

# Clinical Uses of Prostaglandins in Human Reproduction

Prostaglandins are highly effective in abortion and in induction of labour. They are also being used in regulation of menstruation and control of post-partum haemorrhage even though the results are not absolutely satisfying. Further research is going on. Mrs. P. BAJAJ, Public Health Nursing Supervisor, R.H.C.S. Project, Ballabgarh, gives an elaborate introduction to this important subject.

## INTRODUCTION

*Definition:* As defined by Von Euler in 1935 "A group of lipids identified in semen samples and observed to have marked smooth muscle stimulating activity, were given the name Prostaglandins in the belief that these substances were secretions of the prostrate glands".

Karim and Hiller (1966-68) indicated the presence of prostaglandins in the female reproductive system and in blood, during menstruation, abortion, and delivery. They suggested the primary role of the Prostaglandins as stimulants of the human uterine musculature for the purpose of evacuation of uterine contents.

Mehta *et al* were the first to apply Prostaglandin (PG) E<sub>2</sub> in clinical practice in India in January 1970, for obstetrically indicated pregnancy terminations and for induction of labour.

In April 1972, the M.T.P. Act was implemented and innumerable researchers in India have confirmed the usefulness of Prostaglandins in clinical medicines.

## Clinical Application

A. *Termination of Midtrimester Pregnancy:*  
1. Unwanted pregnancy of 13 to 20 weeks; 2. Missed abortion; 3. Excessive bleeding in 2nd trimester; 4. Vesicular mole pregnancy, generally from 14 to 24 weeks.

B. *Induction of Labour (24-43 weeks):* 1. Elective inductions. 2. Induction for medical reasons or obstetric condition; 3. Induction for intrauterine foetal death.

## C. Menstrual Regulation

In case of delayed or missed menstrual periods in whom the amenorrhoea has not exceeded 45 days.

## D. Control of Post-Partum Haemorrhage:

TYPES OF PROSTAGLANDINS CLINICALLY USED:

Natural Prostaglandins: (i) PG E<sub>2</sub>; (ii) PG F<sub>2α</sub>

Synthetic Analogues: (iii) 15 Methly PG E<sub>2</sub>; (iv) 15 Methly PG F<sub>2α</sub>

The natural Prostaglandins are not so stable under the ordinary atmospheric conditions. They require special storage facilities. They are rapidly metabolised into an inactive form necessitating frequent or continuous administration and give rise to undesirable side-effects.

## Mechanism of Action

### (A) IN ABORTION

The Prostaglandins directly stimulate the pregnant uterine musculature and brings forth active spasmodic contractions. This results in the rapid dilation of cervix and diminishing of the utero-placental blood flow.

PG F<sub>2α</sub> compounds are avoided in cases suffering from respiratory allergy, bronchial and pulmonary infection and bronchial asthma.

*In Induction of Labour:* The Prostaglandins produce initial and transient rise in the basal tone of the uterus, and almost immediate uterine contractions of increased frequency and low amplitude. With the restoration of normal uterine tone within half-an-hour, the frequency of contractions settles down to two or three in ten minutes, and the intensity or strength of contraction gradually rises to physiological limits of normal labour.

The success of induction and the induction-delivery interval are, as usual, dependent on the cervical status, the gestational period, and the parity of the patient.

### Routes and Doses

In case of abortion, the Prostaglandins may be given by intravenous, intra-amniotic, extra-amniotic, vaginal or intramuscular means. For induction of labour it can be given intravenously, orally, transmucosally, extra amniotically and by means of Titration as well.

The kind of Prostaglandins to be used and the route of administration depend on the choice of a surgeon to a greater extent but it also depends on the reaction or tolerance of a patient. The frequency in administration of the drug also depends upon the condition or responses given by the patient from time to time.

### Results and Side Effects in Stimulation

*In medical termination of pregnancy* : All the four Prostaglandins by all the available routes are highly effective and successful. Uterine activity develops usually within half-an-hour of Prostaglandin administration, and more than 70% of cases about in 24 hours' period, and nearly 95% abort by 48 hours. The average induction abortion time is approximately 20 hrs. The failure rate is less than 2.

The Prostaglandins are the most efficacious and the safest of all the known abortifacients. There are many side-effects of Prostaglandins in abortions.

#### Side Effects in Medical Termination of Pregnancy

| Side Effects                                       | Incidence in Percentage |
|----------------------------------------------------|-------------------------|
| 1. Nausea and vomiting                             | 50—70%                  |
| 2. Diarrhoea                                       | 30—50%                  |
| 3. Phlebitis-IV                                    | 30—50%                  |
| 4. Fever                                           | 15—20%                  |
| 5. Chills & Rigors                                 | 5—10%                   |
| 6. Fall in blood pressure, chest pains tachycardia | 2—5%                    |

Nausea, vomiting and diarrhoea occur too frequently due to stimulation of gastro-intestinal system. Phlebitis along the vein of infusion occurs only in the intravenous method of administration. The side-effects have been minimised in the intra-amniotic and the extra-amniotic methods.

These side-effects can be controlled or avoided by the simultaneous employment of drugs like Diazepam, Siquil, Stemetil, Eskazin and Lomotil.

#### Drugs to Counteract Prostaglandins' Side-Effects in Medical Termination of Pregnancy

1. Pain of uterine spasm: Injection Pethidine.
2. Sedation for nausea, vomiting: Injection Diazepam—5-10 mg. Intramuscularly. Injection Siquil—5-10 mg. Intramuscularly. Injection Eskazine—1-2 mg. intramuscularly. Injection Stemetil 5-15 mg. Intramuscularly.

