

Improving Fertility in Patients with Polycystic Ovary Syndrome: Metformin versus Clomiphene

Shannon Shipman, PA-S

Background

Infertility due to polycystic ovarian syndrome (PCOS) is an area of medicine that is commonly overlooked and requires further research because the diagnosis of PCOS is hard to make, and often made too late.¹ The pathology of PCOS is complex and requires in-depth research and education to aid providers in making correct diagnoses and prevent delayed treatment time for women.

The textbook symptoms to be aware of include polycystic ovaries evidenced on ultrasound, anovulation, and hyperandrogenism. Hyperandrogenism can be seen as hirsutism, acne, alopecia, and acanthosis nigricans.¹

Purpose

There are many comorbidities that women with PCOS may have that can “blind” a provider from making an accurate diagnosis of PCOS. Due to infertility associated with PCOS, many women require the help of medications to improve their chances of becoming pregnant. Some of those medications include metformin and clomiphene citrate.² This research aimed to compare efficacy rates of metformin as a monotherapy versus clomiphene, an ovulation inducer, in increasing pregnancy rates among women with PCOS.

PICOT Question

In patients with polycystic ovary syndrome (PCOS), is Metformin as effective in increasing chances of pregnancy as a monotherapy compared to clomiphene (Clomid)?

Design & Methods

Keywords: : polycystic ovary syndrome, metformin, clomiphene, ovulation, pregnancy, infertility, and live birth rate.

Inclusion: Studies that focused on women with PCOS, comparison of Metformin and Clomiphene, and evaluated birth rate or pregnancy rate.

Exclusion: Studies that involved women without PCOS, and the use of medication for purposes other than infertility treatment.

Table 1: Summary of Evidence Search

Database	Yielded	Reviewed	Included in Analysis
MedLine	721	32	2
Cochrane Library	893	46	1
ScienceDirect	785	29	1
Google Scholar	825	60	1
Total:	3,224	167	5

Table 2: Synthesis of Evidence

Type of Study	Total	Sources
Meta-Analysis	2	Sharpe 2019, Magzoub 2022
Randomized Control Trial	2	Perveen 2018, Agrawal 2019
Prospective Cross-Sectional	1	Airao 2018

Results

Live birth rate was measured to be 22% when given metformin monotherapy compared to 34% with combination therapy of metformin and clomiphene (or any combination therapy).²⁻⁵

Clomiphene given as monotherapy resulted in an increased live birth rate of 81.2% compared to patients who were given metformin as monotherapy at 71% (RR = 0.84 [0.56, 1.25], 95% CI).³

Clomiphene given as monotherapy resulted in a pregnancy rate of only 8%. When patients were given clomiphene plus metformin, the pregnancy rate increased to 24%.⁴

Patients who received metformin alone experienced an increased miscarriage rate compared to those who received clomiphene alone (pooled RR= 2.67 [1.32, 5.39], 95% CI).³

One study contradicted results from the others. It showed that patients who received clomiphene monotherapy resulted in a conception rate of 72.2% while those given clomiphene plus metformin had a conception rate of only 50%.⁶

Best Practice

Discussion

Any treatment as monotherapy was proven to be more beneficial than no treatment at all. The best option for patients seemed to be combination therapy of metformin plus clomiphene. Not only did this increase live birth rates, but it also improved ovulation rates, and clinical pregnancy rates.

Limitations

- Small Sample Size
- Exclusion of women with BMI >30
- Exclusion of women with diabetes

These limitations need to be taken into consideration since many women with PCOS also are obese and have co-morbid diabetes. Those factors alone can cause their own fertility issues, but coupled with PCOS, creates even more of a challenge that needs to be addressed.

Further Study

Women with PCOS and other co-morbid conditions need to be a focus for future research, especially as it relates to fertility and pregnancy complications. Further education for healthcare providers might be needed to help them understand how patients may present to accurately make the diagnosis and treat them appropriately.

Conclusion

Since metformin helps control many of the symptoms and co-morbid conditions associated with PCOS, it was hypothesized that it alone would improve fertility. Research has proven that metformin alone is not as effective at increasing chances of pregnancy compared to any other combination of medications. However, metformin as monotherapy is still a better option than having no treatment at all if a patient is trying to become pregnant.

Metformin plus clomiphene would give a patient the best chance at pregnancy.

References

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