Introduction

Polycystic ovary syndrome (PCOS) is one of the most common causes of anovulatory infertility, affects 4-7% of women(***Ehrmann, 2005).*** It is by far the most common cause of hyperandrogenic anovulatory infertility and was described more than half a century ago, the underlying cause of this disorder is still uncertain ***(Yen, 1999).***

The classic symptoms of the disease are due to increased ovarian androgen production and chronic anovulation (***Tsilchorozidou et al., 2004).*** There are several clinical and laboratory criteria such as infertility due to chronic anovulation, oligomenorrhea, hirsutism, acne, obesity and acanthosis nigricans ***(Mor et al., 2004; Ciampelli et al., 2005).*** Also, there may be an increase in total testosterone and luteinizing hormone to follicle-stimulating hormone ratio (LH/FSH) ***(Eisenhardt et al., 2006).***

Clomiphene citrate has been the front line therapy for ovulation induction (***Holzer et al., 2006).*** Failure to respond to clomiphene citrate occurs in up to 20% of cases which may require the use of injectable gonadotropines as a second line ***(Mitwally and Casper, 2001).***The drawbacks of this approach include its high cost, the potentially life threatening ovarian hyperstimulation syndrome and the significant risk of high order multiple gestations ***(Holzer et al., 2006).***

Nowadays numerous treatment options in ART are widely used for subfertility. In vitro fertilization (IVF) is the most commonly used. The overall pregnancy rate (PR) per cycle after IVF ranges from 23 to 26%, multiple PR from 22 to 36% and the miscarriage rate from18 to 19% . (***Anonymous1998,Gissler & Tiitinen1998).***

Despite the high PR associated with IVF, there are some disadvantages, to which attention must be paid for couples, heavy medication and close monitoring are physically demanding and time- and money-consuming. Recent research has focused on the successful use of aromatase inhibitors (AIs) as letrozole for ovulation induction ***(Mitwally and Casper, 2006).***

Aromatase is a cytochrome P-450 hemoprotein containing enzyme complex (the product of the CYP19 gene) that catalyzes the rate-limiting step in the production of estrogens which is the conversion of androstenedione and testosterone via three hydroxylation step to estrone and estradiol (***Akhtar et al., 1993).*** Aromatase activity is present in many tissues such as the ovaries, adipose tissue, muscle, liver, breast tissue, and in malignant breast tumours. The main sources of circulating estrogens are the ovaries in premenopausal women and adipose tissue in postmenopausal women ***(Cole and Robinson, 1999).***

There are two types of AIs: Steroidal (type I) and non-steroidal inhibitors (type II) ***(Plourde et al., 1994).*** Type II non-steroidal AIs exert their function through binding to the heme moiety of the cytochrome P450 enzyme ***(Brodie and Njar, 1996).*** Anastrozole and letrozole are third generation selective (non steroidal) AIs, available for clinical use for treatment of postmenopausal breast cancer, they are reversible, competitive AIs, which are highly potent and selective ***(Okman et al., 2003).*** The high affinity of AIs for aromatase is thought to reside in the N-4 nitrogen of the triazole ring that coordinates with the heme iron atom of the aromatase enzyme complex ***(Marty et al., 1997).***

Letrozole is rapidly absorbed from the gastrointestinal tract and excreted by the kidney. The elimination half-life of letrozole is about 2 days ***(Mitwally and Casper, 2001).*** AIs can be applied for ovarian stimulation as its administration early in the follicular phase can induce ovulation by releasing the hypothalamus or pituitary from estrogen negative feedback on GnRH and gonadotropin secretion, leading to an increase in gonadotropin production which would stimulate ovarian follicular development ***(Lidor et al., 2000).***

AIs prevent the Androgen-Estrogen conversion and therefore interfere with the negative feedback at the level of the hypothalamus-pituitary. The increased pituitary gonadotropin output will in turn stimulate the ovaries ***(Mitwally et al., 2005).*** Also, they act locally in the ovary to increase follicular sensitivity to FSH. This may result from accumulation of intraovarian androgens, since conversion of androgen substrate to estrogen is blocked. Recent data support a stimulatory role for androgens in early follicular growth ***(Al-Omari et al., 2001; Metawie, 2001).***

In some studies, letrozole in contrast to C.C increases endometrial thickness by upregulation of estrogen receptors, so it increases pregnancy rate ***(Fatemi et al., 2003; Mitwally et al., 2005).***Therefore, it seems reasonable to consider simpler and inexpensive therapies such as controlled ovarian hyperstimulation (COH) combined with intrauterine insemination (IUI) - for first-line treatment in subfertility.

It has been demonstrated that three cycles of IUI result in the same cumulative pregnancy rate as IVF (***Goverde et al.2000,Philips et al.2000).***

Crosig- nani et al. 1991 reported that The PR achieved after superovulation alone appeared to be inferior to that achieved with superovulation together with IUI .

Aim of the Work

To evaluate the ovulation and pregnancy rates by COH/IUI useing letrozole among CC-resistant PCOS .