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Comparison of the Effects of Cyproterone Compound-Spironolactone, Metformin, and Pioglitazone on Serum Levels of High Sensitivity C-Reactive Protein and Complement System in Polycystic Ovarian Syndrome: A Randomized Double-Blind Clinical Trial

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ABSTRACT

Introduction: Polycystic ovarian syndrome (PCOS) is one of the most common hormonal disorders affecting women of reproductive age. Numerous studies have suggested the involvement of inflammation in the pathogenesis of PCOS. As a result, drugs with anti-inflammatory effects may offer therapeutic benefits for this condition. The standard medications used in treating PCOS include cyproterone compound (cyproterone acetate + ethinyl estradiol) combined with spironolactone, metformin, and pioglitazone. This study aimed to compare the effects of these drugs on the serum levels of inflammatory markers, including hs-CRP, C3, and C4, in women with PCOS.

Materials and methods

Ninety women with PCOS were randomly assigned to three treatment groups for 90 days as follows: Group CC-SP received cyproterone compound (cyproterone acetate 2 mg + ethinyl estradiol 35 µg) daily, along with 100 mg/day spironolactone; Group M received metformin (1500 mg/day); and Group P received pioglitazone (30 mg/day). Serum levels of hs-CRP, C3, and C4 were measured before and after treatment.

Comparisons of changes in variables between groups were performed using the ANOVA test. Additionally, covariance (ANCOVA) analysis was used to examine differences between groups, adjusting for confounding variables. Probability values of ≤ 0.05 were considered statistically significant.

Results

The C3, C4, and hs-CRP levels were increased in the CC-SP group while significantly decreased in the pioglitazone group ($p<0.05$). These changes were not statistically significant in the metformin group.

Conclusions

Pioglitazone reduces the serum levels of inflammatory markers and may be effectively combined with cyproterone and spironolactone in the treatment of PCOS.

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Introduction

Polycystic ovarian syndrome (PCOS) is the most common endocrine disorder among women of reproductive age, with a global prevalence of 5-10%. It is associated with a wide range of adverse outcomes, including infertility, gestational diabetes, diabetes mellitus, hypertension, dyslipidemia, cardiovascular disorders, and endometrial cancer (1). The etiology and pathogenesis of PCOS are multifactorial, with genetic and environmental factors contributing to

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design further research to explore the mechanisms of inflammation in the pathogenesis of PCOS to develop new drugs with combined anti-androgenic and anti-inflammatory properties.

Conclusion

This randomized clinical trial demonstrated that pioglitazone benefits the serum levels of inflammatory markers C3, C4, and hs-CRP. It can be used as an adjunct to other drugs, such as the combination of cyproterone and spironolactone, in the treatment of PCOS patients.

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Statement of Ethics

The study protocol complied with the Declaration of Helsinki and was approved by the Local Ethics Committee of Shiraz University of Medical Sciences (Reference No.: CT-P-9145-4025). The study was registered in the Clinical Trials Registry (ClinicalTrials.gov ID: NCT02689843). The patients were informed about the research protocol and the medications' effects and side effects. Each patient gave a written informed consent.

Conflict of Interest

The authors have no conflicts of interest to declare.

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