Prediction of therapeutic effect of metformin in patients with polycystic ovary syndrome

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Context: Insulin resistance (IR) plays a major role in pathogenesis of PCOS and is observed in 50-70% cases. Insulin sensitizers, in particular metformin (Mf), are used in treatment of the syndrome more than 20 years. However its effectiveness is about 60% in menstrual cycle (MC) restoration and rarely correlates with IR and hyperinsulinhemia (HI) existence. Prediction of therapy effectiveness is important to reveal nonresponders.

Objective: to determine clinical, hormonal and metabolic markers of Mf therapy effectiveness in patients with PCOS.

Methods: transvaginal sonography, AMH, LH, FSH, total testosterone (Tt), androstendione (A) levels evaluation, dual-energy X-ray absorptiometry and oral glucose tolerance test were performed before and 6 months after treatment. Statistic analysis was carried out with SPSS (IBM Statistical Package for the Social Sciences 21).

Patients: 143 women with PCOS (mean age – 26.4±4.6 years, mean BMI – 23.8±4.8 kg/m2) were divided into two groups: group 1 – patient with restored MC (responders, 53.1%), including 33 women who achieved pregnancy, group 2 – with lack of therapy effect (nonresponders, 36.3%). Women with partial effect (10.6%) were excluded from the study.

Interventions: Mf 1500 mg per day during 6 month.

Results: Proportion of the androgen and nonandrogen phenotypes was similar (p>0.05). After 6 month of Mf Tt level decreased by 26.3%, A level – by 26.7%, AMH – by 22.1%, SHGB level increased by 33.5% in group 1 (p<0.05). In group 2 the levels did not change significantly (p>0.05). Index A/G decreased only in the group with complete MC restoration (p<0/05). There was no initial difference in prevalence of HI, IR and impaired glucose tolerance (p>0.05). Mean AMH, Tt levels and A/G index were higher in group1 (p<0.05). ROC-analysis in prediction of period restoration after Mf treatment showed that the area under the curve (AUC) for AMH model was 0.705 (cut-off level - 13.3 ng/ml, sensitivity and specificity 67% and 66% respectively), AUC for Tt- 0.622 (cut-off level – 1.81 ng/ml, sensitivity and specificity 65% and 65% respectively), AUC for index A/G 0.698 (cut-off level – 0.9, sensitivity and specificity 90% and 50% respectively).

Conclusion: in each 2nd women who was prescribed with Mf therapy MC was restored. AMH and Tt levels, A/G index can be used as the predictors of response to Mf therapy, with high sensitivity and specificity. This approach can optimize the management of patients with PCOS.

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