Reviewer's report

**Title:** Ethinylestradiol30µg-drospirenone and metformin: could this combination improve endothelial dysfunction in polycystic ovary syndrome?

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**Reviewer:** Neoklis Georgopoulos

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In the manuscript entitled “Ethinylestradiol30µg-drospirenone and metformin: could this combination improve endothelial dysfunction in polycystic ovary syndrome? by Ioana Rada Ilie, Ioan Marian, Teodora Mocan, Razvan Ilie, Lucian Mocan, Dana Bartos and Carmen Emanuela Pepene the effect of the association ethinylestradiol30µg-drospirenone 3mg (DRP/EE30µg) plus metformin and weight loss on endothelial status and C-reactive protein (hsCRP) levels in polycystic ovary syndrome (PCOS) has been investigated. Despite the interesting findings of the study, certain points need to be further elucidated.

**MAJOR POINTS**

1. Although flow-mediated dilatation (FMD) (%) was significantly increased (p=0.033) after 6 months of treatment, no significant increase in FMD was reported in either obese (p=0.133) or non-obese (p=0.161) group. The authors should comment on the discrepancy.

2. The effect of DRP/EE30µg and metformin 850mg/day on PCOS women (no improvement of adiposity and deterioration of TG, IL-6) was compared to the effect of DRP/EE20µg + metformin 1500mg/day (improvement of insulin sensitivity, increase in HDL-cholesterol concentrations and no significant change in TG levels) in non-insulin resistant and non-obese young PCOS women. The effect of the combined administration of DRP/EE + metformin on lipid metabolism cannot be evaluated, since doses of metformin and EE as well as basal metabolic profile were different between the groups of the studies.

3. In the present study, it was hypothesized that metformin and DRP/EE30µg may have either different or even opposing effects on chronic inflammation that may balance the risk out and neutralize it overall or may both have neutral effects on hsCRP. The aforementioned hypothesis should be elaborated and supported by data sources from the literature.

4. Different effects of metformin, oral contraceptives and anti-androgens on CRP and hsCRP have been reported in the literature. Could the authors provide possible mechanisms implicated in each one of the agents? Additionally, the authors should comment on the findings of the present study.

**MINOR POINTS**
1. Page 4: Women with polycystic ovary syndrome (PCOS) frequently cluster…
2. Page 15: …metformin 850 mg/day + DRP/EE30µg does not influence the insulin resistance
3. Page 16: …the total PCOS group and obese and non-obese subgroups.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests