

# Antipsychotics Can Spur ‘Metabolic Train Wreck’

*Studies in youth show olanzapine confers highest risk of weight gain, risperidone the lowest risk.*

BY MICHELE G. SULLIVAN

EXPERT ANALYSIS FROM A  
PSYCHOPHARMACOLOGY UPDATE,  
SPONSORED BY THE AMERICAN ACADEMY  
OF CHILD AND ADOLESCENT PSYCHIATRY

NEW YORK – With new national data finding that 17% of the country’s youngsters are obese, physicians who treat children with antipsychotics face even tougher medication choices.

Because many of the drugs are tied to increases in weight and obesity-driven diseases, it’s not hard to see the looming metabolic train wreck, Dr. Christoph U. Correll said at the meeting.

The newest NHANES (National Health and Nutrition Survey), released in January, found that more than one-third of U.S. adults and almost 17% of youth were classified as obese in 2009-2010.

“We are now seeing obese children with type 2 diabetes, and we know that this disease has the same 8-year risk as a myocardial infarction for [another] heart attack,” said Dr. Correll of the Zucker Hillside Hospital in Glen Oak, N.Y. “We will see obese children who will not outlive their parents, and we must admit that our treatments are contributing to this.”

Studies show that many antipsychotic medications are associated with signifi-

cant weight gain, much of that leading to metabolic syndrome, Dr. Correll said. A 2011 meta-analysis of 3,000 children found that those taking olanzapine gained almost 4 kg within just 1 month of starting the medication (Euro. Psychiatry 2011;26:144-58). Quetiapine was associated with a gain of 2 kg over 4 weeks, and risperidone with a gain of 2 kg over 7 weeks. Patients taking aripiprazole gained 1 kg over 6 weeks, whereas those taking a placebo had no weight change.

This phenomenon is directly related to the onset of metabolic syndrome, and its associated cardiovascular risks of lipid abnormalities and hypertension, Dr. Correll said. “The longer you treat, the higher are these rates. And the longer you have cardiovascular risk factors, the greater your chance of death.”

A 2006 study illustrates his point. By 10 years of treatment, 21% of patients had metabolic syndrome; by 20 years of treatment, 34%, and after 20 years, 39%.

Age played a significant role, as expected, but a significant difference was found between the general population and patients taking the drugs. Among patients aged 35-45 years, 35% had metabolic syndrome, compared with 6.5% of nonpatients. By 55 years, the prevalence had doubled in the general population,

to about 14%, while it increased significantly less in patients, to 38%.

“This shows that we are shifting the metabolic burden to earlier in life. These patients are prematurely metabolically demented, and we are doing this by not taking care of their weight and metabolic problems.”

This leaves psychiatrists on the horns of a dilemma, Dr. Correll said. Patients need treatment, but the drugs come with a high physiological price. To decrease patients’ exposure to metabolic risks, he advises starting treatment with the lowest metabolically driven medications, and moving to other drugs only if the less risky ones aren’t controlling symptoms.

Studies suggest that, in most patients, olanzapine confers the greatest risk of weight gain, and risperidone the lowest. Lurasidone is doing “quite well” in adult studies, as far as weight gain goes (Drugs Today [Barc.] 2011;47:807-16), but it has not been examined in children or adolescents. “I think this is something we as pediatric psychiatrists should be trying to get our hands on,” Dr. Correll said.

A newly published, randomized trial suggests that valproate might change some of the metabolic activity that drives weight gain in patients taking antipsychotic medications.

Patients with treatment-resistant schizophrenia, schizoaffective disorder, or bipolar disorder were randomized to olanzapine or risperidone alone, or to ei-

ther of the drugs plus valproate as a mood stabilizer. Every one of those taking olanzapine plus valproate experienced significant weight gains, whereas the weight gain occurred in 60% of those taking olanzapine alone.

Weight gain was less common in both risperidone groups. But the addition of valproate seemed to enhance risperidone’s weight-neutral effect: Some 15% of those taking the combination gained significant amounts of weight – significantly fewer than the 30% who gained weight on risperidone alone (J. Clin. Psychiatry 2011;72:1602-10).

The same pattern held with other metabolic measures, including changes in body mass index, glycosylated hemoglobin, total cholesterol, and the triglyceride/HDL cholesterol ratio.

