

# Induction of Ovulation in Polycystic Ovarian Disease

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**Summary:** A prospective study was undertaken among PCOD subjects to know the efficacy of various modes of ovulation induction. Altogether 100 patients entered the study, 96 of them were married and 92 of them presented with infertility. These group of patients who presented with infertility underwent various modalities of induction. CC was the initial choice and patients who were unresponsive to CC were considered for other modalities of induction. A 75 gm oral glucose tolerance test was performed on all patients and patients who had abnormal GTT were put on diet or insulin depending on the degree of severity in abnormal GTT. A small group of patients who were resistant to medical modes of induction underwent laparoscopic ovarian drilling as a method of ovulation induction. Pregnancy rates were 23.52% with Clomiphene Citrate, 14.28% with FSH, 33.33% with HMG and 21% with diet. 2 out of 3 patients who underwent insulin therapy conceived with a pregnancy rate of 66.66%. But the number of patients who underwent insulin therapy is too small to comment on pregnancy rate. Two out of 17 patients who underwent laparoscopic ovarian drilling conceived with a pregnancy rate of 11.76%. Only one patient underwent GnRH short flare up protocol and she developed hyperstimulation in the same cycle where she conceived. CC remains the most effective modality of induction in PCOD. CC resistant subjects may be considered for other alternate modality of inductins. Patients with abnormal GTT do benefit from diet and insulin therapy.

## Introduction

Polycystic ovarian disease remains an incompletely understood entity that appears with regularity in the practice of most gynecologists. Most of these patients present with infertility.

Infertility in this group of patients is due to chronic oligoovulation or anovulation and restoration of ovulatory function is of paramount importance. Many treatment schemes have been proposed and implemented to circumvent intrinsic block to ovulation and thus restore fertility. Various medical agents and surgical procedures have been used to treat infertility in these patients. The purpose of this study is to compare the various agents used to treat infertility in PCOD subjects.

## Materials and Methods

The study was conducted among PCOD patients attending the Gynaecology Dept. and the infertility clinic-Manipal Assisted Reproduction Centre of Kasturba Medical College, Manipal. The study was done during a 2 year period from Dec 1994 to Dec 1996. The diagnosis was based mainly on the basis of transvaginal sonography picture showing multiple subcapsular follicles measuring less than 10 mm in diameter. The number of follicles varied from 6-16.

Patients with infertility were induced with Clomiphene Citrate or Gonadotrophins. Patients were initially given 2-4 cycles of Clomiphene Citrate. Clomiphene failure subjects were treated with gonadotrophins in a sequential manner with Clomiphene Citrate. Either HMG or

pure FSH was used depending on the situation. In a sequential regimen Clomiphene Citrate 50mg was used from Day2-Day5 and HMG or FSH 75 IU was used from Day7-Day 10. Follicular imaging was done from Day 11 onwards and a timely intrauterine insemination was done using "swim-up" technique.

A 75gm Oral Glucose tolerance test was performed on all patients with PCOD. Patients with abnormal Glucose Tolerance test were put on diet or insulin depending on the severity of abnormality in Glucose Tolerance Test.

Seventeen patients underwent laparoscopic ovarian drilling so as to induce ovulation. Pregnancy rates with various induction protocols were critically analysed.

## Results

Out of the 100 patients having PCOD 96(96%) were married and 04(04%) unmarried. Among 96 married subjects 72(75%) presented with primary infertility, 20(20.83%) presented with secondary infertility and 4(3.14%) presented with proven fertility (At least one live child) (Table 1)

**Table - I**  
**Fertility Status**

| Fertility status      | No. of Patients | Percentage |
|-----------------------|-----------------|------------|
| Primary infertility   | 72              | 75%        |
| Secondary infertility | 20              | 20.83%     |
| Fertile               | 4%              | 3.14%      |

Pregnancy rates after each mode of induction were critically analysed. Sixteen out of 68 patients who received Clomiphene Citrate conceived with a pregnancy rate of 23.52%. Pregnancy rates were 14.28% with CC+FSH, 21% with CC-hMG, 21% with Diet, 11.76% with laparoscopic ovarian drilling and 66.66% with insulin. Only one patient underwent GnRH short flare up protocol. She developed hyperstimulation in the cycle where in she con-

ceived. Though pregnancy rates were high after insulin the patients who underwent insulin therapy were too small to comment on the pregnancy rate (Table II).

