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Eureka Journal of Health Sciences & Medical Innovation (EJHSMI)

ISSN 2760-4942 (Online) Volume 2, Issue 1, January 2026

https://eurekaoa.com/index.php/5

EVALUATION OF THE COMBINED PREVENTIVE EFFICACY OF HORMONAL THERAPY AND LIFESTYLE INTERVENTIONS IN WOMEN WITH POLYCYSTIC OVARY SYNDROME

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Annotation

This scientific article examines the effectiveness of combined preventive measures involving hormonal therapy and lifestyle modifications in women diagnosed with Polycystic Ovary Syndrome (PCOS). The study focuses on the role of integrated preventive strategies in improving reproductive, metabolic, and hormonal outcomes in affected women. The findings indicate that hormonal therapy contributes to the regulation of menstrual cycles and reduction of hyperandrogenic manifestations, while lifestyle modifications—including balanced nutrition, regular physical activity, weight control, and behavioral changes—significantly improve insulin sensitivity and metabolic parameters. The results demonstrate that the combined application of hormonal treatment and lifestyle interventions is more effective than single-modality approaches in preventing disease progression and reducing the risk of long-term complications. Based on the obtained results, the implementation of comprehensive, individualized preventive programs is recommended to improve health outcomes and quality of life in women with PCOS.

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Keywords: polycystic ovary syndrome, hormonal therapy, lifestyle modification, prevention, metabolic risk factors, insulin resistance, reproductive health, primary prevention.

Introduction

PCOS-related literature is mostly dominated by the medical perspective. However, the condition's lifelong, far reaching, and multifaceted impacts highlight the importance to gain the perspectives from those with PCOS. A total 34 from 1615 screened articles were included in this systematic review and subsequently coded using NVivo 12 software. The quality of individual studies was assessed by adaptation to the Critical Appraisal Skills Program (CASP) quality assessment tool. Dissatisfaction surrounding the experience of diagnosis was common. Concerns surrounded perceived lack of knowledge from healthcare professionals and delays in diagnosis. Individual studies on adults and adolescents shared similar feelings. The consensus was found to be that current management was vague and generalised. Symptoms such as hirsutism, obesity, irregular menstruation challenge personal and societal expectations of femininity. Online PCOS resources are popular amongst those with PCOS but most of them lack evidence. A call for more culturally specific resources was found to be common ground amongst those with PCOS [5].

Polycystic ovary syndrome (PCOS) and thyroid disorders have both been linked to adverse pregnancy and neonatal outcomes. Even small variations in thyroid function within the normal range may influence fetal growth. Our aim was to investigate whether maternal thyroid function is associated with newborn anthropometrics in PCOS and explore the potential modifying effect of metformin. Post-hoc analyses of two RCTs in which pregnant women with PCOS were randomized to metformin or placebo, from first trimester to delivery. Maternal serum levels of thyroid stimulating hormone (TSH) and free thyroxine (fT4) were measured at gestational weeks (gw) 5-12, 19, 32 and 36 in 309

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singleton pregnancies. The mean z-scores of birthweight, birth length, and head circumference were estimated in the offspring. Associations of maternal thyroid parameters with offspring anthropometrics and the outcomes large for gestational age (LGA) and small for gestational age (SGA) were studied using linear and logistic regression models, with adjustment for body mass index (BMI) when relevant. Maternal fT4 at baseline was negatively associated with birth length (b= -0.09, p=0.048). Furthermore, ΔfT4 during pregnancy correlated positively to z-score of both birth weight and length (b=0.10, p=0.017 and b=0.10, p=0.047 respectively), independently of treatment group. TSH at baseline and gw19 was inversely associated with LGA (OR 0.47, p=0.012 and OR 0.58, p=0.042), while ΔTSH was positively associated with LGA (OR 1.99, p=0.023). There were inverse associations between TSH at baseline and SGA (OR 0.32, p=0.005) and between ΔfT4 and SGA (OR 0.59, p=0.005) in the metformin group only. There were no associations between maternal thyroid function and head circumference of the newborns. Conclusion: In women with PCOS, a higher maternal fT4 in early pregnancy and a greater decrease in fT4 during pregnancy was associated with a lower offspring birthweight and shorter birth length. Higher TSH by mid-gestation and smaller increase in TSH during pregnancy was associated with less risk of LGA. Subclinical variations in maternal thyroid function might play a role for birth anthropometrics of PCOS offspring [10].

