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A STUDY OF INDUCTION OF OVULATION WITH VARIOUS AGENTS

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ABSTRACT

AIM AND OBJECTIVE: Ovulation induction is the method for treating anovulatory infertility. For patients with hypogonadotropic hypogonadism, the treatment involves administration of both FSH and LH, while hCG is injected for follicle rupture. In polycystic ovary syndrome (PCOS), the first treatment choice is clomiphene citrate. Our study aims to assess the efficiency of various Ovulation inducing agents, to evaluate the patients compliance with these drugs, to study their side effects and to identify the percentage of patients who conceive after induction with various agents.

MATERIAL AND METHOD: This prospective observational study was conducted in the Department of Obstetrics and Gynaecology, Smt. S.C.L. General Hospital, Saraspur, Ahmedabad, Gujarat from November 2017 to November 2018 in 85 OPD patients.

RESULT: This study showed that in an anovulatory and otherwise normal patients of infertility, Clomiphene citrate and Letrozole have shown approximately 70% and 80% ovulation rates respectively. Following that pregnancy rates were also gratifying in such patients.

CONCLUSION: In rightly chosen patients, clomiphene citrate and letrozole have given excellent results in terms of ovulation and pregnancy rates.

KEYWORDS :

I. INTRODUCTION

Infertility is defined as failure of a couple to become pregnant after 1 year of regular unprotected intercourse [1]. Ovulatory disorders account for 30 to 40 percent of female infertility [2]. Approximately 85 to 90 percent of healthy young couples conceive within 1 year. Single cycle that will result in pregnancy is called cycle fecundability i.e. 20-25% [3]. Polycystic ovarian disease (PCOD) is one of the common causes for anovulation, characterized by hyperandrogenism, polycystic ovaries, and anovulation [4]. Medicines commonly used to treat infertility and induce ovulation include antiestrogens, gonadotropins, gonadotropin-releasing hormone (GnRH) agonists, GnRH antagonists, and dopamine agonists. The second-line ovulation-inducing agents include gonadotropins such as follicle-stimulating hormone (FSH) and luteinizing hormone (LH) [5].

The ability to induce ovulation and attain pregnancy in anovulatory infertile women remains one of the greatest achievements of reproductive endocrinology [6]. Almost all anovulatory infertile women can be induced to ovulate. Unfortunately, many still do not conceive, for reasons uncertain and vexing.

II. MATERIALS AND METHODS

Study Design: Prospective open label observational study

Study Location: A tertiary care teaching hospital based study done in Department of Obstetrics and Gynaecology, Smt. S.C.L. General Hospital, Saraspur, Ahmedabad, Gujarat

Study Duration: November 2017 to November 2018.

Sample size: 85 patients.

Subjects & selection method: The study population was drawn from OPD cases of primary/secondary infertility in whom ovulation induction was done with various agents and their efficacy was evaluated. Before giving ovulation inducing agents all patient were explained about natural method of conception and fertile period.

Inclusion criteria:

1. History:
- irregular menses
- Oligomenorrhea
- Amenorrhea
- Infertility

2. Clinical Examination:
- Obesity
- Acne, hirsutism, alopecia,
- Acanthosis nigricans

3. USG (TVS):
- Presence of 12 or more cysts of 2 to 9 mm in necklace pattern.
- Ovarian volume equal to or more than 12 cms.
- Bright echogenic stroma.

Exclusion criteria:
- Patients with genetic disorders
- Patients with life threatening diseases.
- Patients with a history of drug or alcohol abuse.

Procedure methodology:

After written informed consent was obtained, a well-designed questionnaire was used to collect the data of the recruited patients retrospectively. The questionnaire included history, general clinical examination including pallor, BMI, systemic examination, Genital examination, per speculum examination, Laboratory investigation [Hb%, CBC, ESR, TFT, S. Prolactin, U-R/M], husband's semen analysis, USG (TVS) and Tubal Patency either by hysterosalpingograghy or laparoscopy.

In this study, ovulation inducing drugs were started from third day of the menses. Clomiphene citrate 50 mg/day was used for 5 days, from 3rd to 8th day of LMP in initial two cycles and increased by 50 mg/day in subsequent cycles as per the response. All patients were followed upto six cycles. Letrozole was given for five days from 3rd to 8h day in dose of 2.5 mg/day and the patients who do not ovulate after 3 cycles, were given 5 mg/day dose for five days. These patients were also followed upto six cycles. The patient was followed sonographically starting from 10th day of menses.

