

# Is metformin and spironolactone better than metformin alone for improving polycystic ovarian syndrome symptoms?

Christine Huang DO

Lehigh Valley Health Network, [Christine.Huang@lvhn.org](mailto:Christine.Huang@lvhn.org)

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## Published In/Presented At

Huang, C. (2019). Is metformin and spironolactone better than metformin alone for improving polycystic ovarian syndrome symptoms?. *Evidence-Based Practice*, 22(3), 31-32. doi: 10.1097/EBP.0000000000000207.

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EMS 2473

Title: Metformin plus spironolactone for PCOS

Word count: 457

# Is metformin and spironolactone better than metformin alone for improving polycystic ovarian syndrome (PCOS) symptoms?

## Evidence-based answer

Likely not. Metformin 1000-1700mg/day combined with low-dose spironolactone 25-50mg/day shows a greater reduction in hirsutism scores among patients with PCOS than metformin alone however similar symptom scores between groups at follow-up suggest the effect is not clinically significant (SOR: **B**, RCTs). In addition, combination therapy leads to inconsistent improvement in menstrual regularity.

## Evidence summary

A 2013 RCT (N=198) studied the efficacy of metformin and low-dose spironolactone in management of PCOS symptoms<sup>1</sup>. Women with a mean age of 23 who met the 2006 Androgen Excess-PCOS criteria were allocated to 3 different treatment groups, metformin (1000mg/day) plus low-dose spironolactone (50mg/day) or each drug alone. All women had menstrual irregularities defined as oligomenorrhea (menstrual interval greater than or equal to 35 days or less than 8 cycles per year) or amenorrhea (no cycle in the last 6 months or more). Hirsutism was evaluated by a modified FGS score at baseline, 3 months, and 6 months performed by a single observer with a score greater than 7 deemed significant hirsutism. At 6 months, FGS scores improved from 13 to 9.7 ( $P=.001$ ) in the metformin group, and from 14 to 9.6 ( $P=.001$ ) in the spironolactone group. Combination therapy resulted in a greater improvement in FGS scores compared to either drug alone, 13 to 9.1 at 6 months ( $p<.05$ ). Though the improvement reached statistical significance in the combination therapy group, 6 month symptom scores are similar between groups and may not reflect clinical significance. Cycle frequency at six months improved from 6.0 to 10 cycles per year ( $P=.01$ ) in the metformin group, from 6.5 to 10 cycles per year ( $P=.001$ ) in the spironolactone group and from 6.1 to 12 cycles per year ( $P=.01$ ) in the combination therapy group but the differences between groups were not significant. Participant withdrawal due to side effects (gastrointestinal symptoms and menstrual irregularities) was comparable between groups. Results are limited by small sample size, lack of blinding in FGS evaluation at follow-up and lack of a placebo group.

A 2013 RCT (N=56) examined the effect of metformin (1700mg/day) and low-dose spironolactone (25mg/day) versus metformin alone on symptoms of PCOS<sup>2</sup>. Enrolled patients had an average age of 23 years and PCOS as defined by Rotterdam criteria. The Ferriman-Gallway score (FGS) of hirsutism severity was used to assess hirsutism with scores greater than 8 indicating hirsutism presence and scores greater than 15 indicating moderate to severe

hirsutism. Patients in this study had an average FGS of 14 along with either mild oligomenorrhea (7–8 cycles/year) or moderate to severe oligomenorrhea (less than 6 cycles/year). FGS scores were repeated at 6 months post intervention with improvements in both the metformin plus low-dose spironolactone group (15 to 11,  $P<.001$ ) and metformin alone groups (12 to 11,  $P<.001$ ). While improvement in the combination group was statistically significant in comparison to the metformin group ( $P<.001$ ), it is likely not clinically significant as 6 month scores are similar between groups. Improvement is most likely explained by baseline differences between groups FGS scores. Menstrual cycles normalized in 82% of patients treated with metformin ( $P<.001$ ) and 67% of patients in patients receiving combination therapy ( $P<.001$ ). Differences between groups were not statistically significant. This study is limited by small sample size, difference in baseline FGS scores between groups and lack of placebo control group.

**Christine Huang, DO**  
Lehigh Valley Health Network  
Allentown, PA

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