SUMMARY AND CONCLUSION

Polycystic ovarian disease (PCOS) is a condition characterized by disruption of the regular process of ovulation. It is associated with hyperandrogoncmia; normal or elevated estrogen level; raised LH secretion with alteration of normal relationship between LH and FSH leading to a raised LH/FSH ratio. The ovaries -are usually although not always enlarged and lobular. On histological examination the ovaries contain atretic follicles; theca cells hyperplasia and generalized increase in stroma. On ultrasound examination, the ovaries are characterized by peripheral distribution of multiple subcapsular cysts (necklace appearance). PCOS presents in many patients with hirsutism and obesity in addition to oligomenorrhea. Approximately 5-10% of women in general population have this syndrome but it is the cause in about 30% of women with infertility.

The medical treatments of anovulation in include anti-estrogens, adrenal suppression, gonadotropin treatment alone or with gonadotropin-releasing hormone (GnRH) analogues (gonadotropin-releasing hormone antagonist). Surgical treatments include ovarian wedge resection, laparoscopic or transvaginal ovarian puncture approaches.

Inhibition of estrogen feedback at the level of hypothalamus-pituitary has been associated with a surge in FSH secretion. This surge in FSH secretion is associated with growth of Graafian follicle and an increase in estrogen secretion. When successful, the Graafian follicle continues to enlarge and eventually ruptures releasing an ovum i.e. ovulation. Approximately 80% of PCOS women treated with clomiphene citrate; ovulate and approximately 20%-40% become pregnant.

Clomiphene citrate is usually given in dose of 100mg daily for 5 days. Clomihene citrate is associated with higher than normal incidence of multiple births.

CC is associated with thin endometrium, poor cervical mucous, reduction of the glandular density and slows down uterine blood flow during the early luteal phase and the implantation stage.

Recently the new aromatase inhibitor, letrozoel has been used for induction of ovulation. Letrozole reversibly inhibits the enzyme responsible for estrogen biosynthesis.

By decreasing the estrogen levels in the body it may release the hypothalamus and/or pituitary from the negative feed back of estrogen on the release of gonadotropins. This will result in an increase in endogenous FSH and LH, which stimulate the development of ovarian follicles.

This mechanism is similar to the proposed mechanism of action of clomiphene citrate. However, Letrozole may have another peripheral mechanism of action directly in the ovaries. Letrozole is eliminated from the body in a few days after last administration (in contrast to CC which may last up to few months). Also, it does not have a direct antiestrogen action by itself as in CC. So there should be no unwanted peripheral antiestrogen effects on the endometrium, and the cervix. Letrozole (***Femara***®, Novartis) is available in 2.5 & 5 mg tablets. It is an approved drug that was developed to inhibit the estrogen production in postmenopausal women with breast cancer. Therefore, it has been tested and tolerated very well when administered continuously for several months. Side effects of letrozole are usually mild in the form of headache, mild GIT upsets, hot flushes and easy fatigue.

Letrozole is associated with thicker endometrium favorable cervical mucous and better uterine blood flow.

The aim of this work was to compare the aromatase inhibitor (Letrozole) with clomiphene citrate (CC) for induction of ovulation and its effect on the endometrium with subsequent pregnance in infertile women due to polycystic ovarian syndrome. The study included 60 infertile women diagnosed as having PCOS. Women were randomized into two groups. Group I included 30 women who were given the aromatase inhibitor, letrozole (Femara, Novartis) orally in a dose of 5mg (two tablet) daily from day 3 to 7 of the menstrual cycle.

Group II included 30 women who were given the CC orally in a dose of 10c mg (2 tablet) daily from day 3 to 7 of the menstrual cycle.

In this study, letrozole at a dose of 5 mg showed more efficacies in ovulation induction than Clomiphene citrate. In group I, the number of follicles 18 mm in diameter or more ranged from 1 to 5 with mean ± SD of 2.2 ± 1.18. in group II, the number of follicles 18mm or more ranged from 1 to 3 with a mean ± SD of 1.5 ± 0.77 mm. (p=0.0001). likewise, in group I, the endometrial thickness (measured by transvaginal ultrasonography) ranged from 6 to 14 with a mean ± SD of 8.86 ± 2.37mm. In group II, the endometrial thickness ranged from 4 to 9 with a mean ± SD of 5.56 ± 1.61mm. (p=0.000).

Consequently, pregnancy was more significantly recorded after using Letrozole than CC, 11 cases (36.7%) in group I and 5 cases (16.7%) in group II, respectively this difference in the number of pregnant cases was highly significant between women of the two studied groups.

Comparison of the side effects of letrozole on CC showed that both drugs are generally tolerated with no significant difference in relative incidence of side effects.