Comparison of Letrozole and Clomiphene citrate on ovulation in achievement of successful Pregnancy

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Abstract

Objective: to compare the efficacy of letrozole and clomiphene citrate in terms of pregnancy achievement and in anovulatory infertile women. Study Design: A randomized controlled trial. Place and Duration: study conducted at the department of obstetrics and gynaecology DG Khan Teaching Hospital. DG Khan from March 2017 to March 2018. Methodology: Two hundred and ten patients were included in this study. The patients were equally divided into two Groups as Group A and Group B by random number method. Study was started after permission from hospital ethical committee. Study variables were age and duration of infertility. SPSS version 24 was used to analyze data. T test and chi square test were applied and p \leq 0.05 was taken as significant. Results: the mean age and duration of infertility of Group B was 25.66±3.39 years and 3.72±2.01 years, respectively. There were 73.3% patients between 18-30 years and 26.7% in 31-40 years of age. There were 79% patients had <5 years of duration of infertility and 21% had >5 years of duration of infertility. The difference was statistically significant (p=0.000) for age. The efficacy of Group A and B was observed as 16.2% and 45.7%, respectively. The difference was statistically significant, (p=0.000). Conclusion: use of Letrozole is safe and more effective for achieving pregnancy in anovulatory infertile women as compared to clomiphene citrate.

Keywords: Letrozole, Clomiphene Citrate, Ovulation, pregnancy rate, Infertility.

Introduction:

Ovulation is a biochemical mechanism which results in maturation process of egg in the hypothalamic pituitary ovarian (HPO) axis¹. Ovulation is orchestrated via neuro endocrine system and terminates in the ovary. Failure of the ovulation process is the main cause of reproductive failure or infertility in the infertile couples². Frequency of this disorder is about 30 to 40% in infertile women. Ovulation induction therapy like fertility medication should target the HPO axis for successful outcome³.

Letrozole and clomiphene citrate are two main drugs commonly used drug in ovulation induction therapy⁴. Many injectible medicines are also available like menopuror, follistim, repronex and gonil f which can be used intrauterine insemination. This process also named as in vitro fertilization⁵. Used of oral fertility drugs are most common and successful ovarian disfunction therapy. Ovarian stimulation can be increased by endogenous gonadotropin through antagonising the negative response of estrogen hormone at the level of hypothalamus with clomiphene citrate which is a selective estrogen receptor modulator⁶,⁷.

Clomiphene also has some disadvantages like high multiple pregnancy rate, overall poor efficacy and some adverse effects like hot flashes and mood swings⁸. Another useful drug is letrozole which converts the endrogens by activating the arometaseenzyme and blocks the estrogen senses, letrozole directly affect the pituitary gland in the hypothalamic area and interfere with ovarian function and enhance the rate of pregnancy⁹. Letrozole have advantages of less side effects, low multiple pregnancy rate and mood swings with fewer vasomotor effect and early clearance¹⁰,¹¹.

In this study we aim to compare the efficacy of clomiphene and letrozole for ovulation and induction of pregnancy in anovulatory infertile women.

Methodology:

This is a randomized controlled trial was conducted at the department of obstetrics and gynaecology DG Khan Teaching Hospital. DG Khan from March 2017 to March 2018. All anovulatory infertile women having age limit 18 to 40 years were included in the study and females with previous pelvic surgery, hyperprolactenemia, hypothyroidism (on the basis of history and medical record) and patients allergic to study drugs were excluded from the study. Non probability consecutive sampling technique was used. Patients having sexual intercourse
more than one year without any contraceptive pills by lateral normal tubal patency, normal pelvic ultrasonography and healthy male factor were labeled as anovulatory infertility.

Efficacy was assessed by measuring the beta HCG after fifth day of missed menstrual cycle if beta HCG levels is more than or equal to 5 mIU/ml after fifth day was labelled as yes otherwise no. Patients were divided into two equal groups (A and B) by random number method. Patients in group A were given clomiphene citrate by oral once a day for five days up to five menstrual cycles. Patients in group B were given letrozole 2.5mg once a day by oral up to five menstrual cycles. All patients were evaluated to see the occurrence of pregnancy after complete of every cycle by measuring the beta HCG cycle at fifth day and efficacy was noted.

