Lipid Monitoring in Patients With Schizophrenia Prescribed Second-Generation Antipsychotics

Ellen M. Weissman, M.D., M.P.H.; Carolyn W. Zhu, Ph.D.; Nina R. Schooler, Ph.D.; Raymond R. Goetz, Ph.D.; and Susan M. Essock, Ph.D.

Objectives: Treatment with second-generation antipsychotic (SGA) medications has been linked with increased rates of the metabolic syndrome (i.e., dyslipidemia, obesity, and hyperglycemia). Several sets of published recommendations now provide clinicians with guidelines for monitoring metabolic parameters in individuals with schizophrenia treated with SGAs. However, few data are available regarding actual metabolic monitoring practices in this patient population. The objectives of the study were to determine baseline lipid monitoring rates for individuals with schizophrenia prescribed SGAs during the period prior to the publication of monitoring guidelines and to determine whether individuals with abnormal lipid levels received follow-up monitoring sooner than individuals with normal levels.

Method: Lipid monitoring rates for 408 individuals with schizophrenia who were prescribed SGAs from October 1999 to October 2003 were examined using administrative data from a Veterans Affairs facility. Survival analysis was used to examine time to follow-up lipid measurement and to compare time to follow-up measure for individuals with normal initial lipid levels versus those with elevated initial lipid levels.

Results: Eighty-five percent of individuals had at least 1 measurement for total cholesterol or triglycerides in a 4-year period. Abnormal initial measurements predicted significantly earlier follow-up monitoring ($p < .005$ for total cholesterol, $p < .05$ for triglycerides, $p < .001$ for low-density lipoprotein cholesterol). However, median time to follow-up measure was 304 days (approximately 10 months) for individuals with elevated total cholesterol levels, which is too long for optimal clinical follow-up.

Conclusion: Program managers and clinicians should assess adequacy of monitoring and support quality improvement initiatives in this area.

(J Clin Psychiatry 2006;67:1323–1326)

Received Oct. 12, 2005; accepted Feb. 20, 2006. *From the Mental Illness Research, Education and Clinical Center VISN 3, Bronx VA Medical Center, Bronx, N.Y. (Drs. Weissman, Goetz, and Essock); the Department of Psychiatry, Mt. Sinai School of Medicine, New York, N.Y. (Drs. Weissman, Goetz, and Essock); the Geriatric Research, Education and Clinical Center, Bronx VA Medical Center, Bronx, N.Y. (Dr. Zhu); the Mental Illness Research, Education and Clinical Center VISN 5, Washington VA Medical Center, Washington, D.C. (Dr. Schooler); and the Department of Psychiatry, Georgetown University School of Medicine, Washington, D.C. (Dr. Schooler).*

This work was supported by the Mental Illness Research, Education and Clinical Center of the Veterans Integrated Service Network 3.

The authors report no additional financial affiliation or other relationship relevant to the subject of this article.

The authors thank David Kaplow, M.S., VA New York Harbor Healthcare System, for assistance with data acquisition for this study.

Corresponding author and reprints: Ellen M. Weissman, M.D., Mental Illness Research, Education and Clinical Center, Bronx VA Medical Center, 130 West Kingsbridge Rd. (OOMH), Bronx, NY 10468 (e-mail: ellenweissman@optonline.net).

Medical specialty groups and researchers have developed guidelines for monitoring metabolic parameters in patients treated with second-generation antipsychotic medications (SGAs) in response to growing concern about metabolic abnormalities among patients receiving these agents.[1,2] Individuals with schizophrenia and related disorders are at increased risk for developing what is called the metabolic syndrome, which includes dyslipidemia, obesity, and hyperglycemia.[3–7] The risk may be further elevated for individuals with particular demographic characteristics (e.g., Hispanic Americans,[8] women[7]). Treatment with certain SGAs also exacerbates metabolic risk.[9–14]

Little is known regarding rates of metabolic monitoring among patients prescribed SGAs. A study in the United Kingdom found that lipid levels were recorded in charts of only 3.5% of 606 inpatients prescribed antipsychotic medications.[15] We are unaware of any published studies documenting rates of metabolic monitoring among patients prescribed SGAs in the United States. Understanding current monitoring practices is essential for developing interventions to improve monitoring.

