Prevalence of Diabetes Mellitus Among Outpatients With Severe Mental Disorders Receiving Atypical Antipsychotic Drugs

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Background: Recent studies have suggested that patients receiving atypical antipsychotic drugs are at increased risk for developing diabetes mellitus. The purpose of this study is to examine the prevalence of diabetes in a group of adults with schizophrenia and other severe mental disorders receiving atypical antipsychotic drugs within a community mental health center setting.

Method: A retrospective chart review was conducted on 436 outpatients receiving either atypical antipsychotic or decanoate antipsychotic drugs at a community mental health center. Diagnosis of diabetes was established through the presence of documentation in the medical record. Patients with a history of diabetes prior to age 18 years were excluded. Data were gathered from April 2001 through September 2002.

Results: The mean (SD) age of patients was 42.5 (10.8) years, and 57.3% were men. Patients were 61.5% white, 31.8% black, 5.3% Hispanic, and 2.3% other. Seventeen percent of patients had a positive family history of diabetes. Point prevalence of diabetes was 14.2% for the entire group. Chi-square analysis for the group revealed significant effects of age ($\chi^2 = 16.514$, $p < .001$), family history of diabetes ($\chi^2 = 27.128$, $p < .001$), and gender ($\chi^2 = 14.114$, $p < .001$). A trend was noted toward a higher prevalence of diabetes among patients receiving atypical drugs (15.2%) compared with those receiving decanoate drugs (6.3%) ($\chi^2 = 2.984$, $p = .078$).

Conclusion: Prevalence of diabetes mellitus among outpatients with severe mental disorders receiving atypical antipsychotic drugs is substantially higher than that reported in the general population. Results of this study are limited by the retrospective methodology, which may underestimate actual prevalence by failing to detect undiagnosed cases.

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Patients with severe mental disorders receiving antipsychotic drugs have an increased risk for developing diabetes mellitus. Reviewing large national samples of patients with schizophrenia, Dixon and colleagues[1] found the prevalence of treated diabetes to range from 9% to 14%. These rates were significantly higher than the 1.2% and 6.3% rates found in the general population for ages 18 to 44 and 45 to 64, respectively, by the National Health Interview Survey.[2] Multiple factors most likely contribute to this difference. Persons with schizophrenia and other severe mental disorders share many well-established demographic risk factors for diabetes with the general population. These risk factors include a positive family history of diabetes, age > 40 years, and black, Hispanic, or other minority race/ethnicity. However, the extent to which demographic factors are associated with risk of developing diabetes among persons with severe mental illness receiving antipsychotic drugs has not been well studied.

Some evidence suggests that individuals with schizophrenia may have additional risk due to the disease of schizophrenia itself. Prior to the discovery of chlorpromazine, several studies reported the presence of reduced glucose tolerance among patients with schizophrenia.[3–9] However, fasting blood glucose among patients with

schizophrenia was usually normal in these studies. Mukherjee et al.[10] reported that diabetes was more common among patients not receiving antipsychotic drugs than in those receiving such treatment, but their medication-free group numbered only 8 patients. In a recent study of drug-naïve patients with schizophrenia by Ryan and colleagues,[11] patients were found to have higher fasting blood glucose levels and more insulin resistance than were controls, although none had diabetes.

The role of antipsychotic medications as a risk factor for development of diabetes mellitus among persons with severe mental disorders has received considerable attention since the introduction of chlorpromazine. Initial reports were published in the 1950s and 1960s of diabetes associated with phenothiazine treatment.[12–19] Examining a group of 528 hospitalized women with various psychotic disorders, Thonnard-Neumann[19] reported in 1968 that 8.6% of phenothiazine-naïve patients had diabetes, while 27% of those receiving phenothiazines had diabetes. More recently, some studies have suggested that patients receiving the newer "atypical" antipsychotic drugs may be at particularly high risk for developing diabetes. In a study of 38,632 patients with schizophrenia within the Veterans Affairs system, those receiving atypical drugs were 9% more likely to have diabetes than were those receiving typical drugs.[20] In a naturalistic study by Henderson and colleagues[21] of 82 outpatients with schizophrenia or schizoaffective disorder receiving clozapine, 36.6% were diagnosed with diabetes over a 5-year period.

While these studies show a high prevalence of diabetes mellitus associated with antipsychotic drugs, there is a paucity of research examining incidence rates of diabetes associated with individual medications. Also, few studies to date have examined large samples of outpatients treated in community mental health center settings. In addition, relatively little is known about the contribution of established demographic risk factors to the development of diabetes among persons with severe mental illness. The purpose of this study is to examine the prevalence of diabetes within a community mental health center setting among adults with schizophrenia and other severe mental disorders receiving treatment with atypical antipsychotic drugs. The study will also examine the relationship between established demographic risk factors for diabetes and the prevalence of diabetes within the target population.