The findings point out just how much remains unknown about the metabolic effects of antipsychotic medications. For now, Dr. Correll said, the best path is to start with the lowest metabolically active drug appropriate for that patient, and closely monitor any metabolic changes.

“At each visit, obtain both weight and body mass index,” he said. “Measure waist circumference at least once a year, and provide counseling on diet and exercise.”

Dr. Correll disclosed that he is a consultant for and is on the advisory boards of numerous drug companies, and also receives research support and honoraria from many of them. ■

## Duodenal Switch May Excel at Type 2 Diabetes Resolution

BY PATRICE WENDLING

FROM THE ANNUAL MEETING  
OF THE CENTRAL SURGICAL  
ASSOCIATION

MADISON, WIS. – Total complication rates are high but comparable over the long term between duodenal switch surgery and Roux-en-Y gastric

a study that focused on the long-term outcomes of 178 consecutive patients who underwent duodenal switch (DS) surgery and 139 propensity matched patients undergoing RYGB. In addition to a chart review, the University of Minnesota Bariatric Surgery Outcomes Survey tool was used to prospectively track

patients’ weight, comorbid illnesses, adverse outcomes, readmissions, and general health status. Mean follow-up was 3.7 years in the DS group and 6.2 years in the RYGB group.

There were five deaths in the

DS group (postop day 38 and months 5, 7, 16, and 66) and three deaths in the RYGB group (postop months 3, 7, and 72), leaving 173 patients and 136 patients, respectively, in the analysis, Dr. Dorman said at the meeting.

Notably, weight loss in the two groups was comparable, decreasing from an average body mass index of 52 kg/m<sup>2</sup> to 31

kg/m<sup>2</sup> in the DS group and from 51 kg/m<sup>2</sup> to 34 kg/m<sup>2</sup> in the RYGB group, said Dr. Dorman, a surgery resident at the University of Minnesota, Minneapolis.

Resolution of type 2 diabetes, hypertension, and hyperlipidemia was greatest among DS patients at 82%, 67%, and 81%, respectively, compared with 64%, 39%, and 55%, respectively, among RYGB patients.

DS patients, however, experienced significantly more loose stools, bloating, and heartburn than did RYGB patients, who had significantly more constipation. Nausea and emesis were comparable between the two groups.

With regard to complications, DS patients were significantly more likely to visit the emergency department than were RYGB patients (40% vs. 25%) and to experience hair loss (67% vs. 41%), Dr. Dorman said.

There was also a nonsignificant trend for DS patients to be readmitted more often than RYGB patients (25.4% vs. 23.5%) and to have more gastrointestinal leaks (1.7% vs. 0%), abdominal reoperations (29% vs. 23%), total parenteral nutrition/tube feeds (7.6% vs.

3%), and infusion therapy (28.5% vs. 23.5%). The RYGB patients, however, underwent more endoscopy (22% vs. 14%).

Dr. Dorman said providers should explain to patients the adverse symptoms they can expect following DS, but noted that the investigators “still feel DS should be limited to surgeons and centers with experience.”

Invited discussant Dr. James Wallace, a bariatric and general surgeon from the Medical College of Wisconsin, Milwaukee, described the 40% rate of ED

visits in the DS group as “extreme,” and questioned the use of nutritional, vitamin, and protein supplementation – particularly in light of the observed hair loss. “I’m unconvinced that the incremental improvement in weight loss and resolution of metabolic derangements justifies the increased nutritional risk of the duodenal switch,” he said.

Dr. Dorman responded that the ED visits may represent a “knee-jerk reflex” on the part of DS patients when they experience a complication. ■

VITALS

**Major Finding:** Resolution of type 2 diabetes, hypertension, and hyperlipidemia was greatest among duodenal switch patients, at 82%, 67%, and 81%, vs. 64%, 39%, and 55% among Roux-en-Y gastric bypass patients.

**Data Source:** Data were taken from a chart review and prospective survey of 309 superobese patients.

**Disclosures:** Dr. Dorman reported no relevant conflicts of interest.

bypass, according to a propensity matched analysis of 309 superobese patients.

“Duodenal switch is a valid alternative to the Roux-en-Y gastric [RYGB] bypass,” especially if diabetes is present, Dr. Robert B. Dorman said. Duodenal switch appears to provide superior resolution of type 2 diabetes.

His conclusion is drawn from



Duodenal switch seems to provide superior resolution to type 2 diabetes than Roux-en-Y gastric bypass, said Dr. Robert B. Dorman.

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