Metformin versus myoinositol: which one is better in obese PCOS patients?  
A crossover study on clinical, endocrine and metabolic effects

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Study question: Which is the more effective insulin-sensitizing drug between metformin and myoinositol on hormonal, clinical and metabolic parameters in obese patients with polycystic ovary syndrome (PCOS)?

What is known already: Due to the central role of metabolic abnormalities in the pathophysiology of PCOS, insulin sensitizers have been proposed as a feasible treatment option. The biguanide metformin is still the most used, but alternative molecules were recently evaluated. Myoinositol, an insulin second messenger, seems able to restore spontaneous ovarian activity in PCOS patients. However, previous reports evaluated the effects of formulations containing myoinositol plus folic acid and no direct comparisons with metformin are available in literature.

Study design, size, duration: This is a crossover, active-treatment-controlled, randomized study. 21 PCOS obese women were randomized to receive metformin (850 mg twice a day) or myoinositol (500 mg three times a day) for six months. After a three month washout, the same subjects received the other compound for the following six months.

Participants/materials, setting, methods: We recruited 21 obese women with PCOS diagnosed according with the Rotterdam criteria (age: 25.62 ± 4.7; BMI: 32.55 ± 5.67). The investigations, performed during the early follicular phase, included menstrual pattern, anthropometric characteristics, hirsutism score evaluation, hormonal assays, oral glucose tolerance test, euglycemic hyperinsulinaemic clamp and lipid profile.

Main results and the role of chance: 13 patients completed the study without protocol violations. Both metformin and myoinositol significantly reduced the insulinaemic response to OGTT (p< 0.05 and p< 0.01 respectively). Both treatments induced an improvement in insulin sensitivity documented by the increase of M value during the euglycaemic hyperinsulinaemic clamp, though these differences did not reach the statistical significance. Metformin was able to significantly decrease body weight (p< 0.01), improve menstrual pattern (p< 0.01) and the Ferriman-Gallwey score, to reduce androstenedione (p< 0.05), FAI and AMH levels (p< 0.01), and to significantly decrease LH and estradiol levels (p< 0.05). None of these clinical and hormonal changes were observed during the myoinositol administration period.

Limitations, reasons for caution: The sample size was limited for a randomized trial. Despite the considerable number of studies in literature, treatment schedules for both metformin and myoinositol are not well standardized. It could be conceivable that an higher myoinositol dosage could be more effective on PCOS features.

Wider implications of the findings: This is the first study directly comparing the efficacy of metformin vs myo-inositol administration on hormonal, clinical and metabolic features in PCOS patients. At variance with previous reports, the novelty of the present trial relies on the use of a pure myoinositol formulation and on the cross over design, which allows to compare the efficacy of different drugs in the same patient.