Summary and Conclusion

Anovulation is a common problem which presents in a variety of clinical manifistations, including amenorrhea, irregular menses and hirsutism. One of the serious consequences of chronic anovulation is infertility. Normal ovulation requires coordination of the controlling endocrine system of menstruation at all levels.

Clomiphene citrate, a triphenyl ethylene derivative non steriodal synthetic compound with both estrogenic and anti-estrogenic activity, is the most common agent in clinical use for ovulation induction with minimal side effects of a clinically acceptable frequency. Its application for induction of ovulation has resulted in high success rates of 55 % to 99 %, however, conception rates of patients are only between 25 % and 43 %.

This discrepancy between ovulation and conception rates has been attributed to several clomiphene citrate induced factors, including inadquate maturation of the endometrium. The effects may involve steroid receptor mechanism.

Several studies has been done to study the effect of clomiphene citrate treatment on endometrial estrogen receptor levels with controversal results.

The present study aimed to study the effect of clomiphene citrate on late secretory endometrial estrogen receptors level and its effect on endometrial dating to find out a possible cause for the discrepancy between the incidence of induction of ovulation using it and the occurrance of pregnancy.

Thirty females were the subjects of this study. They were classified into two groups. The first group was included (10) normally ovulating volunteers who were using barrier contraceptive methods or having tubal ligation. The second group was included (20) infertile non ovulating females, who were given 150 mg C.C. at the fifth day of the cycle for 5 days. Monitoring of ovulation was done by basal body temperature records and by ultrasonic folliculometry and was confirmed by the endometrial biopsy.

Premenstrual endometrial biopsy (day 25 - 28) was taken from the uterine fundus for each participant. B - HCG estimation was done for women on C.C. and women who use barrier contraceptive methods to roll out fertilization before taking the biopsy.

Endometrial tissue specimen was placed into formalin and endometrial dating was done according to the criteria of Noyes et al. (1950), also qualitative and quantitative estimation of endometrial estrogen receptor levels was performed according to methods of **(Hsu et al., 1981)** and **(Greene et al., 1986 and Waich et al., 1992)** respectively.

In this study we found that C.C. 150 mg / day has a suppressive effect on the estrogen receptor levels in late secretory phase as there was a significant decrease of estrogen receptors levels among C.C. users in comparison to normally ovulating females. Also we found that the histological biopsy date was significantly inferior to the actual biopsy date in C.C. induced cycles and there was a positive correlation between histological date and endometrial estrogen receptor levels in both groups indicating that decreased level of estrogen receptors with clomid may be the cause of altered endometrial maturation.

Conclusion :

Inspite of occurrance of ovulation with C.C. therapy, the histological endometrial appearance was significantly out-of-phase pointing to luteal phase defect.

The cause of defective endometrial maturation among C.C. users may be due to the suppressive effect of C.C. on endometrial estrogen receptor levels.

Delayed endometrial maturation and defective endometrial estrogen receptors may be one of the causes that explain the discrepancy between ovulation and pregnancy rates with C.C. therapy.

The mechanism (s) through which C.C. altered endometrial estrogen receptors, whether direct or indirect via hormonal milieu changes, is still unclear and can be a subject of futher intersting researches.

Supplementary estrogen in the pre-ovulatory phase and pregesterone in the second half of the menstrual cycle may logically improve the pregnancy rates with C.C. therapy through improving endometrial maturation.