This study examined lipid monitoring rates for outpatients with schizophrenia treated with SGAs at the Bronx Veterans Affairs (VA) Medical Center (Bronx, N.Y.). Be-

  © Copyright 2006 Physicians Postgraduate Press, Inc.

cause the VA is an integrated health care system, monitoring may be provided either in the psychiatric setting or elsewhere in the system. All clinicians have access to results via a single electronic medical record. Therefore, the VA is a good place to examine baseline rates of monitoring minimally constrained by communication barriers across psychiatric and nonpsychiatric clinics. This report provides preliminary data from an ongoing comprehensive study of metabolic monitoring practices at multiple VA sites in the New York metropolitan region. Given the lack of published data on monitoring practices and growing recognition of the importance of the metabolic syndrome, these preliminary data are of interest to the field.

The aims of the study were to determine baseline lipid monitoring rates and whether individuals with abnormal lipid levels received follow-up monitoring sooner than individuals with normal baseline levels.

METHOD

The study is a retrospective analysis conducted using administrative data from the local VA databases. The Bronx VA Institutional Review Board granted a waiver of informed consent for the study. Patients prescribed any antipsychotic medication from October 1999 to October 2003 were identified using data from local VA databases. The study population was limited to individuals under age 65 with schizophrenia or schizoaffective disorder diagnosed at 2 or more mental health visits who had at least 60 days of exposure to SGAs. Diagnoses at mental health visits were tabulated for schizophrenia/schizoaffective disorder, bipolar disorder, and other psychotic disorders, and individuals who had a plurality of diagnoses for either bipolar disorder or other psychotic disorder were excluded from the study population. Individuals 65 years of age or older were excluded for this analysis in order to minimize the potential impact of medical complications of aging as a confounder on monitoring rates. Frequency of measurements for total cholesterol, triglycerides, high-density lipoprotein (HDL), and low-density lipoprotein (LDL) during the 4-year study period were examined.

The proportion of individuals receiving any monitoring for total cholesterol was determined. For individuals with at least 1 measurement, the initial total cholesterol level was categorized as normal (< 200 mg/dL) or abnormal (≥ 200 mg/dL) based on National Cholesterol Education Program Adult Treatment Panel III (ATP III) guidelines for desirable total cholesterol levels.[16] Time to follow-up measure for individuals with normal (desirable) total cholesterol levels was compared to that for individuals with abnormal levels (borderline high or high) using survival analysis and log-rank tests. As a sensitivity analysis, the analysis was repeated using total cholesterol ≥ 240 mg/dL to define abnormal values (this time categorizing individuals with borderline high total cholesterol as having normal values).

Similar analyses were performed for triglycerides, HDL cholesterol, and LDL cholesterol. In accordance with ATP III guidelines, normal triglycerides were defined as < 150 mg/dL, normal HDL cholesterol as ≥ 40 mg/dL, and normal LDL cholesterol as < 130 mg/dL (including "optimal" and "near optimal" levels). Sensitivity analyses were performed using cutoff points of 200 mg/dL (triglycerides), 60 mg/dL (HDL), and 100 and 160 mg/dL (LDL) to define normal values. These cutoffs were chosen for the sensitivity analyses based on definitions for borderline lipid levels set forth by ATP III.

RESULTS

The study population included 408 individuals, 383 (94%) male and 25 (6%) female, with a mean ± SD age of 45.9 ± 8.7 years. One hundred ninety-six individuals (48%) were never married, 135 (33%) were divorced or separated, 75 (19%) were married or widowed, and 2 (0%) were of unknown marital status. Three hundred fifteen individuals (77%) were not employed, 30 (7%) were employed full-time, and the rest were either employed part-time or retired.

Of 408 individuals in the sample, 348 (85%) had at least 1 total cholesterol measure, of whom 111 (27%) had only one measurement. Time to follow-up measure was significantly shorter for individuals with abnormal first measurements (Figure 1). Median time to follow-up measure was 412 days (304 days if initial measure was ≥ 200 mg/dL vs. 552 days if initial measurement was normal) ($\chi^2 = 10.5$, df = 1, $p < .005$). The sensitivity analysis yielded a similar pattern when abnormal cholesterol was defined as ≥ 240 mg/dL.

