

Effects of a combination of resveratrol and alpha-lipoic acid on body weight and adipose composition in women with PCOS: a preliminary pilot study

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Abstract. – OBJECTIVE: Polycystic ovary syndrome is associated with reproductive and metabolic dysfunction; in fact, treatment aims in PCOS focus on optimizing healthy weight, improving underlying hormonal disturbances, preventing future reproductive and metabolic complications, and improving quality of life.

PATIENTS AND METHODS: This pilot study considered 8 overweight females (BMI > 30) in reproductive age with PCOS. Patients were treated with a galenic preparation mixture containing resveratrol and alpha-lipoic acid in association with vitamin D, B and folic acid for 12 weeks, after which anthropometric assessment was conducted.

RESULTS: After 12 weeks of treatment, BMI, anthropometry and bioimpedance parameters were all reduced in the treated patients compared to baseline.

CONCLUSIONS: The present nutraceutical combination resulted beneficial for improving the metabolic profile of women with PCOS, paving the way for new nutraceutical strategies for the management of metabolic disturbances in PCOS.

Key Words:

PCOS, Resveratrol, Alpha-lipoic acid, Metabolic syndrome.

Introduction

Polycystic ovary syndrome (PCOS) affects 5% to 15% of reproductive-aged women and is asso-

ciated with reproductive and metabolic dysfunction¹. Obesity worsens the presentation of PCOS and weight management (weight loss, maintenance of weight or prevention of excess weight gain). In fact, treatment aims in PCOS patients include optimizing healthy weight, improving underlying hormonal disturbances, prevention of future reproductive and metabolic complications, and improving quality of life. Lifestyle interventions (dietary, exercise, behavioral or combined) are recommended as first-line management in an international evidence-based guideline on PCOS².

Both prevalence and incidence of the metabolic syndrome is very high in women with PCOS. Obesity and visceral fat enlargement play a dominant role in determining the final phenotype of type 2 PCOS³. Women with PCOS present abdominal fat excess that is related to their androgen and/or insulin excess. Altered fat distribution plays an important role in the increased metabolic and CV risk observed in PCOS.

Women with PCOS present a number of systemic symptoms in addition to those related to the reproductive system. It has been associated with functional derangements in adipose tissue, metabolic syndrome, type 2 diabetes, and an increased risk of cardiovascular disease (CVD)⁴.

Natural polyphenol resveratrol has attracted significant interest as a therapeutic strategy to reduce obesity and related metabolic disorders⁵. Resveratrol has many properties and many clinical and animal studies have demonstrated the improvement of metabolic dysfunction as well as menstrual dysfunction, clinical signs (i.e., acne and hair loss), and the biochemical evidence of hyperandrogenism in the context of PCOS⁶⁻⁸. Alpha-lipoic acid (LA) plays a key role in many physiological processes, exerting anti-inflammatory, immunomodulatory, antioxidant, detoxifying, and insulin sensitizing activities⁹. Many clinical studies¹⁰⁻¹³ have focused on the combination of LA with other compounds, such as inositols for the treatment of PCOS women. Our proposed mechanism of action shows how the combination of resveratrol and LA in adipose cells may counteract the metabolic syndrome and the increase in BMI in PCOS (Figure 1). Specifically, resveratrol acts on AMPK, a key protein in the mechanisms of energy regulation, and promotes the translocation of GLUTs on the membrane and the conversion of white adipose tissue into brown adipose tissue¹⁴. Furthermore, alpha-lipoic acid has a synergistic activity with resveratrol in the reduction of insulin resistance, thanks to the action on the signaling of the insulin receptor through the PI3K/Akt pathway that determines the translocation of GLUTs on the membrane¹⁵.

We aimed at evaluating the effects of a novel nutraceutical treatment based on LA and resveratrol supported on a magnesium dihydroxide

in improving anthropometric (weight and body composition), metabolic and quality of life factors in PCOS patients.

Patients and Methods

We included 8 overweight females of reproductive age (postmenarcheal and premenopausal) with PCOS. Inclusion Criteria: women with PCOS and BMI ≥ 30 .

