Countering Antipsychotic-Induced Weight Gain

Metformin and lifestyle interventions seemed to offset weight gain and improve insulin and glucose levels.

BY MARY ANN MOON
Contributing Writer

Metformin and lifestyle changes, either alone or in combination, counteracted the weight gain caused by atypical antipsychotic medications after an initial episode of schizophrenia, according to the findings of a prospective study.

These approaches also decrease waist circumference, body mass index, fasting glucose levels, insulin levels, and insulin resistance index in schizophrenia patients taking the drugs, compared with placebo, Dr. Ren-Rong Wu and associates at Central South University, Changsha, China, reported.

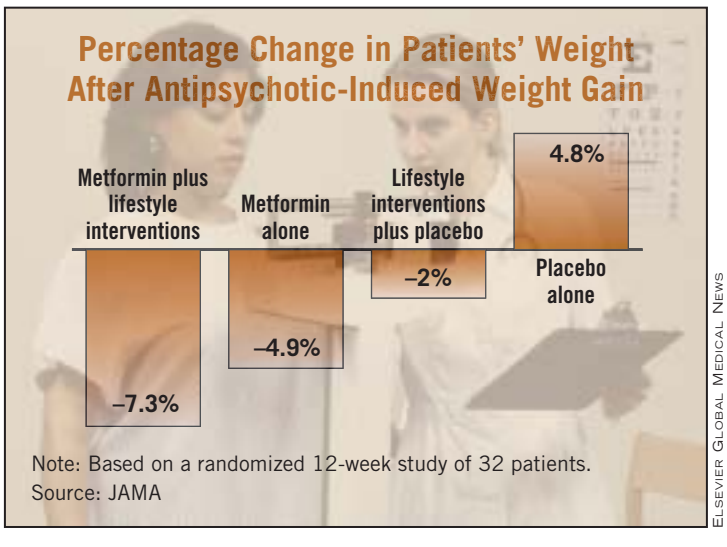
In what they described as the first double-blind placebo-controlled study to directly compare metformin and lifestyle interventions in a population of first-episode schizophrenia patients, the investigators randomly assigned 32 patients each to receive either 750 mg metformin alone daily, a placebo tablet alone, lifestyle interventions plus metformin, or lifestyle interventions plus placebo tablet, for 12 weeks.

All of the study subjects had developed their first episode of schizophrenia during the preceding year and had gained more than 10% of their predrug body weight during therapy with clozapine (Clozaril), olanzapine (Zyprexa), risperidone (Risperdal), or sulpiride. Most had been of normal weight before beginning treatment, and most were young adults.

All the subjects were living in the care of their parents or caregivers, who assisted with adherence to the interventions.

The lifestyle interventions included counseling; prescription of what the American Heart Association formerly called the step 2 diet—now known as the Therapeutic Lifestyle Changes diet—which allowed less than 30% of total calories from fat but did not decrease total daily caloric intake; and exercise such as walking, jogging, bicycling, sports, and vigorous activity such as chopping wood.

The subjects' weight decreased by 7.3% with metformin plus lifestyle interventions, by 4.9% with metformin alone, and by 2% with lifestyle interventions plus placebo. In contrast, weight continued to rise by 4.8% with placebo alone.



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Similarly, all three treatment approaches significantly reduced mean fasting glucose, insulin levels, and insulin resistance index, while these measures significantly increased with placebo.

No major adverse events were attributed to the interventions. Ten of the subjects failed to complete the study, five of whom required hospitalization for exacerbation of psychosis.

For patients with schizophrenia who are taking atypical antipsychotic medications, "we recommend that lifestyle intervention[s] plus metformin be considered first for those with weight gain. If patients cannot tolerate or adhere poorly to lifestyle intervention[s], they should consider metformin alone," Dr. Wu and associates said (JAMA 2008;299:185-93).

The authors noted that their study results may not be generalizable to Western populations, to people with schizophrenia who live independently, or to patients who have long-standing schizophrenia or who are older or more obese than these study subjects were when they began treatment. ■

Insulin Addition Need Not Lead to Weight Increase in Type 2 Patients

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

Weight gain does not necessarily follow the institution of insulin therapy in type 2 diabetes patients already taking oral hypoglycemics, results of a 7-year longitudinal study suggest.

Study investigators concluded that weight gain following the addition of insulin therapy is mostly the result of a correction of the glycemia that often causes weight loss, and brings most patients closer to their normal physiologically controlled weight.

