater with PG methods compared to the saline method. None was however, serious. The side effects of diarrhoea and fever were more common with multiple dose amongst prostaglandin groups.

Summary

1. A comparative blind study of mid trimester pregnancy terminations is being carried out at Nowrosjee Wadia Maternity Hospital, using three trans-abdominal intra-amniotic methods: (i) Hypertonic saline 20 per cent 200 ml., (ii) PG single dose 50 mg. PGF_{2α}, (iii) PG multiple dose, 25 mgm PGF_{2α} given at 0, 6, 24 and 30 hours.

2. 100 cases were included in the preliminary study to give the following distribution, 33 cases in 20 per cent hypertonic saline, 34 cases in PG single dose method and 33 cases in PG multiple dose method.

3. The abortion rate at the end of 72

hours in each of the above method were 96 per cent.

4. The side effects were minimum with the saline method. Only in one case of PG multiple dose method was there a serious side effect of bronchospasm.

5. Surgical interference was required in 3 cases of saline, 15 cases of PG single dose and 6 cases of PG multiple dose method to complete the abortion.

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