Outpatient Metformin Management of Obese Individuals With Schizophrenia

To the Editor: Antipsychotic medications are indispensable for the treatment of schizophrenia, but side effects of weight gain and obesity,[1] often accompanied by type 2 diabetes, are significant contributors to diminished life expectancy for patients with the schizophrenia.[2] The type 2 diabetes drug metformin is effective for weight loss among schizophrenia patients receiving antipsychotics in controlled research studies.[2–4] Whether metformin can be similarly effective after discharge when treatment is provided by local mental health outpatient clinics remains undemonstrated.

Method. Recently admitted patients with *DSM-IV* chronic schizophrenia or schizoaffective disorder, with body mass index (BMI) ≥ 30, serum creatinine ≤ 1.5 μmol/L, and no history of type 2 diabetes (glycated hemoglobin [HbA_{1c}] ≤ 6.4% and fasting blood sugar [FBS] ≤ 110 mmol/L), participated in our program of metformin sustained release (1,500 mg/d), individualized exercise, and dietary counseling. All patients were receiving a multitude of psychotropic agents.[5] Metformin was prescribed therapeutically after a full and witnessed patient-clinician discussion (noted in the hospital chart) of the risks and benefits of the drug; Declaration of Helsinki guidelines were followed in the absence of an ethical review committee. Measures included weight, HbA_{1c}, FBS, and a metabolic panel with a lipid profile. Of 47 qualified patients, 35 with BMI ranging from 30.2 to 51.9 (mean ± SD = 38.9 ± 5.5) and aged from 20 to 63 years (mean ± SD = 41.6 ± 11.1) were still in hospital and evaluated at 8 weeks. The 16 patients still in hospital at 16 weeks were again evaluated. Metformin was well tolerated by all patients. At discharge, patients were assigned a state-certified peer wellness counselor to facilitate program compliance and were entered into an outpatient program for 3 months of follow-up. Outpatient physicians were asked to prescribe metformin.

Results. Nonparametric statistics were used. For the 35 patients who were still in hospital at 8 weeks, mean ± SD baseline and 8-week weights were 108.6 ± 17.1 and 105.4 ± 15.7 kg, respectively, which represented a significant loss of 3.2 kg ($Z = -4.10$, $P = .00$, Wilcoxon matched-pairs signed rank test[6]). For the 16 patients still in hospital at 16 weeks, baseline, 8-week, and 16-week weights were 106.3 ± 17.1, 103.6 ± 17.7, and 103.5 ± 19.7 kg, respectively. Friedman analysis of variance[6] for baseline, 8 weeks, and 16 weeks indicated an overall effect of metformin ($\chi^2_2 = 8.18$, $P = .02$), with a significant 2.7-kg loss from baseline to 8 weeks ($Z = -3.02$, $P = .00$, Wilcoxon test[6]) and a nonsignificant 2.8-kg loss from baseline to 16 weeks ($Z = -1.60$, $P = .11$, Wilcoxon test[6]). No other measure showed significant change. Of the 35 patients discharged into 3-month follow-up, 20 could no longer be located by 3 months; of the remaining 15, 10 were still taking metformin and 5 were not, with weights of 109.2 ± 13.3 and 107.4 ± 19.4, respectively. There was no significant difference in weight between these 2 groups at 3 months ($Z = -0.74$, $P = .46$, Mann-Whitney rank sum test[6]), or between baseline and 3-month postdischarge weights in either group.

Our findings corroborate inpatient weight reduction with metformin for obese patients receiving polypharmacy, but discharged patients did not sustain weight loss at 3 months after discharge, since baseline and 3-month weights did not differ. There was also no weight difference between patients who did and did not remain on metformin, although small sample size and high variability may have precluded observing any difference. Of utmost importance, however, is that our single peer wellness coach and limited resources were inadequate to ensure compliance or monitor patient activity. Also, physicians were reluctant to prescribe metformin for nondiabetic patients. If the long-term benefits of metformin for managing obesity and its long-term consequences in patients receiving psychoactive drugs in the community are to be realized, major commitments to community aftercare services and physician education will be required.

REFERENCES

1. Allison DB, Mentore JL, Heo M, et al. Antipsychotic-induced weight gain: a comprehensive research synthesis. *Am J Psychiatry*. 1999;156(11):1686–1696.
2. Correll CU, Sikich L, Reeves G, et al. Metformin for antipsychotic-related weight gain and metabolic abnormalities: when, for whom, and for how long? *Am J Psychiatry*. 2013;170(9):947–952.
3. Jarskog LF, Hamer RM, Catellier DJ, et al; METS Investigators. Metformin for weight loss and metabolic control in overweight outpatients with schizophrenia and schizoaffective disorder. *Am J Psychiatry*. 2013;170(9):1032–1040.
4. Chen CH, Huang MC, Kao CF, et al. Effects of adjunctive metformin on metabolic traits in nondiabetic clozapine-treated patients with schizophrenia and the effect of metformin discontinuation on body weight: a 24-week, randomized, double-blind, placebo-controlled study. *J Clin Psychiatry*. 2013;74(5):e424–e430.
5. Winsberg B, Yeager C, Hobbs B, et al. Metformin provides weight reduction for hospitalized patients receiving polypharmacy. *J Clin Psychopharmacol*. 2010;30(3):345–346.
6. SPSS Version 12.0.1 for Windows [computer program]. Chicago IL: SPSS, Inc; 2003.

Bertrand Winsberg, MD
bgw436@aol.com
Ronald Wei, MD
Natarajan Elangovan, MD
Janet Camp-Lifshitz, MPhil

Author affiliations: Private Practice, Great Neck, New York, and Department of Psychiatry, Robert Wood Johnson Medical School, University of Medicine and Dentistry of New Jersey, New Brunswick (Dr Winsberg); Essex County Hospital Center, Cedar Grove (Dr Wei), New Jersey; Private Practice, Staten Island (Dr Elangovan); and Psychiatric Research Consultant, Pomona (Ms Camp-Lifshitz), New York.

Potential conflicts of interest: None reported.
Funding/support: Supported in part by grant CDC1H75DP003079-01, Centers for Disease Control and Prevention, Atlanta, Georgia.
Published online: November 6, 2014.
Prim Care Companion CNS Disord 2014;16(6):doi:10.4088/PCC.14l01687