3. Diarrhoea—Lomotil Tablets 3/4, 4 Hrly.

4. Dehydration: Intravenous Fluids.

### (B) IN INDUCTION OF LABOUR

The Prostaglandins for induction of labour have given success rates of 85-98% as compared to other conventional methods of induction. In cases of unfavourable or unripe cervical status, the Prostaglandins give superior outcome of induction of labour than the oxytocin. This is also used for difficult induction of labour, missed abortion and intrauterine foetal death.

The incidence of side-effects in cases of induction of labour have not been serious or significant and have never warranted stoppage of therapy.

#### Complications

*In Abortion* : This gives rise to incomplete abortion from 25-50%. Therefore, surgical evacuation of retained placenta and its membrane are required:

Atomic post-abortion bleeding : 2—5%; Cervical Tear: 2—5%; Uterine rupture: 0.5%.

*In Induction of Labour* : Hypertonicity and disordered uterine action: 5-7%; Foetal distress due to induction: 0.5 to 2%; Uterine rupture: very rare; Hyperbilirubinaemia in new born—rare unless high dose: No complication—Serious.

### (C) FOR MENSTRUAL REGULATION

Prostaglandins are being used for delayed or missed menstrual periods either through vagina or extra amniotic. The administration by the vaginal route has to be repeated six to eight times in 24 hours, while a single dose is administered by the extra-ovular method.

After the administration, the bleeding often continues for two weeks and in case of pregnancy surgical intervention is almost invariably called for. It has side effects of nausea, vomiting and diarrhoea, and discomforts of severe uterine cramps pose additional problems and make the use of Prostaglandins for menstrual regulation almost unacceptable.

### (D) FOR CONTROL OF POST-PARTUM HAEMORRHAGE

To control effectively and instantaneously the post-partum haemorrhage, the Prostaglandins have to be injected directly into the uterine wall. The other routes are not able to have rapid action without ill-effects. Prostaglandins do not, therefore, play significant pharmacological and therapeutic roles in the control of post-partum haemorrhage.

### Research Work

341 Healthy Pregnant Women, between 10-20 weeks of gestation, sought Medical Termination of Pregnancy at the All-India Institute of Medical Sciences, New Delhi, by three different techniques : 1. Intra-Amniotic; 2. Extra-Amniotic; 3. Intra-Muscularly.

This study was conducted by Dr. V. Hingorani and Dr. N. Aggarwal in the Department of Gynaecology.

**Intra-Amniotic Schedule :** No. 8 Needle—Administer the drug in abdomen at a suitable point. The area was first infiltrated with xylocaine 1% for local Anaesthesia. The drug was administered only if clear liquor was obtained. In case of blood-tap, another point should be tried. If blood comes again then this route is given up. The patient is carefully observed till the time of abortion. The trial is considered successful if the patient is aborted completely or incompletely within 48 hours.

#### Schedule for Intra-Amniotic Administration

| Drug & Doze          | No. of Cases | Success Rate | Abortion Within |
|----------------------|--------------|--------------|-----------------|
| PGF 2 a 40 mg        | 48           | 85%          | 48 hrs          |
| PGF 2 a 50 mg        | 30           | 90%          |                 |
| 15 ML-PG F 2z 2.5 mg | 86           | 98.8%        |                 |

**Extra-Amniotic Schedule :** No. 8 Catheter is used to introduce fluid extra-amniotically. Patient is kept in lithotomy position with the head end lowered. After instillation, the patient is asked to lay down for 20 minutes to avoid expulsion of the drug. Patient is carefully observed till the time of abortion and the trial is considered successful if complete or incomplete abortion occurs within 36 hours.

**Side-Effects :** Vomiting; diarrhoea; flush and fever are to be treated symptomatically.

#### Schedule of Extra-Amniotic Administration

| Drug and Doze        | No. of Cases | Success Rate | Abortion Time  |
|----------------------|--------------|--------------|----------------|
| 15 ml. PGF 2a 750 mg | 50           | 96%          | Within 36 hrs. |
| 15 ml. PGF 2a.       | 45           | 86.6%        | 920 mg.        |

**Intra-Muscularly :** Abortion takes place completely or incompletely within 30 hours after the induction of the drug. 200 mg. of 15 ME-PG F2A was given and followed by 400 mg. after every 3 hrs. 30 minutes before each of 3 injections, each patient received 2 tablets of Diphemoxylan Chloridium 2.5 mg. and Atropin 25 mg orally as prophylaxis against diarrhoea. The method is used when intra-amniotic and extra-amniotic methods are technical failures in the instance of blood-tap. It is feasible when pregnancy is less than 15 weeks. The Intra-Muscular schedules have been

well tolerated and accepted by the patients. Best results have been obtained in multiparous with pregnancies less than 14 weeks.

#### Intra-Muscular Administration

| Drug & Doze.                                      | No. of Cases | Success Rate | Abortion Within. |
|---------------------------------------------------|--------------|--------------|------------------|
| 15 Mc. PG F2 a 400 mg/300 mg — 3 hrly injections. | 30           | 76.6%        | 30 hrs.          |
| 15 Mc. PG P2 a—300 mg/300 mg                      | 52           | 86.5%        |                  |

#### NURSING CARE : IMPORTANT POINTS

1. Prepare the patient as desired for administration of the Prostaglandins.
2. Use aseptic technique for the collection of the equipment and introduction.
3. Attend to the personal hygiene of the patient especially in case of Intra- and Extra-Amniotic methods.
4. Watch for side-effects, report and treat as ordered.
5. Prepare articles for abortion and observe the condition of the patient from time-to-time.
6. Keep Intra-Venous fluids and injections ready for the safety of the mother.

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