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SYMPOSIUM

Treatment with Sitagliptin or Metformin Does Not Increase Body Weight Despite Predicted Reductions in Urinary Glucose Excretion

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Abstract

Background:

We used a mathematical model to estimate the contribution of urinary glucose excretion (UGE) to reported changes in body weight (BW) following oral antihyperglycemic agent (AHA) therapy. This modeling approach was used to gain novel insight into the mechanisms by which oral AHA affects BW.

Methods:

Twenty-four hour glucose profiles were used to predict UGE before and after treatment with oral AHA. Model-predicted changes in BW due to reduced UGE were compared with reported changes in BW to quantify non-UGE-dependent effects (fluid retention, food intake, and energy expenditure).

Results:

In type 2 diabetes patients [hemoglobin A1c (HbA1c) >7.3%], the energy lost to UGE is predicted to decrease an average of 100 kcal/day for each 1% decrease in HbA1c. This effect, alone, is predicted to increase BW 1.4 kg after 6 months. Differences from this value reported for changes in BW with oral AHA therapy (+1.4 kg for pioglitazone and rosiglitazone; –0.4 kg for glyburide; –0.9 kg for sitagliptin and vildagliptin; –2.3 kg for metformin) are therefore predicted to be due to additional, non-UGE-dependent mechanisms.

Conclusions:

Weight gain following thiazolidinedione therapy is predicted to result from both reduced UGE and non-UGE-dependent mechanisms. Reduced UGE alone is predicted to account for most of the weight gain reported following sulfonylurea therapy. Weight loss observed in response to metformin and weight maintenance observed in response to dipeptidyl peptidase-4 inhibitors may result from an increase in satiety, energy expenditure, or both.

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Abbreviations: (AHA) antihyperglycemic agent, (BW) body weight, (DPP-4) dipeptidyl peptidase-4, (GFR) glomerular filtration rate, (GLP1) glucagon-like peptide 1, (HbA1c) hemoglobin A1c, (SD) standard deviation, (SEM) standard error of the mean, (T2D) type 2 diabetes, (TZD) thiazolidinedione, (UGE) urinary glucose excretion

Keywords: body weight, diabetes, glyburide, HbA1c, mathematical modeling, metformin, pioglitazone, rosiglitazone, sitagliptin, urinary glucose excretion

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