OBSERVATIONS

Changes in Weight and Glucose Tolerance During Treatment With Mirtazapine

Weight gain is a serious problem with numerous psychotropic drugs (1), and drug-induced weight gain may be associated with health risks typically linked to obesity such as type 2 diabetes. Some second generation antipsychotics are known to lead to weight gain and to impair glucose tolerance (2), but little is known about the influence of weight gain–inducing novel antidepressants such as mirtazapine on glucose tolerance.

In a naturalistic study, we assessed weight, glucose tolerance, and plasma levels of insulin and cortisol, which are major players regarding glucose metabolism (3), in 11 inpatients (7 males and 4 females; age [mean ± SD]: 46.7 ± 20.5 years; weight: 73.3 ± 5.5 kg) with major depression according to the ICD-10 and Diagnostic and Statistical Manual of Mental Disorders Fourth Edition receiving mirtazapine during psychiatric hospital treatment of 2–6 weeks. After the initial baseline examination, mirtazapine treatment was started and the dosage adjusted according to clinical needs. At baseline and at the end of treatment, patients were weighed and underwent an oral glucose tolerance test (OGTT) over 4 h.

During treatment with mirtazapine, subjects gained on average 2.17 ± 1.97 kg (t = 3.65, df = 10, P = 0.004). However, basal serum glucose (102 ± 14 vs. 96 ± 6 mg/dl; t = 2.23, df = 10, P = 0.05) and glucose tolerance as measured by 120-min glucose (150 ± 83 vs. 128 ± 83 mg/dl; t = 2.25, df = 10, P = 0.048) and glucose area under the curve during OGTT (df = 10, P = 0.028) improved in parallel. Also, 120-min insulin levels decreased during treatment (from 51 ± 27 to 37 ± 34 μU/ml; t = 2.33, df = 10, P = 0.042). Indexes of insulin sensitivity (4) showed no statistically significant changes during the treatment period (homeostasis model assessment: from 4.91 ± 1.44 to 5.01 ± 1.19; t = −0.22, df = 10, P = 0.827; Matsuda and DeFronzo index: from 4.42 ± 1.71 to 4.89 ± 2.12, t = −1.00, df = 10, P = 0.339). Cortisol levels did not decrease significantly from baseline to the end of therapy but did between baseline and treatment week 2 (from 195.11 ± 58.29 to 162.98 ± 34.54 μg/l; t = 2.28, df = 9, P = 0.049).

The present study confirms that treatment with mirtazapine is likely to be associated with weight gain. Although weight gain is expected to impair glucose tolerance, mirtazapine had the opposite effect in the present study.

Improved glucose tolerance during treatment with mirtazapine may, at least in part, be mediated by a reduction of cortisol secretion, because cortisol plasma levels are reported to be elevated in depressed patients (5), and it was found that they can be lowered by antidepressant treatment with mirtazapine (6).

Usually, depression goes along with a decrease in physical activity, appetite, and food intake but a relative excess of carbohydrates and a preference for sweets (7). Recovery from depression might therefore lead to favorable changes in nutritional preferences and physical activity. Additionally, mirtazapine unfolds α-adrenergic antagonism effects by blocking α2-receptors (8). It is possible that this α-adrenergic antagonism is responsible for the drop in glucose, similar to the effect of the α-adrenergic antagonist doxazosin, which has been reported to lead to a decrease in plasma glucose during OGTT without changing the plasma insulin response (9).

Depression has been significantly linked with the development of type 2 diabetes (10), making it highly desirable to gain further knowledge on the effect of antidepressants on glucose metabolism.

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References

Retrospective Review of Metformin in Inpatients and Outpatients at the University of Michigan

Metformin is a hypoglycemic agent that is used in the treatment of type 2 diabetes. It is considered the drug of choice in patients who are overweight with no contraindications to...