EVALUATION OF PROSTAGLANDIN F\textsubscript{2} ALPHA AND HYPERTONIC SALINE AS ABORTIFACIENTS

by

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The intraamniotic instillation of various abortifacients is becoming increasingly popular as a simple, ambulatory, nonsurgical method of termination of midtrimester pregnancies. It is in this context that hypertonic solutions, specially 20% saline, and the more recently discovered prostaglandins of the E and F series have featured prominently in large abortion series. Though extensively used safely now, hypertonic saline had gone into disrepute following the high maternal mortality rate Waga'suma (1965) and reports of fatal complications Cameron and Dayan (1966). Prostaglandin-induced abortions have not been marred by any reports of fatalities, but are characterised by irksome gastrointestinal side effects Anderson et al (1972). This study was designed to compare these two midtrimester abortifacients as regards the efficacy, in terms of success-rate and induction-abortion interval, and their acceptability in terms of course of abortion, side-effects and complications.

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Material and Methods

Eighty women seeking medical termination of pregnancy of 14-20 weeks' gestation, at the All India Institute of Medical Sciences Hospital, were selected for this study. In 40 women, PGF\textsubscript{2} alpha was administered intraamniotically, while 20% saline was used in another group of 40 women. Women with metabolic, renal, respiratory, cardiovascular or liver disease, and those with uterine scar or malformations or with pelvic inflammation were excluded from this study. The choice of the abortifacient to be used for each patient was randomized, so as to make the study unbiased and strictly comparable.

The average age of patients was 25 years (range 16-37 years) in the PGF\textsubscript{2} alpha group and 24 years (range 15-42 years) in the saline group. Parity of patients ranged between 0-8, with a preponderance of primigravidas, the latter comprising 45% of patients in the PGF\textsubscript{2} alpha group, and 57.5% of cases in the saline group. Pregnancies terminated were between 14-20 weeks of gestation, the maximum being in late midtrimester. Thus, 40% of women in the PGF\textsubscript{2} alpha group and 52.5% of cases in the saline group sought termination at 20 weeks of gestation.
Intraamniotic Administration of \( \text{PGF}_2 \) Alpha

After the patient evacuated the bladder, amniotomy was done per abdomen with due aseptic precautions, using an 18 gauge needle with stylette and selecting a site in the midline a little above the pubic symphysis. The stylette was withdrawn, and after ensuring a free flow of clear liquor, a polyethene catheter was threaded through the needle into the amniotic cavity, and the needle was then removed. \( \text{PGF}_2 \) alpha was then injected through this indwelling catheter. The first dose of 23 mg \( \text{PGF}_2 \) alpha (5 mg/ml solution) was injected very slowly to detect untoward reactions like bronchospasm or tetanic uterine contractions. The second dose of 25 mg \( \text{PGF}_2 \) alpha was administered 6 hours later.

The patient was asked to report about any symptoms of extravasation of saline, like pelvic pain, tingling and numbness and feeling of intense thirst, during the instillation.

In each case, the vital signs of the patient before and during instillation and during the induction-abortion period, as well as during the course of abortion were regularly noted.

Results

Success Rate

In each group, the trial was considered successful if abortion (complete or incomplete) occurred within 48 hours of induction. The success-rate was 87.5% in the \( \text{PGF}_2 \) alpha group and 95% in the saline group, the difference not being statistically significant (Fig. 1). In the PG group, 4 of the 5 ‘failed’ trials were ‘interrupted’, because due to premature rupture of membranes, following administration of the first dose, the second dose of \( \text{PGF}_2 \) alpha could not be given. One failure was due to non-responsive-ness to the drug. While in the saline group, one of the ‘failed’ trial was due to “ interruption” of saline instillation, as

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Intraamniotic Administration of Hypertonic Saline

200 ml of hypertonic saline was injected into the amniotic cavity over a period of 20 minutes after withdrawing about 50 ml of liquor. The method used was the same as that described above for \( \text{PGF}_2 \) alpha instillation, except that no indwelling catheter was left in this case.