**Table II**  
**Pregnancy rates after various induction protocols**

| Method              | No. of Patients | Pregnancy | Percentage |
|---------------------|-----------------|-----------|------------|
| CC                  | 68              | 16        | 23.52%     |
| CC+FSH              | 35              | 05        | 14.28%     |
| CC+HMG              | 09              | 03        | 33.33%     |
| Diet                | 19              | 04        | 21%        |
| Insulin             | 03              | 02        | 66.66%     |
| Laparoscopic        |                 |           |            |
| Ovarian drilling    | 17              | 02        | 11.76%     |
| GnRH short flare up | 01              | 01        | 100%       |

There is an overlap between patients in these table as same patients underwent different modes of induction.

## Discussion

The present study was undertaken to evaluate the efficacy of various modes of induction ovulation in polycystic ovarian disease. Induction of ovulation in PCOD remains a challenge to the reproductive endocrinologist. We observed a high pregnancy rate after CC(23.52%). Clomiphene citrate can be used with minimal Gracia monitoring techniques. The risk of multiple gestation and ovarian hyperstimulation are low with Graeva et al 1977 clomiphene citrate; Ninley et al, 1985. Gracia et al (1977) observed a pregnancy rate of 40% with clomiphene citrate.

Human menopausal gonadotrophins is the next therapeutic option for patients who have failed to ovulate on CC. Use of gonadotrophins on patients who have failed to ovulate on CC is well established (Kelly, 1990). Today's readily available monitoring technology (ultrasonography and rapid E2 measurements) makes gonadotrophin therapy safe in terms of the risks of multiple gestation and OHSS. Although pure FSH use in PCOD has a

physiologically sound basis in the setting of elevated LH levels, in the clinical trials to date, it has not lived up to its original promise of being an 'ideal drug' (Kelly, 1990). We observed a pregnancy rate of 14.28% with FSH. Kelly et al (1990) in a review article found a pregnancy rate of 14-21% with pure FSH. Pregnancy rate with HMG in the present study was 33.33%. Wang Gemcell (1980) observed a pregnancy rate of 28% with HMG. However the number of patients who received HMG in the present study is too small to comment on the pregnancy rate.

Considerable number of patients with PCOD exhibit abnormal glucose tolerance. (Frank, 1995). An improvement in ovarian function has been noted with diet and calorie restriction in PCOD subjects. We observed a pregnancy rate of 21% with diet in those group of patients who had an abnormal GTT. Kiddy et al (1992) observed a pregnancy rate of 38.46% with diet. Two out of 3 patients who received insulin conceived with a pregnancy rate of 66.66%. The number of patients who received insulin is too small to comment on the pregnancy rate.

Out of the 17 patients who underwent laparoscopic ovarian drilling 2 conceived with a pregnancy rate of 11.76%. Barry et al (1995) observed a pregnancy rate of 20% with laparoscopic ovarian drilling. Thus patients resistant to medical modes of induction may benefit from ovarian drilling.

The patient with PCOD remains a challenge to the reproductive endocrinologist. Although successful induction of ovulation can often be achieved using a standard therapeutic regimen of CC or gonadotrophins is group of anovulatory patients often fails to respond as expected. No one method is productive in all patients, these varied regimens offer us a number of options in dealing with this difficult problem. CC remains the most effective modality of induction in PCOD. CC resistant subjects may be considered for other alternate modes of induction. Patients with abnormal GTT do benefit from diet and insulin therapy.

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