Impact of a supplement containing antioxidants, inositols and probiotics on IVF cycles in patients with polycystic ovarian syndrome and overweight or obesity: a pilot randomised controlled study

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INTRODUCTION

Polycystic ovarian syndrome (PCOS) is linked to hormonal imbalance, oxidative stress, and altered microbiota, which may impair fertility, especially in women with higher BMI. This study evaluated the effects of a supplement containing inositols, antioxidants, and probiotics on reproductive hormones, microbiota function, oxidative stress, and IVF outcomes in women with PCOS and BMI ≥ 25 kg/m² (1,2)

METHODS

This pilot double-blind randomized controlled trial included 20 patients with PCOS, BMI≥25kg/m², recruited from March 2021-2023. Patients were randomly allocated (1:1) to placebo (P) or supplementation (S): D-chiro-inositol, myo-inositol, selenium, vitamin D, melatonin, Lacticaseibacillus rhamnosus, Lactobacillus crispatus and Lactiplantibacillus plantarum. Reproductive hormones and vaginal and intestinal short-chain fatty acids (SCFA) were assessed before supplementation and 3 months later, before ovarian stimulation.

Ovarian stimulation and oocyte and embryo variables were analysed. During oocyte retrieval, thiobarbituric acid-reactive substances (TBARS) and total antioxidant capacity (TAC) were assessed in follicular fluid (LF) and serum by colorimetric techniques, using internal and quality controls. Besides, embryo kinetic variables obtained through time-lapse technology were analyzed, including morphokinetic parameters of cell-division timings up to the 8-cell stage (t2, t3, t4, t5, t6, t7, and t8). Statistical study included Levene's test, T-test and Mann-Whitney U test. Results were expressed as mean and standard deviation (SD).

RESULTS

Patients in group S showed hormonal changes between the start of supplementation and its completion: a trend to lower serum concentrations of total testosterone (32.8[10.0] ng/dL vs. 40.7[22.7] ng/dL, p=0.09), free index testosterone (3.3 [2.0] vs. 4.2[2.6], NS), androstenodione (213.3[67.1] ng/dL vs. 240.8[97.3] ng/dL,NS) and AMH (7.8[4.4]ng/mL vs. 9.4[5.4]ng/mL, NS), whereas no changes were detected in P.

An increase in propionic acid (p<0.001) and butyric acid levels (p=0.031) was observed in rectal samples from patients treated with S (**Figure 1**) , in comparison with P. Treatment with S was also associated with a lower number of follicles ≥12 mm. at trigger (11.7[5.9] vs.17.8[8.8], p=0.09), but a trend to a higher number of oocytes 12.2[8.2] vs. 8.7[5.5], NS), MII (8.4[7.2] vs. 6.8[4.5], NS) and a higher MII/number of follicles ≥12 mm. at trigger ratio (0.64[0.30] vs. 0.39[0.23], p=0.05).