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Fig. 1
the patient complained of severe pain after 50 ml was injected. The second failure was due to the cervix remaining undilated even at 48 hours after induction. In 4 of the 5 failure with PGF$_2$ alpha and both the failed trials with saline, oxytocin supplementation was used to complete the abortion in each case. Hysterotomy with ligation was done in one ‘failed’ trial in the PG group.

**Cumulative Abortion Rates**

The cumulative abortion rates for the two groups (Fig. 2) suggested that a greater percentage of patients aborted faster with PGF$_2$ alpha than with saline, though by 48 hours there was no difference between the two groups. In the PGF$_2$ alpha group, 15% patients aborted within 12 hours of induction, 42.5% in 18 hours, 62.5% in 24 hours, 75% in 30 hours, 87.5% in 36 hours and 95% in 48 hours. In the saline group 2.5% patients aborted within 12 hours of induction, 18% in 18 hours, 27.5% in 24 hours, 70% in 30 hours, 80% in 36 hours, 92.5% in 42 hours and 95% in 48 hours.

**Type of Abortion**

The percentage of complete abortions was significantly higher in the saline group as compared to the PGF$_2$ alpha group (P 0.02). Thus, whereas 78.8% of successful abortions in the saline group were complete, only 48.6% of successful abortions in the PG group were complete (Fig. 3). Vacuum aspiration and digital evacuation of the placenta or oxytocin drip were the supplementary methods used in cases of incomplete abortion. The higher incidence of complete abortions with saline is probably due to a better line of cleavage of placental separation in these cases, due to the subchorionic necrosis induced by saline Christie et al (1966). PGF$_2$ alpha acting as a direct myometrial stimulant Csapo (1972), fails to achieve this.

**Induction-Abortion Interval**

The induction-abortion interval in the PGF$_2$ alpha group was 24.5 hours on the average, the range being 7-47 hours. The mean induction-abortion interval in the saline trials, was 27.2 hours, with a
range of 10-46 hours. The difference was not statistically significant. No significant relationship could be established between the age and parity of the patient or the period of gestation with the induction-abortion interval in both groups. However, it was observed that while multigravidas aborted faster than primigravidas in the PGF₂ alpha group, in the amniotic fluid was lower, the latter being more in volume in these cases as compared to that in cases where gestation period was shorter.

**Course of Abortion**

The course of abortion was also significantly different (P<0.001) in the two groups (Table IV and Fig. 4). The in-

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**TABLE I**

<table>
<thead>
<tr>
<th>Parity</th>
<th>PGF₂ Alpha</th>
<th>Saline</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Average</td>
<td>Range</td>
</tr>
<tr>
<td>Primigravidas</td>
<td>25.1</td>
<td>8.7 - 47</td>
</tr>
<tr>
<td>Multigravidas</td>
<td>24.1</td>
<td>7 - 46</td>
</tr>
</tbody>
</table>

**TABLE II**

<table>
<thead>
<tr>
<th>Gestation in weeks</th>
<th>Average Induction-Abortion Interval (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>14 - 16</td>
<td>PGF₂ Alpha 22.0 26.4 Saline</td>
</tr>
<tr>
<td>16 - 20</td>
<td>23.3 27.6</td>
</tr>
</tbody>
</table>
EVALUATION OF PROSTAGLANDIN AND HYPERTONIC SALINE

TABLE III
Latent Period and Effective Contractions in Relation to Abortifacient Used