Statins are one of the most prescribed classes of drugs worldwide. Atorvastatin, the most prescribed statin, is currently used to treat conditions such as hypercholesterolaemia and dyslipidaemia. By reducing the level of cholesterol, which is the precursor of the steroidogenesis pathway, atorvastatin may cause a reduction in levels of testosterone and other androgens. Testosterone and other androgens play important roles in biological functions. A potential reduction in androgen levels, caused by atorvastatin might cause negative effects in most settings. In contrast, in the setting of polycystic ovary syndrome (PCOS), reducing excessive levels of androgens with atorvastatin could

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be beneficial. To quantify the magnitude of the effect of atorvastatin on total testosterone in both males and females, compared to placebo or no treatment. Secondary objectives. To quantify the magnitude of the effects of atorvastatin on free testosterone, sex hormone binding globin (SHBG), androstenedione, dehydroepiandrosterone sulphate (DHEAS) concentrations, free androgen index (FAI), and withdrawal due to adverse effects (WDAEs) in both males and females, compared to placebo or no treatment. These searches had no language restrictions. We also contacted authors of relevant articles regarding further published and unpublished work. Selection criteria: RCTs of daily atorvastatin for at least three weeks, compared with placebo or no treatment, and assessing change in testosterone levels in males or females. Data collection and analysis: Two review authors independently screened the citations, extracted the data and assessed the risk of bias of the included studies. We used the mean difference (MD) with associated 95% confidence intervals (CI) to report the effect size of continuous outcomes,and the risk ratio (RR) to report effect sizes of the sole dichotomous outcome (WDAEs). We used a fixed-effect meta-analytic model to combine effect estimates across studies, and risk ratio to report effect size of the dichotomous outcomes. We used GRADE to assess the certainty of the evidence. Main results: We included six RCTs involving 265 participants who completed the study and their data was reported [7].

Background Metformin and liraglutide have been gradually used in the treatment of polycystic ovary syndrome (PCOS) due to their metabolic benefits, but also with some adverse reactions. Evidence suggests that gut microbiota imbalance plays an important role in the pathogenesis of PCOS. This study comprised a clinical trial to evaluate the efficacy of metformin, liraglutide, and their combination in PCOS women, and a parallel animal experiment to explore the potential involvement of gut microbiota. In an open-label randomized controlled trial, sixty overweight/obese women with PCOS were randomized to: the MET group received oral metformin (0.85 g twice daily; n=20), the LIRA group

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received subcutaneous liraglutide (1.2 mg once daily; n=20), and the COM group received both treatments (n=20) for 12 weeks. In a separate animal study, female Sprague-Dawley rats were divided into five groups: (1) PCOS model group (letrozole 1 mg/kg orally); (2) MET group (letrozole + metformin 200 mg/kg orally); (3) LIRA group (letrozole + liraglutide 0.2 mg/kg subcutaneously); (4) COM group (letrozole + metformin + liraglutide at above doses); and (5) healthy controls (no treatment). All treatments lasted 4 weeks. Women in MET, LIRA, and COM groups showed significant reductions in body weight, blood glucose, blood lipid, and the LH/FSH ratio. Notably, body weight, BMI, visceral fat area, and body fat percentage decreased more significantly in the COM group than in the MET group ($P<0.05$). Compared with the MET group, the COM group was more effective in reducing free testosterone ($P=0.01$). In the animal experiment, the body weight, estrus cycle, and ovarian morphology of rats in the COM group were significantly improved. Letrozole-induced PCOS rats showed intestinal flora disorder, which was improved by metformin, liraglutide, and their combination by altering the alpha and beta diversity and relative abundance of the gut microbiota. Metformin combined with liraglutide significantly improved metabolic and endocrine characteristics in PCOS women [6].