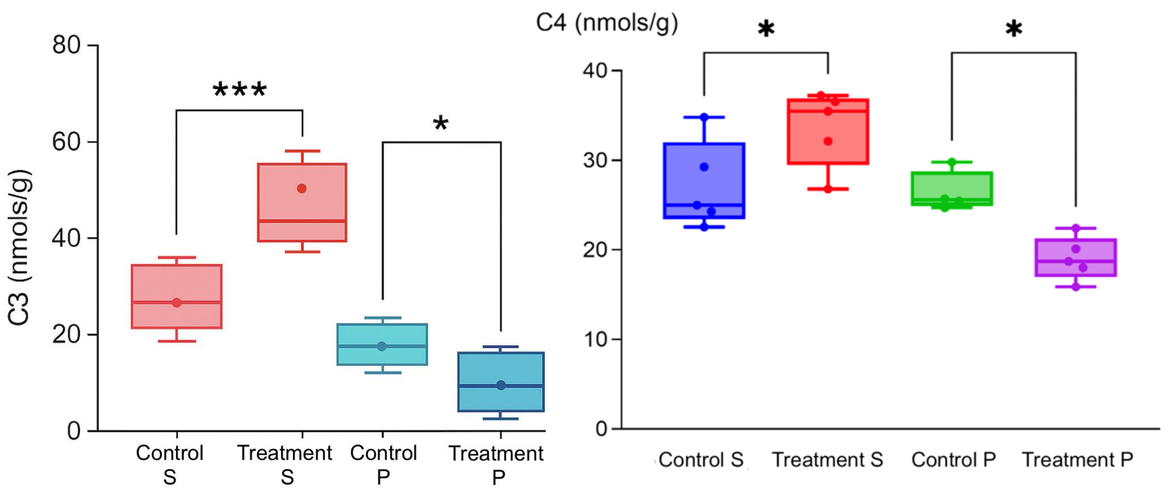

Figure 1. Acid propionic (C3) and butyric (C4) before (control) and after the intervention (treatment) in the nutraceutical (S) and placebo (P) groups. Data are shown as boxplots. Asterisks indicate statistically significant differences (*p < 0.05, **p < 0.01, ***p < 0.001).

We detected a trend to lower serum TBARS in group S compared to P (5.7[0.3] vs 6.2[0.5], p=0.4), **Figure 2**. Time-lapse incubator data showed that embryos from S group exhibited faster embryo development compared to P: t2, (26,1[4,2],35.0[9,4], p=0.001), t3, (35.2[5.4],40.2[5.3], p=0.001) and t4 (36.7[4.8], 42.4[4.5], p=0.001), **Figure 3**.

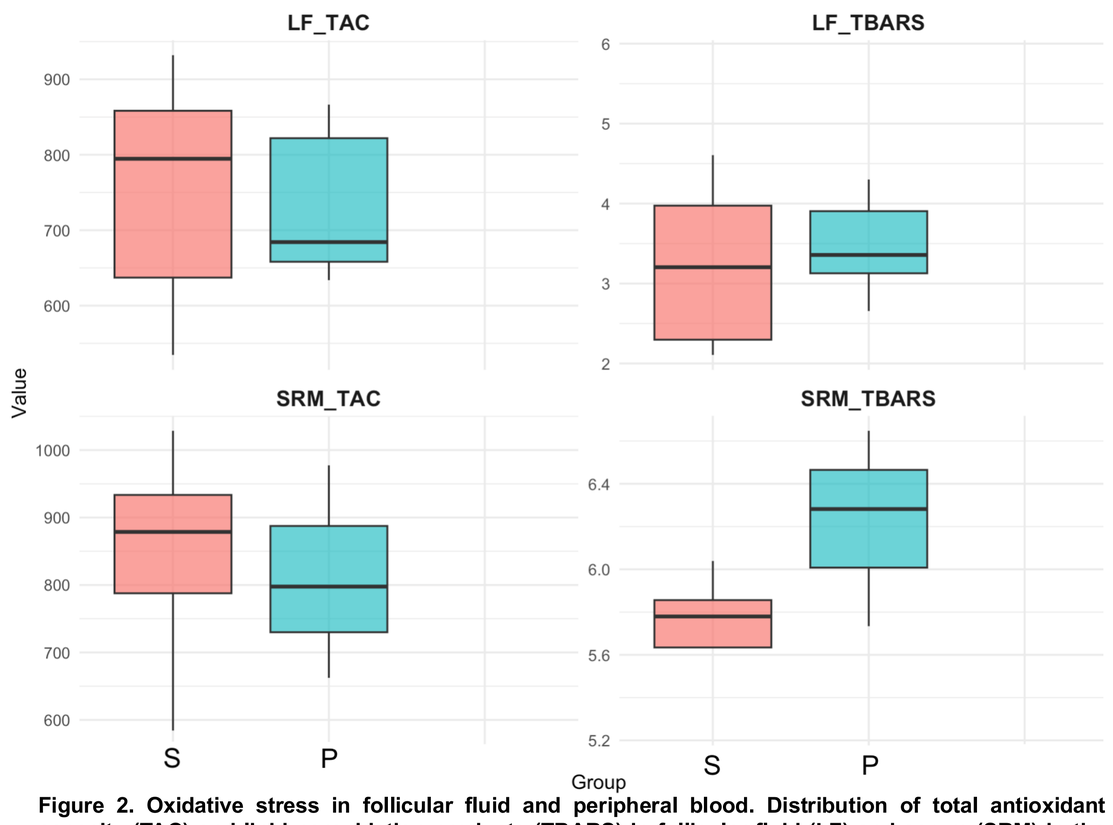

Figure 2. Oxidative stress in follicular fluid and peripheral blood. Distribution of total antioxidant capacity (TAC) and lipid peroxidation products (TBARS) in follicular fluid (LF) and serum (SRM) in the nutraceutical (S) and placebo (P) groups. Data are shown as boxplots.. In peripheral blood, the nutraceutical group showed a trend toward lower TBARS accompanied by a parallel reduction in TAC.

