Polycystic ovarian syndrome in patients at a public fertility clinic – The role of metformin and letrozole vs letrozole monotherapy in live birth rates

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Introduction

Infertility affects 1 in 6 Australian couples (1). Obesity affects ovulation, response to fertility treatment, pregnancy rates and outcomes (2). PCOS is a leading cause of infertility, accounting for as many as 90-95% of women who attend infertility clinics with anovulation (3). Many women with PCOS are obese, which confounds their infertility. Letrozole is now first line management for ovulation induction in anovulatory patients. Despite the prevalence of PCOS in anovulatory infertility, the role of combination therapy of metformin and letrozole for ovulation induction is not well studied, with a literature review revealing a single RCT of 100 women in Pakistan supporting metformin in addition to letrozole for ovulation induction (4). At our regional public infertility clinic, we examined the role of PCOS diagnosis and metformin with letrozole vs letrozole alone on rates of live birth for women presenting to the service.

Objectives

To examine the role of metformin with letrozole against letrozole monotherapy in achieving live birth rates in women with PCOS. Secondary objectives included identifying the obesity rates in the infertile PCOS population, and explore the importance of PCOS diagnosis in availing appropriate care in a sub fertile population.

Methodology

We retrospectively examine the records of patients presenting to a single centre regional public infertility clinic over a 5 year time period. We identified 346 patients who presented and examined their records to identify those who were diagnosed with PCOS, and the implications of that diagnosis. Obesity rates were also examined in the identified population. Treatment with letrozole monotherapy and letrozole and metformin were compared to pregnancy and live birth outcomes.

Results

We found a higher live birth rate (0.27) for women diagnosed with PCOS who were treated with metformin and letrozole compared to letrozole alone (0.25), CI 95% CI (0.22 - 0.19), p value 0.87, which did not reach statistical significance at the 5% level. We postulate this is due to small sample size.
Examining BMI, 47% of records were excluded due to missing BMI data. Given the confounding role obesity has in both PCOS and infertility, lack of documented BMI is a significant weakness in record keeping. BMI was categorised according to the WHO classification system. BMI rates were as follows:

Underweight (BMI < 18.5)	1.5%
Normal weight (BMI 18.5-24.9)	23%
Pre-Obesity (BMI 25-29.9)	18%
Obese (BMI > 30)	58%

Conclusion

We believe that metformin in addition to letrozole improves live birth rates in anovulatory PCOS patients, when compared to letrozole monotherapy. Our data did not have significant weight to support this conclusion due to low population numbers. Further studies are needed to evaluate the role of metformin in combination with letrozole on the live birth rate of women with PCOS.
The rate of obesity in a sub-fertile PCOS population is extremely high. Diet and lifestyle interventions should be the cornerstone of fertility treatment for these individuals. It is both cost effective and carries a multitude of benefits (3, 5) .
Metformin and letrozole may well be superior to letrozole alone in improving pregnancy and live birth rates in anovulatory PCOS patients

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