Exclusion criteria: women with reproductive symptoms associated to PCOS, including congenital adrenal hyperplasia, Cushing's syndrome, hyperprolactinemia, thyroid disease and androgen secreting tumors. Participants were not excluded based on type 2 diabetes, co-morbidities or medication use for clinical or metabolic features of PCOS. The study protocol was approved by the local ethics committee, and all participants provided written informed consent. The study design includes age, marital status, menstrual cycle regularity, medical history, and physical examination findings.

Patients were treated with a galenical preparation mixture containing (cps): 104 mg Revi-fastlipo[®] (24 mg alpha lipoic acid and 38.5 mg Resveratrol, Prolabin&Tefarm), 38.5 mg resveratrol, 76 mg lipoic acid, 12.5 mg Polydatin, 39 mg magnesium, 200 mg folic acid and 12.5 mcg vitamin D. Patients were instructed to take 2 cps a day, one in the morning and one in the evening preferably on an empty stomach.

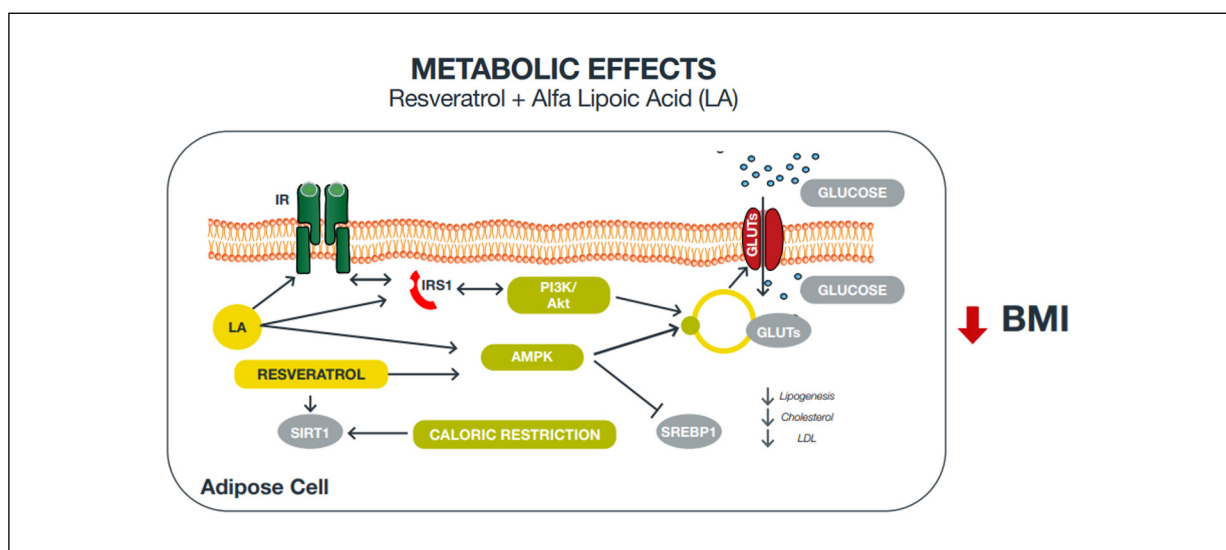


Figure 1. Schematic mechanism of action of Lipoic acid (LA) and resveratrol in PCOS and metabolic syndrome.

Anthropometry

BMI and waist circumference (WC) were determined at the first visit and at the 12-week end-point. BMI (kg/m²) was calculated as the ratio of body weight (kg) and body height (m) squared. WC was measured at the midpoint between the lower border of the rib cage and the iliac crest by using a flexible centimeter tape. Waist hip ratio were recorded.

Bioimpedance Analysis (BIA)

Abdominal fat was measured using an innovative bioimpedance device (Bia-TANITA AB140 ViScan, BIO, Tanita Europe B.V., Amsterdam, The Netherlands)¹⁴, consisting of a laser beam guided band pointing to the navel with four electrodes placed directly on the abdomen, being the subject in the supine position. To ensure highly accurate and repeatable results, waist circumference (WC) was measured using the base unit itself with an infrared system. WC, trunk fat (TF), and percent visceral fat (VF) were thus evaluated at enrollment and after 12 weeks of treatment.

