HUMAN MENOPAUSAL GONADOTROPINS IN COMBINATION WITH AROMATASE INHIBITOR OR WITH CLOMIPHENE CITRATE FOR CLOMIPHENE CITRATE RESISTANT CASES

Thesis
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By

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Introduction

Ovulation dysfunction represents one of the most common problems in couples presenting for infertility evaluation ***(Gysler et al., 1982).***

Low ovarian response may be a result of diminished ovarian reserve, which can be due to advanced age, prior ovarian surgery and environmental and genetic factors. Also, other factors such as endometriosis and pelvic infections may impair ovarian function. However, in most patients, low ovarian response remains unexplained ***(Mitwally and Casper, 2001).***

The rationale for controlled ovarian stimulation (COS) in women with unexplained infertility, who by definition have regular ovulatory menstrual cycles, is to enhance the likelihood of pregnancy by increasing the number of oocytes available for fertilization and to overcome a possible subtle defect in ovulatory function not uncovered by conventional testing ***(Fisch et al., 1989).***

Intrauterine insemination, by increasing the density of motile sperm available to these oocytes, might further increase the monthly probability of pregnancy ***(Guzick et al., 1998).***

Gonadotropin therapy is the mainstay of most forms of infertility treatment and adds considerably to the cost of the assisted reproduction therapies ***(Guzick et al., 1999).***

Clomiphene citrate (CC) has been used in the treatment of anovulatory infertility since 1962. By depleting the estrogen receptors, CC acts as an anti-estrogen on the central nervous system ***(Adashi., 1984, Dickey and Holtkamp., 1996, Kousta et al., 1997).***

Recently, sequential CC and gonadotropins (hMG or FSH) therapy has become an increasingly utilized method of COS for patients who fail CC treatment *(**Kemmann and Jones., 1983, Rose., 1992, Dickey et al., 1993b, Lu et al., 1996).***

The value of adding CC during COS is to decrease the FSH dose required for optimum stimulation. However, CC use is associated with lower pregnancy rates because of its peripheral antiestrogenic effects offsetting the FSH dose reduction benefit *(**Mitwally and Casper, 2003a).***

Mitwally and Casper showed that aromatase inhibition is successful in inducing and augmenting ovulation without anti-estrogenic effects ***(Mitwally and Casper, 2000a; b; c; 2001).***

Mitwally and Casper hypothesized that it may be possible to mimic the action of CC, without depletion of estrogen receptors, by administration of aromatase inhibitors (AI) in the early part of the menstrual cycle *(**Mitwally and Casper, 2003a).***

Aromatase inhibitors were related with higher pregnancy rates and lower multiple pregnancy rates than CC and similar pregnancy rates to gonadotropins

(Mitwally and Casper, 2001, 2002, 2003b, 2005).

Aim of the work

To study the use of aromatase inhibitor [anastrozole (Arimidex ®; AstraZeneca)] and human menopausal gonadotropin (hMG) in comparison to clomiphene citrate (CC) and (hMG) in controlled ovarian stimulation (COS) in CC resistant cases (as regards follicles number and size, serum E2 level, endometrial thickness, ovulation rate and cancellation rate).

Patients and methods

Type of study: Randomized prospective study

The patients will be selected from infertility clinic of Ain Shams Maternity Hospital and inpatients of Ain Shams OB/GYN. Hospital.

Method of selection of patients:-

Inclusion criteria:-

1- Age: 25-39 years

2- Have a previously documented dominant follicle or follicles (≤ 12mm mean diameter) while receiving CC at the 100-mg dose but failed to ovulate (CC-resistance).

3- Normal hormonal profile (TSH and PRL).

4- Normal pelvic genital organs, proved by clinical assessment and ultrasonography (except polycystic ovary).

Exclusion criteria: -

1- If patient has pelvic infection or systemic disease.

2- If patient receives hormonal treatment (for ovulation induction) in last three months.

The study will include 40 women with CC-resistance divided into two groups:

1- Group A (first study group) :(20 cases)

They will receive the aromatase inhibitor, anastrozole (Arimidex®; AstraZeneca) 1mg/day orally from day 3 to day 7 of the menstrual cycle, plus human menopausal gonadotrotropin (hMG) (Humegon®; Organon) [75-150 IU/day] i.m. injection starting on day 7 until the day of human chorionic gonadotrophin (hCG) (Choragon®; Ferring).

2- Group B (second study group): (20 cases)

They will receive Clomiphene Citrate (CC) (Clomid®; Aventis) 100 mg/day orally from day 2 to day 6 of the menstrual cycle plus hMG injection [75-150 IU/day] starting on day 6 until the day of hCG.

Each patient will receive one treatment regimen in one treatment cycle only.

The development of the ovarian follicles will be monitored by transvaginal ultrasound measurement of the mean follicular diameter every 3 days during the follicular phase. The patient monitoring will be performed, depending on the menstrual cycle start date. Endometrial thickness will be also monitored by ultrasound.

The dose and duration of hMG treatment will be adjusted during the monitoring of the follicular development according to the patient's response including the number of the growing follicles.

The controlled ovarian stimulation goal is to achieve less than three mature ovarian follicles with a mean diameter of >18 mm on the day of hCG stimulation. HCG will be given as a single i.m. injection of 10 000 IU to trigger ovulation when

there is less than three ovarian follicles with mean dimeter of >18 mm.

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