<table>
<thead>
<tr>
<th>Phase</th>
<th>PGF$_2$ alpha</th>
<th>Saline</th>
<th>Contrast between two groups*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Latent period</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average length (hours)</td>
<td>5.3</td>
<td>18.4</td>
<td></td>
</tr>
<tr>
<td>% of I-A time</td>
<td>21%</td>
<td>66.5%</td>
<td>P 0.001</td>
</tr>
<tr>
<td>Effective contractions</td>
<td>19.2</td>
<td>8.8</td>
<td>33.5%</td>
</tr>
<tr>
<td>% of I-A time</td>
<td>79%</td>
<td>33.5%</td>
<td>P 0.001</td>
</tr>
</tbody>
</table>

I-A Induction Abortion
* Cochran's modified $r$ test

TABLE IV
Parity in Relation to Latent Period and Effective Contractions in PGF$_2$ Alpha Inductions

<table>
<thead>
<tr>
<th>Parity</th>
<th>Latent period</th>
<th>Effective contractions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Average length (hours)</td>
<td>% of I-A time</td>
</tr>
<tr>
<td>Primigravidas (P)</td>
<td>4.0</td>
<td>19.8</td>
</tr>
<tr>
<td>Multigravidas (P)</td>
<td>7.0</td>
<td>22.5</td>
</tr>
<tr>
<td>Primigravidas (S)</td>
<td>16.7</td>
<td>63.5</td>
</tr>
<tr>
<td>Multigravidas (S)</td>
<td>19.9</td>
<td>67.9</td>
</tr>
</tbody>
</table>

P: PGF$_2$ Alpha Trials  S: Saline Trials

Production-abortion interval comprised of two phases of uterine activity. The time from induction and the first palpable uterine contraction or the first painful uterine contraction felt by the patient was taken as the "latent period." The period from the onset of palpable or painful uterine contractions to the time of abortion constituted the phase of "effective contractions" or "labour." PGF$_2$ alpha-induced abortions were characterized by a short 'latent period' (21% of induction-abortion interval) and a long "labour" (66.5% of induction-abortion time). In the saline group, the induction-abortion interval was comprised of prolonged latent period (66.5%) and a short "labour" (35.5%). However, frequency of analgesic required was about the same in the two groups as 47.5% patients in the PGF$_2$ alpha group and 42.5% in the saline group, needed analgesics during the trial period. Early onset of uterine contractions in PGF$_2$ alpha group is probably due to the direct myometrial stimulating effect of PGF$_2$ alpha Csapo et al (1972). With saline myometrial contractility is induced only indirectly by one of various mechanisms accounting for prolonged latency. The mechanisms include withdrawal of placental hormonal support Laumas et al (1974) oxytocin or prostaglandin release Hendricks et al 1969; Gustavii 1973) and foetal death consequent to instillation of hypertonic saline into the amnio-
LATENT PERIOD AND EFFECTIVE
CONTRACTIONS IN PGF_{2}\alpha AND
HYPERTONIC SALINE ABORTIONS.

- Latent Period.
- Effective Contraction.

\[ P < 0.001 \]

\( \text{PGF}_{2}\alpha \)
\( \text{20\% Saline} \)

Fig. 4

PARITY IN RELATION TO LATENT PERIOD
AND EFFECTIVE CONTRACTIONS IN PGF_{2}\alpha
AND HYPERTONIC SALINE ABORTIONS.

- Latent Period.
- Effective Contraction.

\( P \) PRIMIGRAVIDAS.
\( M \) MULTIGRAVIDAS.

Fig. 5

Side Effects and Complications

There were significantly more side-effects in PGF_{2} alpha-induced abortions than in saline-induced ones (Table V and Fig. 6). Thus, gastrointestinal symptoms occurred in 32.5% of cases in the PGF_{2} alpha group and in 2.5% cases in the saline group, the difference being statistically significant (\( P < 0.001 \)).