Statistical Analysis

Considering 8 PCOS women in this pilot study, $p = 0.05$, and the use of the χ^2 test, the study was estimated to have an 80% power rejection of the null hypothesis that the nutraceutical supplementation does not change the parameters in PCOS women. The power of the study was calculated using PS Power and Sample Size Calculation, version 3.0 (2009). Continuous variables were presented as median values \pm standard deviation (SD), and catoric data were presented as percentages (%). Quantitative variables were compared by means of a paired Student's *t*-test baseline vs. 12-weeks treatment. Differences were considered to be significant for values of $p \leq 0.05$. All calculations were performed using SPSS version 22.0 (IBM Corp., Armonk, NY, USA).

Table I. Patients' characteristics.

Subjects (n)	8
Age	31 \pm 4.3

Results

Eight women with PCOS were accessed. Mean age and BMI at baseline are reported in Table I. Investigated parameters notably improved in the treatment group with respect to baseline. Table II shows that BMI, anthropometry levels and bioimpedance parameters after 12 weeks of treatment all decreased.

Discussion

Since the etiopathogenesis of PCOS remains poorly understood, up to date, different medical approaches are used for the management of this complex syndrome. Many focus on the metabolic aspects and among them inositols, metformin, vitamin D and alpha-lipoic acid are commonly used. Insulin-sensitizer agents, such as metformin and inositol-based supplements to date remain the most widely used. Some studies^{16,17} have shown that inositols have a key role in PCOS. Myo-inositol (MYO) and d-chiro-inositol (DCI) are second messengers of insulin. Generally, these supplements are based on MYO, DCI or a combination of both. Very often, these molecules are also associated with other compounds, such as alpha-lipoic acid¹⁸, melatonin¹⁹ and vitamin D²⁰ in order to enforce their biological activity on the metabolic aspects of PCOS. However, this novel formulation, based on resveratrol and alpha-lipoic acid without the presence of either form of inositols, could be of great interest paving the way for new nutraceutical strategies for the management of metabolic disturbances in PCOS.

Table II. Variation of clinical characteristics after 12 weeks.

	Baseline	12 weeks
BMI (kg/m ²)	34.78 \pm 4.1	32.12 \pm 2.9
Waist circumference (cm)	114.8 \pm 8.15	109.57 \pm 4.17
Waist/hip ratio	0.89 \pm 0.08	0.83 \pm 0.05
Trunk fat level (%)	45.43 \pm 5.03	41.31 \pm 6.22
Visceral Fat level (%)	23.57 \pm 5.4	20.07 \pm 5.99

Limitations

Our pilot trial had a small sample size that made it difficult to detect significant effects due to treatment. Our research was also limited to selected clinical parameters; therefore, further investigation will need to be conducted to fully determine the effects and impact on metabolic parameters of this treatment in PCOS women.

Conclusions

Supplementation with resveratrol alpha-lipoic acid combination exerted positive effects on BMI, total and trunk adipose mass, and lean tissue mass in obese PCOS women. Supplementation with these dietary substances may be beneficial for weight loss, glycemic control, or both. Previous studies^{21,22} have showed the benefits on anthropometric parameters and metabolic profile of resveratrol in combination with D-chiroinositol on overweight pregnant women²¹ and overweight prediabetic patients²².

Preclinical trials²³ suggest that resveratrol mimics the metabolic effects of calorie restriction. In experimental animals, this potential translates into prevention or improvement of inflammation, disglycemia, cancer, and nonalcoholic fatty liver disease. Many studies^{10-12,24} have also demonstrated alpha-lipoic acid may be beneficial in PCOS. Therefore, the present combination could be beneficial for improving the metabolic profile of women with PCOS. Only further controlled clinical studies will determine the significant impact of the parameters observed in this pilot study.

Conflict of Interest

The Authors declare that they have no conflict of interests.

Informed Consent

All patients recruited for the study were fully counseled and signed a written informed consent.

Ethical Approval

All procedures performed in this study were in accordance with the ethical standards of international research committee.

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