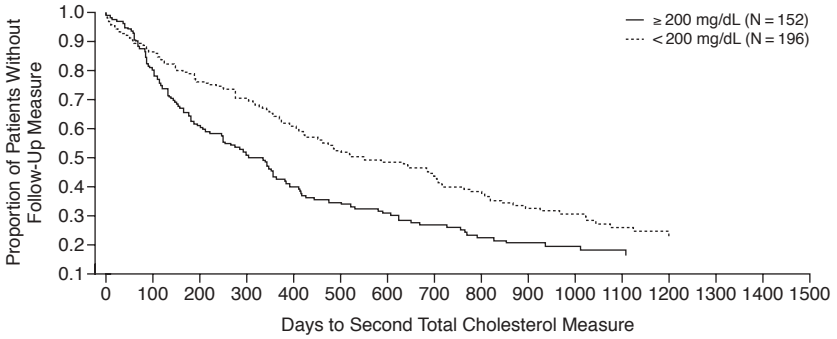
Results for triglyceride monitoring were similar to those for cholesterol. Three hundred forty-eight individuals (85%) had at least 1 triglyceride measurement, of whom 111 (27%) had only 1. Median time to follow-up measure was 412 days (347 days if initial measure was ≥ 150 mg/dL vs. 490 days if initial measure was normal) ($\chi^2 = 4.00$, df = 1, $p < .05$). A similar pattern was seen using ≥ 200 mg/dL to define abnormal triglycerides; however, the difference was not statistically significant.

Three hundred one individuals (74%) had LDL measurements, of whom 113 (28%) had only 1. Median time to follow-up measure was 486 days (344 days if initial measure was ≥ 130 mg/dL vs. 641 days if initial measure was normal) ($\chi^2 = 13.1$, df = 1, $p < .001$). A similar pattern was seen using LDL ≥ 100 mg/dL as the threshold for abnormal LDL, and a nonsignificant trend toward longer time to follow-up measure was seen when 160 mg/dL was the threshold used.

Three hundred twelve individuals (76%) had HDL measurements. Among those with at least 1 measurement,

  © Copyright 2006 Physicians Postgraduate Press, Inc.

Figure 1. Follow-Up Total Cholesterol Monitoring for Patients With Schizophrenia Treated With Second-Generation Antipsychotic Medications by Initial Total Cholesterol Category[a]



[a]Significantly shorter time to follow-up measurement for patients with elevated initial cholesterol measurement ≥ 200 mg/dL, log-rank test ($\chi^2 = 10.5$, df = 1, $p < .005$).

time to follow-up measurement using either 40 mg/dL or 60 mg/dL as the threshold for abnormal HDL was not statistically significant.

DISCUSSION

This is the first known report to examine the frequency of lipid monitoring for individuals with schizophrenia prescribed SGAs and the first to find more frequent follow-up monitoring among individuals with abnormal total cholesterol. It is somewhat reassuring that these patients are monitored more frequently than individuals with normal levels. However, median time to follow-up of abnormal cholesterol levels was 304 days. Among individuals with elevated cholesterol levels, more frequent follow-up is indicated to assess either the persistence of abnormal values prior to initiating lipid-lowering treatment (indicating the need for intervention) or the effectiveness of ongoing treatment. For example, ATP III recommends assessing the effectiveness of lifestyle changes and/or drug therapy at 6 and 12 weeks, then at 4- to 6-month intervals.[16] Without timely follow-up, additional behavioral or pharmacologic interventions may be unnecessarily delayed. Even when individuals with borderline levels (200–239 mg/dL) were excluded from the abnormal group, median time to follow-up measure was 250 days.

The relationship between abnormal initial measurement and earlier follow-up was strongest for total cholesterol and LDL. Comparisons of time to follow-up monitoring for normal versus abnormal initial LDL measurement are complicated because LDL target levels vary with the number of cardiac risk factors an individual exhibits. The same patients who had levels for total cholesterol also had triglyceride levels monitored, with nearly universal overlap on the dates, suggesting that these had probably been ordered as part of a lipid panel.

The study is limited to 1 VA setting. The findings may not be generalizable, particularly to settings where primary care and psychiatry are not integrated into a single health system. However, our results suggest that even in an integrated setting (a "best case" system scenario for monitoring), improvement in monitoring for individuals with abnormal lipids is needed. The VA has a further advantage; most veterans pay low fees for their care, and care is minimally constrained by payment issues. These results may reflect higher monitoring frequencies than could be expected in public settings with less integration and less generous funding, underscoring the importance of improving monitoring across these settings.

The present study does not assess the impact of specific patient and provider factors on monitoring. However, all patients were treated for schizophrenia or schizoaffective disorder and received SGAs for at least 60 days during the observation period. Thus, we report prevalence of metabolic monitoring in a previously unstudied cohort. Our primary purpose was to examine monitoring rates in this population and to compare lipid monitoring for individuals with normal versus abnormal levels at the index lipid measurement. Thus, we did not examine monitoring in a control group without schizophrenia. Results reported here are limited to lipid monitoring; other metabolic measures such as glucose and body mass index are also important components of the metabolic syndrome. These results represent a first step in assessing current metabolic monitoring practices. This study examined practice prior to publication of the American Psychiatric Association/American Diabetes Association[2] or Mount Sinai[1] monitoring guidelines and provides a baseline for future studies assessing the impact of guidelines on monitoring rates.