Table V
Side-effects in Relation to Method of Induction

<table>
<thead>
<tr>
<th>Side Effects</th>
<th>PGF_{2} Alpha</th>
<th>%</th>
<th>Saline</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal</td>
<td>13</td>
<td>32.5</td>
<td>1</td>
<td>2.5</td>
</tr>
<tr>
<td>Nausea</td>
<td>3</td>
<td>7.5</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Vomiting</td>
<td>9</td>
<td>22.5</td>
<td>1</td>
<td>2.5</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>1</td>
<td>2.5</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Fever</td>
<td>1</td>
<td>2.5</td>
<td>1</td>
<td>2.5</td>
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<tr>
<td>Dyspnoea</td>
<td>1</td>
<td>2.5</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Flush</td>
<td>2</td>
<td>5.0</td>
<td>1</td>
<td>2.5</td>
</tr>
<tr>
<td>Uterine tetany</td>
<td>1</td>
<td>2.5</td>
<td>1</td>
<td>2.5</td>
</tr>
</tbody>
</table>
EVALUATION OF PROSTAGLANDIN AND HYPERTONIC SALINE 807

SIDE-EFFECTS AND IMMEDIATE COMPLICATIONS IN PGF₂ AND HYPERTONIC SALINE ABORTIONS

PGF₂ alpha group, 2.5% cases had diarrhoea, 2.5% had nausea and 22.5% had vomiting, whereas in the saline group only 2.5% had vomiting. Fever occurred in 2.5% cases in both groups and the cause was genital tract infection associated also with an induction-abortion interval of more than 24 hours. Flushing was noted in 5% patients in the PGF₂ alpha group and 2.5% cases with saline, while dyspnoea was seen in 2.5% cases with PGF₂ alpha.

Marked postabortal haemorrhage due to incomplete abortion, necessitating blood replacement for resuscitation was seen in 2 patients in the PGF₂ group and in 1 case in the saline group. Unexplained collapse characterized by dyspnoea, tachycardia, cyanosis and hypotension occurred in 1 patient in the saline group, shortly before abortion. Blood coagulation studies, blood urea, electrolytes, X-ray chest, E.C.G. were all within normal limits. The etiology could not be established, but the patient was resuscitated, and had an uneventful postabortion period.

A febrile postabortion period was experienced by 2 patients in the PGF₂ group and 3 in the saline group. Incomplete abortions were treated on follow-up in 2 cases in the PGF₂ group. In one curettage was done. In other multiparous patient who continued to bleed even after curettage, hysterectomy was performed and she was found to have a placental polyp.

Hospital Stay

Hospital stay of patients in the two groups was short and comparable, being three days on the average, thus, stressing the ambulatory nature of the abortion methods.

Follow-up Study

The menstrual pattern of patients reporting for follow-up 1-3 months after the abortion, was unchanged in 96.9% cases in the PGF₂ alpha group, as compared to 76.9% cases in the saline group. Menorrhagia occurred in 3.1% cases in the PG group and 15.4% cases with saline, while amenorrhoea was noted in 77% cases in the saline group alone. They, however, responded to treatment.
Conclusions

The high success rate and acceptably short induction-abortion interval along with the short hospital stay of patients induced by PGF$_2$ alpha and saline, suggest the efficacy of these midtrimester abortifacients. This experience is also reflected in the series of PGF$_2$ alpha induced abortions of Brenner et al (1972) and Anderson et al (1972), and also in the saline abortion series of Kerenyi (1971) and Stim (1972). The relatively low morbidity rates and the absence of fatal complications stress the safety of the abortion-method for even fairly advanced pregnancies.

On a comparative basis, except for an insignificantly longer induction-abortion interval, hypertonic saline seems to have some advantages over PGF$_2$ alpha as a midtrimester abortifacient. The fewer side effects, better success rate, short active "labour" and the greater percentage of complete abortions in the saline trials, are in favour of saline. Although there were more menstrual changes subsequent to saline than to PGF$_2$ alpha-induced abortions, they were all amenable to treatment. Besides, saline is less expensive and more easily available than PGF$_2$ alpha and from the results of this study promises to be a good substitute to prostaglandins as an effective and safe midtrimester abortifacient for use in crowded abortion centres.

References