INTRODUCTION

Polycystic ovary syndrome (PCOS) is the most common endocrinopathy among women of reproductive age; the prevalence varies between 2.5 and 7.5% ***(Taylor, 2000)***. The prevalence of PCOS may be higher in other ethnic groups ***(Wijeyaratne et al., 2002)***. It is characterized by chronic anovulation and hyperandrogenism ***(Asuncionet al., 2000)***. Consequently, it is the most common cause of anovulatory infertility, oligomenorrhea, amenorrhea, and hirsutism ***(Balen and Michelmore, 2002)***. The recent consensus conference concluded that any two out of the three parameters (polycystic ovary appearance at ultrasound examination, clinical or biochemical hyperandrogenism, and oligo-amenorrhea) with the exclusion of other cause of hyperandrogenism such as adult onset congenital adrenal hyperplasia, hyperprolactinemia and androgen secreting neoplasms was sufficient to diagnose PCOS ***(Rotterdam et al., 2004).***

Clomiphene citrate (CC) has been used in the treatment of anovulatory infertility since 1962. By depleting the estrogen receptors (ERs), CC acts as an anti – estrogen on the central nervous system. This increases the pulse frequency of FSH and LH, giving a moderate gonadotrophin stimulus to the ovary and thus, overcoming ovulatory disturbances and increasing the number of follicles reaching ovulation ***(Kousta et al., 1997).***. Clomiphene induces ovulation at a high rate (70-90%) and, although the pregnancy rate is lower (10 – 40%), in properly selected patients with no other causes of infertility it can be as high as 60% after six cycles ***(Messinis, 2002)***. Peripheral anti – estrogenic effects are frequently cited as a possible explanation for the relatively low pregnancy rates with clomiphene despite the high rate of ovulation

observed. Prolonged endometrial estrogen receptor depletion results in the significant thinning of the endometrium (endometrium thickness = 8mm) that is associated with clomiphene cycles compared with natural cycles and in clomiphene / hMG cycles compared with hMG alone. This endometrial thinning has been observed in 15% - 50% patients on clomiphene ***(Opsahl et al., 1996 and Nakamura et al., 1997).*** .

Mitwally & Casper (2001) hypothesized that it may be possible to mimic the action of CC without depletion of estrogen receptors (ERs) by administration of an aromatase inhibitor in the early part of the menstrual cycle. This would result in release of the hypothalamic / pituitary axis from estrogenic negative feeback, increasing gonadotropin secretion and resulting in stimulation of ovarian follicle development ***(Mitwally & Casper, 2001)***. In several studies, ***Sammour et al. (2001)*** and ***Mitwaily & Casper (2002)*** found that patients responded well to aromatase inhibitors (AI). These studies reported that treatment with aromatase inhibitors in this group of patients is associated with a good ovulation rate, thick endometrium, and a considerable number of pregnancies ***(Sammour et al., 2001 and Mitway & Casper, 2001)***. Aromatase inhibitors have a relatively short half – life (≈48 h) compared with CC, and therefore would be eliminated from the body rapidly. In addition, since no estrogen receptor down - regulation occurs, no adverse effects on estrogen target tissues, as observed in CC – treated cycles, would be expected ***(Sioufi et al., 1997)***. This thesis focuses on comparison between C.C and letrozole as a new low cost oral method of ovulation induction.