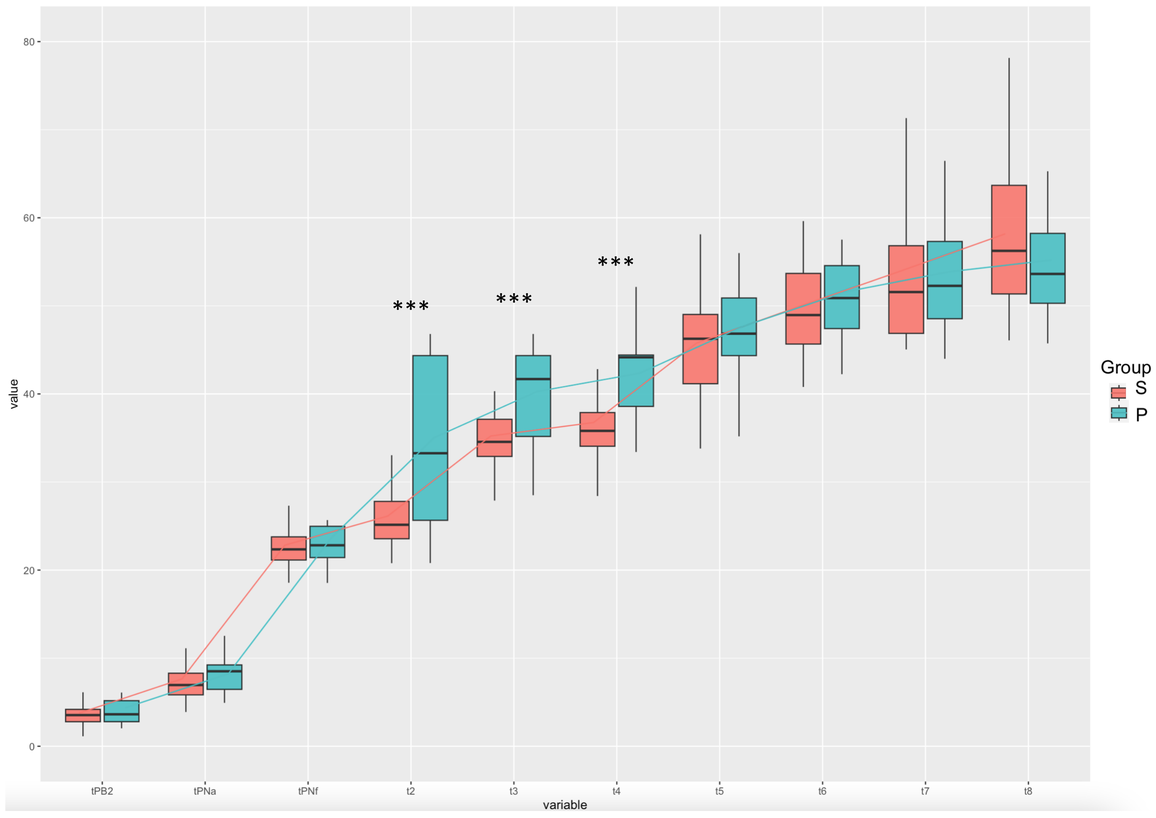

Figure 3. Boxplot comparison of embryo development kinetics between the placebo (P) and supplement (S) groups. The figure illustrates the time-lapse parameters measured at key developmental stages: second polar body extrusion (tPB2), time of pronuclei appearance (tPNa), time to pronuclear fading (tPNf), and the timing of divisions to 2, 3, 4, 5, 6, 7, and 8 cells (t2, t3, t4, t5, t6, t7, t8). Differences between these parameters (e.g., t8–t2, t8–t3, etc.) were also evaluated.

CONCLUSION

In women with PCOS and BMI≥25, the studied supplementation was associated with lower androgen levels, better intestinal microbiota function and oxidative stress profile, with improved follicular recruitment, oocyte maturation and embryo development. This pilot study could form the basis for a larger trial to confirm these results

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