
ORIGINAL ARTICLE

Comparison of Clomiphene Citrate and Letrozole in Ovulation Induction and Pregnancy Rate in Polycystic Ovarian Disease

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ABSTRACT

Objectives: To compare the efficacy of letrozole versus clomiphene citrate in ovulation induction and pregnancy rate in patients with polycystic ovarian disease.

Design: Randomized controlled trial.

Place and duration of study: Moula Bakhsh Teaching Hospital And Diagnostic Centre Sargodha from January 2013 to June 2013.

Subject and Method: 200 patients with polycystic ovarian disease selected by non probability purposive sampling were included. Efficacy was determined in terms of ovulation induction when follicular size of more than or equal to 17mm is achieved on transvaginal ultrasound and pregnancy rate is checked by urine for pregnancy test in those patients with successful ovulation induction in the same cycle.

Result: 63.6% patients had successful ovulation induction with letrozole and 29.4% patients having clomiphene citrate showed successful ovulation induction. The pregnancy rate in letrozole group was 23.6% and in clomiphene citrate group it was 9.3%.

Conclusion: Letrozole is superior to clomiphene citrate in achieving successful ovulation induction and subsequent pregnancy rate in patients with polycystic ovarian disease.

Keywords: Polycystic ovarian disease, Ovulation induction, Letrozole, Clomiphene citrate

INTRODUCTION

Anovulation is an important cause of infertility and accounts for 20- 25%¹ of cases and polycystic ovarian disease is one cause of anovulation contributing to infertility significantly. Polycystic ovarian disease is the most common endocrinopathy affecting women of reproductive age². According to Rotterdam Criteria (2003 ESHRE/ASRM Consensus), whereby patients diagnosed with PCOS require presence of two out of three criteria i.e oligomenorrhea and/or anovulation, clinical or biochemical signs of hyperandrogenism, and /or polycystic ovaries on ultrasound. The estimates of prevalence of polycystic ovarian disease in general population are 20-33%. To date, clomiphene citrate has been the first line of drug for ovulation induction but 20-25% of women with PCOS are resistant and fail to ovulate^{4 5} and of 75% who ovulate only 20-40% of them have successful pregnancy⁵. Aromatase inhibitors are safe and effective alternative in this indication. Letrozole, a third generation aromatase inhibitor has the potential to be used for ovulation induction. The use of letrozole has been known to induce ovulation in 75-80% women⁵. It has less chances of miscarriage⁶ and has favourable response on endometrium and cervical mucus as

compared to clomiphene citrate contributing to a higher pregnancy rate^{7 8}.

The aim of study was to compare the efficacy of letrozole versus clomiphene citrate for ovulation induction and pregnancy rate in patients with polycystic ovarian disease.

PATIENTS AND METHODS

The present study was conducted in Moula Bakhsh Teaching Hospital And Diagnostic Centre Sargodha from January 2013 to June 2013. A total number of 200 patients were included in the study. Inclusion criteria were patients of age 20-35 year diagnosed as polycystic ovarian disease according to Rotterdam criteria having either primary and secondary infertility. Exclusion criteria were male factor infertility, tubal factor, medical problems e.g thyroid disorder, renal disease, hyperprolactinemia, liver disease, or having other causes of anovulatory infertility. The patients with even numbers were given 100mg clomiphene citrate and with odd numbers were given 5mg letrozole from day 2 of menstrual cycle for 5 days followed by follicular tracking on day 12 by using transvaginal ultrasound to check successful ovulation induction. Ovulation was diagnosed when dominant size follicle size more than or equal to 17 mm achieved followed by rupture of follicle

and subsequent pregnancy rate was checked in both groups with urine for pregnancy test in those who missed periods in the same cycle. Data was analyzed on SPSS version 14.

RESULTS

Table I: It shows baseline demographic and clinical characteristics of polycystic ovarian syndrome patients of both letrozole and clomiphene citrate group.

Table II: It shows that among 200 patients the successful ovulation induction with clomiphene citrate is 29.4% and with letrozole the number of patients with successful ovulation induction was 63.6% and the patients in clomiphene citrate group who had successful pregnancy rate is 9.3% and in letrozole group 23.6%.

Table I: Baseline demographic and clinical characteristics of PCOS patients for each group.

