Management of Anovulatory Infertility due to Polycystic Ovarian Syndrome Comparing Clomiphene Citrate and Letrozole

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Background & Purpose

Polycystic Ovarian Syndrome (PCOS) is the leading cause of infertility caused by anovulation. Women who have been diagnosed make up to 95% of women presenting for treatment for anovulation.[1]

Clomiphene citrate (Clomid) has historically been first line treatment for anovulatory PCOS. However, there has been recent new development in medications such as letrozole (Femara) in use for anovulatory infertility.[2]

PICOT

In women with polycystic ovarian syndrome (PCOS), what is the effect of letrozole (Femara) on PCOS related infertility compared with clomiphene citrate(Clomid)?

Design & Methods

Keywords: *Clomiphene citrate, clomid, letrozole, infertility, PCOS, and polycystic ovarian syndrome*
Inclusion: Published in last 5 years, in English, full text available, patient with PCOS as diagnosed with Rotterdam criteria, unsuccessful in conceiving for at least 12 months
Exclusion: Other forms of infertility, articles not in English, articles using other treatment options, no full text available

Summary of Evidence

Database	Yielded	Included
Google Scholar	2400	2
Pubmed	29	1
Cochrane Library	25	2
Total	2454	5

Results

Clomiphene Primary Endpoint

	Ovulation	Endometrial Thickness
Najafi et al.[3]		8.3
Zaman et al.[4]	56%	
Ay et al.[5]	55%	
Kareem et al.[6]	81.97%	7.03
Chopra et al.[7]	88%	7.01

Letrozole Primary Endpoint

	Ovulation	Endometrial Thickness
Najafi et al.[3]		11.8
Zaman et al.[4]	81%	
Ay et al.[5]	55.60%	
Kareem et al.[6]	75.63%	7.21
Chopra et al.[7]	92%	9.31

Clomiphene Secondary Endpoints

	Pregnancy Rate	Live Births	Mono/Multifollciles
Najafi et al.[3]	24.50%		
Zaman et al.[4]	9%		
Ay et al.[5]	20%	75%	
Kareem et al.[6]	13.33%		51.16%/48.84%
Chopra et al.[7]	23%		61.7%/35.3%

Letrozole Secondary Endpoints

	Pregnancy Rate	Live Births	Mono/Multifollicles
Najafi et al.[3]	45%		
Zaman et al.[4]	23%		
Ay et al. [5]	33%	66.70%	
Kareem et al.[6]	21.82%		69.57%/30.43%
Chopra et al.[7]	37%		88.6%/11.4%

Letrozole was more likely to result in ovulation .

Pregnancy rates were higher in patients taking letrozole than those taking clomiphene. Multifollicles were more likely to be present in patients taking clomiphene citrate.

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Best Practice

There is a higher probability of ovulation when taking letrozole rather than clomiphene citrate. Higher rates of pregnancy were also seen with letrozole. There is a lower chance of multiple gestations with letrozole as well.

Clomiphene citrate is still an effective medication for anovulatory infertility, but letrozole will have higher probability of ovulation and conception.

When prescribing, providers should consider patient goals including cost of medication, side effects, or if patient desires multiples.

Limitations/Further study

Studies often did not specify for how many cycles they administered treatments or were only treated for one menstrual cycle.
Consider larger populations and study sizes for future trials.

Conclusion

Use of letrozole is more probable to result in ovulation than clomiphene citrate, although clomiphene is not unsuccessful at production of ovulation. Treatment for anovulatory PCOS should be patient goal centered as well as cost and risk should be factored into which medication is prescribed.

References

1. Dennett CC, Simon J. The Role of Polycystic Ovary Syndrome in Reproductive and Metabolic Health: Overview and Approaches for Treatment. *Diabetes Spectr Publ Am Diabetes Assoc*. 2015;28(2):116-120. doi:10.2337/diaspect.28.2.116
2. Melo AS, Ferriani RA, Navarro PA. Treatment of infertility in women with polycystic ovary syndrome: approach to clinical practice. *Clinics*. 2015;70(11):765-769. doi:10.6061/clinics/2015(11)09
3. Najafi P, Pasban-Noghabi S, Afzali N, Mohammadzadeh S. Comparing the Effect of Clomiphene Citrate and Letrozol on Ovulation Induction in Infertile Women with Polycystic Ovary Syndrome. *J Pak Med Assoc*. 2019;70:1. doi:10.5455/JPMA.267607
4. Zaman S, Arshad H, Hafeez S, Rasul S, Khan A, Khan M. Ovulation Induction in Polycystic Ovarian Syndrome (PCO) Related Subfertility: A Comparison of Clomiphene Citrate and Letrozole.
5. Ay SS, Birge Ö, Bakır MS, Yumru AE. Efficacy of letrozole versus clomiphene citrate for infertile women with polycystic ovary syndrome. *Int J Reprod Contracept Obstet Gynecol*. 2021;10(8):2944. doi:10.18203/2320-1770.ijrcog20212938
6. Kareem SM, Kazom SN. Clomiphene citrate or Letrozole as a first line treatment of anovulatory sub fertile polycystic ovarian syndrome women. Published online 2019.
7. Chopra DrS. A randomized clinical study to compare the outcome of two different ovulation induction regimes among PCOS patients. *Int J Clin Obstet Gynaecol*. 2021;5(1):218-221. doi:10.33545/gynae.2021.v5.i1d.819