Future analyses are needed to examine the relationship between monitoring and SGA prescribing (e.g., are baseline metabolic studies done prior to initiating treatment with a new antipsychotic medication? Are individuals

prescribed certain antipsychotic agents or not taking antipsychotic medication monitored at different rates?) as well as the association of patient factors (e.g., demographic variables, comorbid disorders such as obesity and substance abuse, evidence of treatment for hyperlipidemia) and provider factors with differential rates of monitoring.

CONCLUSION

Preliminary results suggest that, in a VA health care network, more than three quarters of individuals with schizophrenia who are prescribed antipsychotic medication receive monitoring for lipids in a 4-year period. While it was encouraging that individuals with abnormal initial measurements were followed up sooner than those with normal initial levels, the median time to follow-up measurement for those with abnormal initial levels was 10 months, too long for optimal clinical care. Monitoring frequency may be even lower in other public settings that lack integrated primary care services. Program managers and clinicians should assess adequacy of monitoring and support quality improvement initiatives in this area.

REFERENCES

1. Marder SR, Essock SM, Miller AL, et al. Physical monitoring of patients with schizophrenia. Am J Psychiatry 2004;161:1334–1349
2. American Diabetes Association, American Psychiatric Association, American Association of Clinical Endocrinologists, and the North American Association for the Study of Obesity. Consensus development conference on antipsychotic drugs and obesity and diabetes. J Clin Psychiatry 2004;65:267–272
3. Saari KM, Lindeman SM, Viilo KM, et al. A 4-fold risk of metabolic syndrome in patients with schizophrenia: the Northern Finland 1966 Birth Cohort study. J Clin Psychiatry 2005;66:559–563
4. Heiskanen T, Niskanen L, Lyytikainen R, et al. Metabolic syndrome in patients with schizophrenia. J Clin Psychiatry 2003;64:575–579
5. Saari K, Jokelainen J, Veijola J, et al. Serum lipids in schizophrenia and other functional psychoses: a general population northern Finland 1966 birth cohort survey. Acta Psychiatr Scand 2004;110:279–285
6. Allison DB, Fontaine KR, Heo M, et al. The distribution of body mass index among individuals with and without schizophrenia. J Clin Psychiatry 1999;60:215–220
7. Homel P, Casey D, Allison DB. Changes in body mass index for individuals with and without schizophrenia, 1987–1996. Schizophr Res 2002;55:277–284
8. Kato MM, Currier MB, Gomez CM, et al. Prevalence of metabolic syndrome in Hispanic and non-Hispanic patients with schizophrenia. Prim Care Companion J Clin Psychiatry 2004;6:74–77
9. Allison DB, Casey DE. Antipsychotic-induced weight gain: a review of the literature. J Clin Psychiatry 2001;62(suppl 7):22–31
10. Sernyak MJ, Leslie DL, Alarcon RD, et al. Association of diabetes mellitus with use of atypical neuroleptics in the treatment of schizophrenia. Am J Psychiatry 2002;159:561–566
11. Lindenmayer JP, Czobor P, Volavka J, et al. Changes in glucose and cholesterol levels in patients with schizophrenia treated with typical or atypical antipsychotics. Am J Psychiatry 2003;160:290–296
12. Newcomer JW. Metabolic risk during antipsychotic treatment. Clin Ther 2004;26:1936–1946
13. Koro CE, Fedder DO, L'Italien GJ, et al. Assessment of independent effect of olanzapine and risperidone on risk of diabetes among patients with schizophrenia: population based nested case-control study. BMJ 2002;325:243–245
14. Lieberman JA, Stroup TS, McEvoy JP, et al. Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. N Engl J Med 2005; 353:1209–1223
15. Paton C, Esop R, Young C, et al. Obesity, dyslipidaemias and smoking in an inpatient population treated with antipsychotic drugs. Acta Psychiatr Scand 2004;110:299–305
16. National Cholesterol Education Program. Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Bethesda, Md: National Institutes of Health; 2001. Publication no. 013670. Available at: http://www.nhlbi.nih.gov/guidelines/cholesterol/atp3full.pdf. Accessibility verified June 23, 2006