Hyperprolactinemia (HPRL) and polycystic ovary syndrome (PCOS) are common causes of infertility in women of reproductive age. A pituitary adenoma (PA) is the most common type of brain tumor that causes HPRL. In the neurosurgical field, the co-existence of PA and PCOS is not common. However, neurosurgeons often treat patients who are referred from gynecology. Because most of these patients are young and reproductive-aged, it is difficult for a neurosurgeon to come up with a treatment plan alone. In this study, we investigated the prevalence of PAs in PCOS patients, the cutoff prolactin (PRL) level to detect PAs, and the treatment strategy, then assessed the relationship between these diseases via a literature review. Methods: Medical records from November 2009 to March 2020 were reviewed at our institute. A total of 657

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PCOS patients were enrolled. Initial prolactin levels were investigated and hyperprolactinemic patients were selected. As a result of sella magnetic resonance imaging (MRI), patients were divided into 2 groups of those with hyperprolactinemia but without PAs (group A) and those with both hyperprolactinemia and PAs (group B), respectively. We then compared and analyzed each group to find the characteristics and statistical differences. Receiver operating characteristic (ROC) curve analysis was performed to determine a cutoff value of the serum PRL level that could detect PAs in hyperprolactinemic PCOS patients[4].

Women with polycystic ovary syndrome (PCOS) have varying difficulties in achieving weight loss by lifestyle intervention, which may depend on adipose tissue metabolism. The objective was to study baseline subcutaneous adipose tissue gene expression as a prediction of weight loss by lifestyle intervention in obese/overweight women with PCOS. This is a secondary analysis of a randomized controlled trial where women with PCOS, aged 18–40 and body mass index (BMI) ≥ 27 were initially randomized to either a 4-month behavioral modification program or minimal intervention according to standard care. Baseline subcutaneous adipose tissue gene expression was related to weight change after the lifestyle intervention. A total of 55 obese/overweight women provided subcutaneous adipose samples at study entry. Weight loss was significant after behavioral modification (−2.2%, $p = 0.0014$), while there was no significant weight loss in the control group (−1.1%, $p = 0.12$). In microarray analysis of adipose samples, expression of 40 genes differed significantly between subgroups of those with the greatest weight loss or weight gain. 10 genes were involved in metabolic pathways including glutathione metabolism, gluconeogenesis, and pyruvate metabolism[3].

Polycystic ovary syndrome (PCOS) is among the predominant endocrine disorders of reproductive-aged women. The prevalence of PCOS has been estimated at approximately 6–26%, affecting 105 million people worldwide. The

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systematic review includes randomization-controlled trials (RCTs) on physical exercise and reproductive functions among women with PCOS. Studies in the English language published between January 2010 and December 2022 were identified via PubMed. A combination of medical subject headings in terms of physical activity, exercise, menstrual cycle, hyperandrogenism, reproductive hormone, hirsutism, and PCOS was used. Results: Overall, seven RCTs were included in this systematic review. The studies investigated interventions of physical activity of any intensity and volume and measured reproductive functions and hormonal and menstrual improvement. The inclusion of physical activity alone or in combination with other therapeutic interventions improved reproductive outcomes. Conclusion: The reproductive functions of women with PCOS can be improved with physical activity[1].

The beneficial effect of probiotics on the improvement of carbohydrate and lipid metabolism, as well as body mass index (BMI), has been demonstrated in various patient groups. We aimed to investigate the effect of a multi-strain probiotic on the hormonal balance of women with PCOS. Ethical approval was obtained from the Bioethical Committee. The study was designed as a 12-week, randomized, double-blind, placebo-controlled clinical study. The probiotic SanProbi Barrier capsules, which contain a unique composition of nine probiotic bacteria strains (Lactobacillus and Biffidobacterium), were used in the study. The mean age of the study participants was a mean of 28.42 ± 5.62 years. A total of 50 women with PCOS, diagnosed based on Rotterdam ESHRE criteria, were included in the study. Among them, 25 women were randomized to a placebo group, and 25 to a probiotic group. Results: A comparison of changes in individual hormone levels between groups confirmed statistically significant differences for TSH, androstenedione, SHBG, and BMI. In the case of LH, the statistical significance of the difference in delta change in the probiotic group was demonstrated with the use of a one-tailed test. Conclusions: Probiotic supplementation may serve as an alternative supporting treatment, especially in the phenotype of women with a

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high FAI index. Probiotic therapy is also effective in reducing BMI in overweight women with PCOS [9].