Feature	Letrozole (n =100)	Clomiphene Citrate (n=100)
Age <30year	69	62
>30year	31	38
Type of infertility		
Primary	53	44
Secondary	47	56
Duration of infertility		
<5year	66	51
>5year	34	49
Menstrual cycle		
Regular	35	41
Irregular	65	59

Table II:

Outcome parameter	Letrozole (n=100)	Clomiphene Citrate (n=100)
Ovulation rate %	63.6	29.4
Pregnancy rate %	23.6	9.3

DISCUSSION

Polycystic ovarian disease has always been a challenging problem for the gynaecologists. It has become a major public health concern causing significant distress to those directly involved, as well as friends and family. In this study women of reproductive age group 20-35years with polycystic

ovarian disease presenting in gynaecology OPD with both primary and secondary infertility were included in the study. The baseline demographic and clinical characteristics of polycystic ovarian syndrome patients for both letrozole and clomiphene citrate group had no effect on the outcome parameters and are described in the table I. Among 200 patients 63.6% patients had successful ovulation induction with letrozole as compared to 29.4% in clomiphene citrate group. This result is same as shown by the study conducted by Kamath MS et al and Kamath MS and George K^{9 10}. Similar results were obtained by Bayar U and Badaway A in their studies^{12 13}. The patients with successful pregnancy were 23.6% in letrozole group as compared to 9.3% in clomiphene citrate group. The studies conducted by Kamath MS and George K, Kamath MS et al, Begum MR and Kar S^{9 10 11 14} showed comparable results regarding pregnancy rates in letrozole and clomiphene citrate group. Previous studies have shown that letrozole is generally safe for use in pregnancy¹⁵. Known complications of clomiphene citrate use include multifetal pregnancy and miscarriage. In this study, no subject had multiple pregnancy or pregnancy loss.

CONCLUSION

Anovulation is an important cause of infertility in polycystic ovarian disease and letrozole which is a newer ovulation induction agent is superior to clomiphene citrate in achieving successful ovulation induction and pregnancy rate in polycystic ovarian disease.

REFERENCES

1. Vogatzi M, Shaw RW. Ovulation Induction. In RW Shaw, D Leuslay and A Monga editors. Gynaecology. London: Churchill Livingstone Elsevier; 2011. 231-50
2. Hendawy SF, Samaha HE. Letrozole versus clomiphene citrate for induction of ovulation in patients with polycystic ovarian syndrome undergoing intrauterine insemination. Clinical Medicine Insight: Reproductive Health 2011;5: 11-6
3. Balen A. Polycystic ovary syndrome. In RW Shaw, D Leuslay and A Monga editors. Gynaecology. London: Churchill Livingstone Elsevier; 2011. P.251
4. Akbari S, Roozbahani MA, Roozbahani FA. Comparing of letrozole versus clomiphene citrate combined with gonadotropins in

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- intrauterine insemination cycles. Iranian J Reprod Med 2012;10:29-32
5. Parihar M, Gada D, Paul PG. Letrozole versus clomiphene citrate in patients with anovulatory infertility. South Asian Federation of Obstet Gynaecol 2009;1:19-23
 6. Ghazizadeh S et al. Comparing the effects of clomiphene-HMG and letrozole-HMG on ovulation induction in infertile women. J Reprod Infertil 2009;10:109-14
 7. Pritts EA. Letrozole for ovulation induction and controlled ovarian hyperstimulation. Current Opinion Obstet Gynaecol 2010;22:1-5
 8. Atay V et al. Comparison of letrozole and clomiphene citrate in polycystic ovaries undergoing ovarian hyperstimulation. J Int Med Res 2006;34:73-6
 9. Kamath MS et al. Aromatase inhibitors in women with clomiphene citrate resistance:a randomized,double-blind placebo-controlled trial. Fertil Steril 2010;94:2857-9
 10. Kamath MS, George K. Letrozole or clomiphene citrate as first line for anovulatory infertility:a debate. Reprod Biol Endocrinol 2011;9:86
 11. Begum MR et al. Comparison of efficacy of aromatase inhibitor and clomiphene citrate in polycystic ovarian syndrome. Fertil Steril 2009;92:853-57
 12. Bayar U et al. Use of an aromatase inhibitor in patients with polycystic ovarian syndrome:a prospective randomized controlled trial. Fertil Steril 2006;80:1447-51
 13. Badaway A et al. Clomiphene citrate or letrozole in women with polycystic ovarian syndrome:a prospective randomized controlled trial. Fertil Steril 2009;92:849-52
 14. Kar S. Clomiphene citrate or letrozole as first line ovulation induction drug in infertile PCOS women:a prospective randomized controlled trial. J human reprod sci 2012;5:262-5
 15. Elizur SE, Tulandi T. Drugs in infertility and fetal safety. Fertil Steril 2008;89:1595-1602