'Concern over an increase in body weight should not deter' from adding insulin and other medications to achieve therapeutic goals.

"Thus, concern over an increase in body weight should not deter patients and physicians from adding insulin and appropriate oral medications in order to achieve therapeutic goals," Dr. Ohad Cohen of Tel Aviv University, and his coauthors wrote in Diabetes Research and Clinical Practice.

The study included 366 adults (mean age 67 years) with type 2 diabetes. Most (310) were on only oral hypoglycemic medications at baseline; the remaining 56 were also taking insulin (Diabetes Res. Clin. Pract. 2008;79:128-32). Compared with those taking oral medications, patients also on insulin had an earlier age of diabetes onset (51 vs. 55 years) and longer duration of diabetes (13 vs. 6 years).

Mean baseline weight was 79 kg; the mean self-reported weight before diagnosis was 83 kg.

Patients followed a stepwise diabetes therapy, beginning with modified nutritional therapy followed by oral medications. Insulin was added if oral therapy failed to reach the glycemic goal of a hemoglobin A_{1c} level of less than 8%.

Weight among those taking only the oral medications stayed constant throughout the 7-year follow-up period, with no changes occurring after the transition from nutritional therapy to oral medication, and no significant difference from baseline to the end of follow-up.

In contrast, patients who added insulin to their treatment regimen experienced significant weight gain, gaining a mean of 2 kg in the period between the change and the end of the study.

However, the investigators noted, insulin was added at a time when the patients' blood glucose levels increased significantly to a mean of 9.4%; this increase was accompanied by a nonsignificant weight decrease. The mean weight increase of 2 kg did not cause patients to exceed their self-reported prediagnosis weight, or to significantly exceed their weight when treated by diet alone.

A large weight increase of more than 10 kg occurred in 22 subjects. Multivariate analysis identified younger age, higher HbA_{1c} levels, lower initial body mass index, and the absence of atherosclerotic heart disease as risk factors for high weight gain.

"The data uniquely present clear evidence that the increase in weight of diabetic patients, who in real life use insulin, is relative to their previous uncontrolled state preceding insulin usage and does not surpass the weight during previous stages of the disease," the authors said. ■

Low–Glycemic Index Diet Also Cuts Glucose Levels

BY JOHN R. BELL
Associate Editor

Patients with poorly controlled type 2 diabetes who for 1 year consumed a diet with a low glycemic index had reductions in their hemoglobin A_{1c} level similar to those seen with the diet recommended by the American Diabetes Association, according to research published in Nutrition.

Dr. Yusheng Ma of the University of Massachusetts, Worcester, and colleagues randomly assigned 40 individuals (age range 33-77 years; mean age 54 years) with type 2 diabetes and an HbA_{1c} of 7% or higher either to a diet based on the ADA recommendations (21) or to a diet that instead encouraged consumption of foods with a low glycemic index (19).

Participants received counseling monthly during the first 6 months and again at months 8 and 10, and completed a 7-day dietary recall at each visit.

In the ADA group, 52% of participants were men compared with 42% in the low–glycemic index (GI) group, though the difference was not statistically significant (Nutrition 2008;24:45-6).

Both mean HbA_{1c} level and total cholesterol level decreased over 12 months, with no significant difference between the two dietary groups.

Over the same period, HDL cholesterol increased in both groups. However, the mean LDL cholesterol level dropped from 89 mg/dL at baseline to 71 mg/dL at 12 months in the ADA group, while in the low-GI group, it rose, from 93 mg/dL at baseline to 95 mg/dL at 12 months.

Mean weight dropped in both groups, but mean waist circumference rose in both. Caloric intake in the ADA group was higher at 6 and 12 months while in the low-GI group it was lower at both time points.

Those participants in the low-GI group also were less likely to add or switch diabetes medications than were those in the ADA group (odds ratio 0.26), but this finding was also significantly associated with higher body mass index, high HbA_{1c} level, and male gender.

These results led the investigators to conclude that a low–glycemic index diet is equally able to reduce and control HbA_{1c} and blood lipids as the ADA-recommended diet, which entails carbohydrate counting without regard to glycemic index.

They acknowledged several limitations of the study, including lower attendance at counseling sessions among the low-GI group, and they cautioned that the findings warrant replication in a larger randomized controlled trial. ■