**Journal of Diabetes Science and Technology** Volume 1, Issue 2, March 2007 © Diabetes Technology Society

# Impact of Treatment with Rosiglitazone or Metformin on Biomarkers for Insulin Resistance and Metabolic Syndrome in Patients with Polycystic Ovary Syndrome

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# Abstract

## Background:

There is increasing evidence that insulin resistance (IR) has an important implication in the pathogenesis of polycystic ovary syndrome (PCOS), a common endocrinopathy in women. This study was performed to investigate the impact of different treatments for IR on five currently discussed markers for insulin resistance: intact proinsulin, adiponectin, retinol-binding protein 4 (RBP4), resistin, and visfatin in patients with PCOS.

### Methods:

Thirty-five women with clinically confirmed PCOS diagnosis were included in the study [age (mean  $\pm$  SD): 24.7  $\pm$  4.8 years; body mass index: 27.4  $\pm$  6.0 kg/m<sup>2</sup>]. They were randomized to receive either metformin (850 mg twice a day) or rosiglitazone (4 mg once a day). Blood samples for measurement of the HOMA<sub>IR</sub> score, visfatin, RBP4, intact proinsulin, resisitin, and adiponectin were taken at baseline and after 6 months of treatment.

### Results:

Both drugs improved ovulation, and an increase in insulin sensitivity was observed, especially in the rosiglitazone arm. Adiponectin levels increased in both treatment arms (metformin:  $8.6 \pm 3.3$  to  $16.7 \pm 7.2$  mg/liter, p < 0.001; rosiglitazone:  $8.2 \pm 3.5$  to  $26.2 \pm 9.5$  mg/liter, p < 0.001), but the increase was more pronounced with rosiglitazone (p < 0.001). While no changes of visfatin concentrations were observed during rosiglitazone therapy ( $15.4 \pm 6.9$  ng/ml vs  $17.4 \pm 4.8$  ng/ml, n.s.), there was an increase in the metformin treatment arm ( $11.9 \pm 4.0$  to  $21.8 \pm 8.3$  ng/ml, p < 0.001). Significant increases demonstrated for RBP4 in both treatment arms were more pronounced in the metformin group (metformin: +66%, rosiglitazone: +33%). All patients were in stage I or II of  $\beta$ -cell dysfunction and none of them showed increased intact proinsulin levels or changes in resisitin at baseline or end point.

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Abbreviations: (ANCOVA) analysis of covariance, (BMI) body mass index, (HOMA) homeostatic model assessment, (IR) insulin resistance, (PCOS) polycystic ovary syndrome, (PPARγ) peroxisome proliferator-activated receptor γ, (RBP4) retinol-binding protein 4

Keywords: adiponectin, insulin resistance, metformin, polycystic ovary syndrome, rosiglitazone

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#### Abstract cont.

#### **Conclusions:**

Both drugs slightly improved ovulation in our PCOS patient population during 6 months of therapy, which was accompanied by improved insulin sensitivity and an increase in adiponectin levels. Metformin increased visfatin concentrations. Despite improved insulin resistance, an increase in RBP4 concentration was seen for both drugs. Rosiglitazone seems to be the more favorable drug under these circumstances. However, our results regarding visfatin and RBP4 contradict other reports and further research is required to clarify their value as diagnostic markers for the metabolic syndrome. In this study, adiponectin appeared to be the most promising indicator of both metabolic status and therapeutic success.

J Diabetes Sci Technol 2007;1(2):211-217