

## Does adding metformin to clomifene citrate lead to higher pregnancy rates in a subset of women with polycystic ovary syndrome?

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**BACKGROUND:** An RCT among newly diagnosed, therapy naive women with polycystic ovary syndrome (PCOS) showed no significant differences in ovulation rate, ongoing pregnancy rate or spontaneous abortion rate in favour of clomifene citrate plus metformin compared with clomifene citrate. We wanted to assess whether there are specific subgroups of women with PCOS in whom clomifene citrate plus metformin leads to higher pregnancy rates.

**METHODS:** Subgroup analysis based on clinical and biochemical parameters of 111 women randomized to clomifene citrate plus metformin compared with 114 women randomized to clomifene citrate plus placebo. The data for age, BMI, waist–hip ratio (WHR) and plasma testosterone were available in all women, 2 h glucose in 80% of women and homeostatic model assessment for assessing insulin sensitivity (HOMA) in 50% of women.

**RESULTS:** Of the women who were allocated to the metformin group, 44 women (40%) reached an ongoing pregnancy. In the placebo group, 52 women (46%) reached an ongoing pregnancy. There was a significantly different chance of an ongoing pregnancy for metformin versus placebo between subgroups based on age and WHR ( $P = 0.014$ ). There was a positive effect of metformin versus placebo on pregnancy rate in older women ( $\geq 28$  years) with a high WHR, a negative effect of metformin versus placebo in young women ( $<28$  years) regardless of their WHR and no effect in older, not viscerally obese women. No significant differences in effect of treatment were found for groups based on BMI, 2 h glucose, HOMA or plasma testosterone.

**CONCLUSIONS:** Metformin may be an effective addition to clomifene citrate in infertile women with PCOS, especially in older and viscerally obese patients.

Key words: clomifene/metformin/polycystic ovary syndrome/pregnancy/subgroup analysis

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