The risk-to-benefit ratio of using combined oral contraceptive pills (COCPs) and/or metformin for comprehensive management of polycystic ovary syndrome (PCOS) in women with obesity is unclear. As there is a lack of robust evidence on the impact of these first-line medications on cardiovascular disease (CVD) risk, we compared the effect of COCPs, metformin or both on prevalence of metabolic syndrome (MetS) in participants with hyperandrogenic PCOS and hypothesized that COCPs would increase prevalence of MetS while metformin would decrease prevalence of MetS. Methods and findings We conducted a multicenter, double-blind, double-dummy, randomized trial (COMET-PCOS) in participants between ages ≥18 and ≤40 years and body mass index (BMI) ≥25 kg/m2 and ≤ 48 kg/m2 with hyperandrogenic PCOS (defined by the Rotterdam criteria). Participants were randomized 1:1:1 to 24 weeks of low-dose COCPs (20 μg ethinyl estradiol/0.15 mg desogestrol), metforminXR (2,000 mg), or both (Combined). The primary outcome, assessed by intention-to-treat analysis, was the effect of the different treatment groups on the prevalence of MetS at the end of study. The analytical model included site, race, and the presence or absence of MetS at the screening visit as covariates. The secondary outcomes included changes in each component of MetS (TG, HDL-C, BP, WC, and fasting glucose levels) over the study period. Of the 240 participants randomly assigned, 20 out of 79 in the COCP group, 16 out of 81 in the metformin group, and 17 out of 80 in the combined group dropped out of the study. A total of 169 participants (70.4%) completed the trial between January 2018 and June 2023 (mean age: 29.5 years; mean BMI: 35.6kg/ m2; 70% were White and 23% were Black). The overall prevalence of MetS was 31% at baseline and comparable across groups. At the end of the study, the prevalence of MetS was 26.2% (17/65) in the metformin group, 28.6% (17/59) in the Combined group, and 28.8% (17/59) in COCP group with no significant difference in trend of MetS prevalence between

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groups (adjusted p=0.26). Waist circumference (mean change (MC) −2.23cm; 95% CI [−3.98, −0.49]; p=0.01), BMI (MC −0.49kg/ m2; 95% CI [−0.88, −0.10[; p=0.01), and android fat mass measured by DXA (MC −167g; 95% CI [−264, −71[; p<0.001) decreased in the COCP group over the study period whilst there was no statistically significant changes in these parameters in the metformin only group when compared to baseline.. In the metformin and Combined groups, the majority of participants (>64%) reported diarrhea, while 24.1% in the COCP group reported uterine bleeding. The main methodologic limitation of the study is the potential lack of power to detect differences in secondary outcomes. Conclusions In participants with hyperandrogenic PCOS and overweight/obesity, low-dose COCPs effectively managed PCOS symptoms without increasing prevalence of MetS. Our findings challenge the current practice of using metformin alone or with COCPs for lowering cardiometabolic risk[2].

Polycystic ovary syndrome (PCOS) is a lifelong chronic condition that affects one in ten females and can be diagnosed in adolescence. As adolescents with PCOS transition to adulthood, counselling for lifestyle management and mental health concerns often transition from involving the family unit to increasingly individual-focused approaches. PCOS is associated with a large range of comorbidities affecting reproductive, metabolic, dermatological, and psychological health. The diagnosis and comorbidities of PCOS are influenced by pubertal hormones and need to be reassessed continuously to ensure that treatment remains appropriate for age and development. As young patients grow up, personal concerns often change, especially in relation to reproductive management. In this Review, we present prevalence rates, screening tools, and treatment recommendations for PCOS-related conditions, and we consider the diagnostic and clinical elements of optimal transition of care models that ensure continuity of comprehensive care for adolescents moving from the paediatric health-care system to the adult health-care system[8].

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Conclusion

Polycystic Ovary Syndrome (PCOS) is a multifactorial endocrine–metabolic disorder requiring an integrated preventive approach. The findings indicate that hormonal therapy effectively improves menstrual regulation and hyperandrogenic symptoms, while lifestyle modifications significantly enhance insulin sensitivity and metabolic outcomes. Evidence suggests that combined interventions are more effective than single-modality treatments in preventing disease progression and reducing long-term complications. Therefore, the implementation of individualized, comprehensive preventive strategies is essential to improve reproductive health and overall quality of life in women with PCOS. Overall, the combined application of hormonal therapy and lifestyle modification appears to be more effective than single-modality interventions in preventing disease progression and reducing long-term complications of PCOS. Therefore, the implementation of comprehensive, personalized, and evidence-based preventive programs is strongly recommended to improve reproductive health, metabolic outcomes, and quality of life in women with PCOS. Future research should focus on long-term outcomes, phenotype-specific interventions, and the integration of patient-reported experiences into preventive and therapeutic strategies.

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