All the recorded data was entered in the computer software SPSS version 23. Mean and standard deviation were calculated for numerical data like age. Frequency and percentages were calculated for qualitative data like effectiveness. Student t test and chi square test were applied to see the association among variables. P value less than or equal to 0.05 was considered as significant.

Results:

Two hundred and ten patients were included in this study. The patients were equally divided into two Groups as Group A=105 and Group B=105 by random number method. The mean age and duration of infertility of Group A was 28.25±4.77 years and 4.01±1.87 years, respectively. There were n=51 (48.6%) patients between 18-30 years and n=54 (51.4%) in 31-40 years of age. There were n=88 (83.8%) patients had <5 years of duration of infertility and n=17 (16.2%) had >5 years of duration of infertility. While, the mean age and duration of infertility of Group B was 25.66±3.39 years and 3.72±2.01 years, respectively. There were n=77 (73.3%) patients between 18-30 years and n=28 (26.7%) in 31-40 years of age. There were n=83 (79%) patients had <5 years of duration of infertility and n=22 (21%) had >5 years of duration of infertility. The difference was statistically significant (p=0.000) for age.

The efficacy of Group A and B was observed as n=17 (16.2%) and n=48 (45.7%), respectively. The difference was statistically significant, (p=0.000). (Table. II).

Discussion:

In our study we observed that letrozole is more efficacious and better in terms of achievement of pregnancy in infertile females who were selected for treatment of an ovulation. Our result shows effectiveness of clomiphene
citrate 16.96% and letrozole group shows 33.04% with p value of 0.005 which is a significant value. Another similar study was conducted by Ibrahim et al. in 2012 and reported 23.07% pregnancy achievement with the use of letrozole and 10.68% with the use of clomiphene citrate. This study was comparable with our study having almost all variables similar to our study.

Another similar study was conducted by Seyedoshoadaei et al. and shows 73.4% ovulation with use of clomiphene citrate and 78% with the use of tamoxifen and letrozole shows efficacy 74%. Rate of pregnancy achievement was 64%, 40%, and 50% in group A, B and C respectively. This study is also similar to our study which shows a better efficacy of clomiphene citrate in achievement of ovulation in infertile women. According to this study an ovulation is a main contributing factor in infertility of female gender.

Another study was conducted by Atay et al. in 2006 and reported that pregnancy achievement is much higher with use of letrozole when compared with clomiphene citrate. Results of this study were statistically significant. Another similar study was conducted by Bayar et al. and reported that there was not significant difference in pregnancy rate in both groups when letrozole and clomiphene citrate were compared in terms of ovulation and pregnancy achievement goals. Both these studies were similar to our study and can be compared.

A study was conducted by Kar et al. on successful ovulation rate of letrozole and clomiphene and reported that clomiphene citrate gives 60.78% ovulation rate and letrozole shows 73.08% ovulation rate but these values were not statistically significant as p value is 0.39. Another study was conducted by Roy et al. on comparison of clomiphene citrate and letrozole for achievement of pregnancy and observed effectiveness of letrozole is such higher 43.8% and compared with clomiphene citrate 26.4%. Both these studies were identical to our study and can be compared with our study.

Hussain et al. also conducted a study in 2013 and compared letrozole and clomiphene citrate and shows 25.3% pregnancy rate in letrozole group and 16% in clomiphene citrate. Here is another study conducted by Parihar M et al. and reported 11.9% pregnancy rate in letrozole group and 8.8% in clomiphene citrate.

Another similar study was conducted by Naeem A et al. and reported that Letrozole is more effective in terms of pregnancy achievement when compared with Clomiphene citrate. Anovulatory is a rising issue in the medical history and should be considered with greater effort and considerations. Results of this study are also similar to our study and can be compared with results.

Conclusion: our results reveal that use of Letrozole is safe and more effective for achieving pregnancy in anovulatory infertile women as compared to clomiphene citrate.

References