III. RESULT

1. Ovulation Induction With Clomiphene Citrate

Total No. of patients induced with C.C.	Total No. of cycles induced with C.C.	No. of cycles in which ovulation occur	Percentage of ovulation	No. of pregnancy	Pregnancy rate
40	187	131	70%	15	37.5%

Total 40 patients were induced for ovulation with clomiphene citrate having total 187 cycles of ovulation induction, out of which 131 cycles show successful ovulation. This suggests that ovulation induction rate with C.C. is 70% whereas cumulative pregnancy rate is 37.5% amongst which maximum patients conceived within first 3 cycles. According to Speroff — 1181, Clomiphene will successfully induce

ovulation in approximately 80% of properly selected women. This response decreases with age, high body mass index, and any associated hyper-androgenemia. Ovulation rate with clomiphene citrate is 80% in anovulatory infertility. Ovulation rate with Clomiphene citrate is 70-90% while cumulative pregnancy rate is 30%.

A. Ovulation Induction With C.C. 50 Mg

Total No. of cycle	Total No. of cycles which with 50 mg c.c	No. of cycles in induced ovulation c.c. occurs	Percentage of Ovulation	No. of patients conceived	Pregnancy rate
187	127	95	74.8%	9	22.5%

B. Ovulation Induction With C.C. 100 Mg

Total No. of cycle	Total No. of cycles induced with 100 mg C.C.	No. of cycles in which ovulation occurs	Percentage of Ovulation	No. of patients conceived	Pregnancy rate
187	43	25	58.1%	5	12.5%

C. Ovulation Induction With C.C. 150 Mg

Total No. of cycle	Total No. of cycles induced with 150 mg C.C.	No. No of patients conceived	Percentage of ovulation	No. of patients conceived	Pregnancy rate
187	17	11	64.75	1	2.5%

In study with 50 mg of C.C., ovulation rate is 74.8%, while with 100 mg of C.C. ovulation rate is 58.1%, while with 150 mg of C.C., ovulation rate is 64.7%. This suggests that most of the patients ovulate with 50 mg C.C. and also pregnancy rate is higher with C.C. 50 mg. When pregnancy is not achieved within 3-6 clomiphene induced ovulatory cycles, the infertility investigations should be expanded to specifically exclude any other infertility factor not yet evaluated or to change the overall treatment strategy if evaluation is already complete.

2. Ovulation Induction With Letrozole:

No. of patients	No. of cycle	Ovulatory cycles	Percentage of ovulation	No. of Pregnancy	pregnancy rate
25	120	96	80%	7(28%)	28%

In my study, ovulation induction rate with Letrozole is 80%, and pregnancy rate is 28%.

3. Ovulation Induction Study By CC Or Letrozole Based On Age

Age years	No. of patients	No. of cycle	Ovulatory cycles	Percentage of ovulation	No. of pregnancy
20-25	38	188	138	73%	14
26-30	35	171	130	76%	12
31-35	9	37	25	67%	0
35>	3	15	4	26%	3

From my study chart, women belonging to age group 20-30 years have maximum ovulation rate. While age group > 35 years have least ovulatory cycles rate. Also out of 29 patients conceived 26 patients belong to age group 20-30 years. According to Speroff, ovulation induction rate and pregnancy rate decreases with age. Fertility rate is peak in between 20-24 years.

IV. DISCUSSION AND CONCLUSION

Several studies comparing different gonadotropin preparations in different doses have been designed to explore the quantitative response (number of oocytes retrieved) in recent years [7]. Discovery of ovulation inducing drugs like C.C. and Letrozole was an important landmark in the history of treatment of infertility. It has been reported that obesity is associated with abnormal function of the hypothalamic-pituitary-ovarian (HPO) axis that contributes to development of PCOD along with altered hormonal profile, clinically represents as hirsuitism (hyperandrogenism) and oligomenorrhea.[8,9,10]. Fertility problems such as anovulation and pregnancy loss are linked with obesity [11]. In my study as well, it is seen clearly that in an anovulatory and otherwise normal patients of infertility, C.C. and Letrozole has shown approximately 70% and 80% ovulation rates respectively. Following that pregnancy rates were also gratifying in such patients. To conclude, in rightly chosen patients, these drugs have given excellent results. All cases of Clomiphene resistance or failure need a complete endocrinal work-up and a diagnostic laparoscopy to rule out any underlying endocrine disorder or pelvic pathology [12]. Diagnostic laparoscopy should be done to evaluate the pelvis after failure of 3 to 6 cycles of clomiphene. Patients who do not ovulate spontaneously with C.C. / Letrozole may have some other problems also and so they require to be investigated in detail as well as may require addition of certain hormonal preparations for ovulation induction like FSH, HMG or hCG [13]. If patient is ovulating with C.C. in every six cycle but is not conceiving, she is a candidate for IUI. Ovulation induction rate and pregnancy rate is maximum during age 20-30 years. With increasing age both ovulation rate and pregnancy rate decreases progressively [14]. So fertility rate decreases with age.

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