METHOD

A review of medical records was conducted on a convenience sample of 436 of approximately 1000 adult outpatients receiving antipsychotic drugs at Strong Ties Community Support Program, Rochester, N.Y. Strong Ties is an ambulatory care program of the University of Rochester Medical Center Department of Psychiatry providing comprehensive treatment for adults with severe mental disorders. The program features an on-site pharmacy and a primary care clinic that offer services to all patients. Study inclusion criteria were: age 18 years or older, presence of a clinical diagnosis of a psychotic disorder or major mood disorder, and treatment with a single atypical antipsychotic drug for at least 3 months (with or without concomitant psychotropic drugs). Patients with history of diabetes onset prior to age 18 years were excluded from the study. Records of patients receiving treatment with either haloperidol decanoate or fluphenazine decanoate were included for comparison purposes. The study was reviewed and approved by the University of Rochester Research Subject Review Board. Data were gathered from April 2001 through September 2002.

Medical records were identified by pharmacy staff through examination of the Strong Ties pharmacy database. Reviews were subsequently performed to collect the following information from each medical record: demographic information, primary DSM-IV Axis I diagnosis, family history of diabetes, current antipsychotic medication with dose and start date, date of first antipsychotic use, and number and type of concomitant medications. Diagnosis of diabetes mellitus was established through documentation in the medical record. Date of diabetes diagnosis, presence of diabetes treatment, presence of concomitant antipsychotic drug treatment at the time of diagnosis, and start date of concomitant antipsychotic drug treatment were recorded from each medical record.

In cases where dates were unclear, the following rules were used. When partial dates were available, either the last day of the month or the last month of the year was used. When dates of multiple psychiatric hospitalizations were available without information on drug therapy before or during the initial hospitalizations, the date of discharge from the second hospitalization was used as the date of first antipsychotic use. When the actual date of diabetes diagnosis was unclear, the first documentation in the medical record of diabetes was used as the date of diagnosis. All data were transcribed into data collection forms and entered into a secure Microsoft Access database (Microsoft Corp., Redmond, Wash.). Data analysis was conducted using SPSS (SPSS, Chicago, Ill.) and SAS (SAS Institute, Cary, N.C.) software.

RESULTS

The mean ± SD age of subjects was 42.5 ± 10.8 years, and 57.3% of patients were men. Patients were 61.5% white, 31.8% black, 5.3% Hispanic, and 2.3% other. The DSM-IV[22] Axis I diagnosis breakdown for the group was 45.0% schizophrenia, 29.1% schizoaffective disorder, 8.0% bipolar disorder, 7.4% major depressive disorder, 6.7% psychotic disorder not otherwise specified, and 3.8% other diagnoses. Seventeen percent of patients had a positive family history of diabetes.

Table 1. Antipsychotic Drug (APD) History and Diabetes Mellitus Prevalence Rates

Current APD	Years On Current APD, Mean (SD)	Total Years On All APDs, Mean (SD)	Patients With Diabetes On Current APD, N (%)	Patients Diagnosed With Diabetes While On Current APD, N (%)	Patients Diagnosed With Diabetes Before Current APD, N (%)
Clozapine (N = 141)	5.64 (3.77)	16.38 (8.05)	22 (15.6)	10 (7.1)	12 (8.5)
Olanzapine (N = 104)	3.87 (1.33)	13.77 (10.11)	15 (14.4)	8 (7.7)	7 (6.7)
Risperidone (N = 86)	3.45 (1.69)	10.52 (9.04)	13 (15.1)	7 (8.1)	6 (7.0)
Quetiapine (N = 57)	2.72 (1.16)	9.98 (8.72)	9 (15.8)	1 (1.8)	8 (14.0)
Fluphenazine decanoate (N = 29)	9.36 (5.78)	21.37 (8.80)	1 (3.4)	1 (3.4)	NA
Haloperidol decanoate (N = 19)	7.26 (5.16)	15.19 (11.16)	2 (10.5)	2 (10.5)	NA
Total (N = 436)	4.72 (3.46)	14.04 (9.50)	62 (14.2)	29 (6.7)	33 (7.6)

Abbreviation: NA = not applicable.

Table 1 summarizes the antipsychotic drug history of the study group and prevalence rates of diabetes by antipsychotic drug type. Of the 33 patients diagnosed with diabetes prior to receiving their current antipsychotic drug, 8 were diagnosed prior to receiving any antipsychotic drug, 6 were receiving typical drugs, 3 were receiving risperidone, 2 were receiving olanzapine, 1 was receiving quetiapine, 1 was receiving clozapine, and 1 was receiving ziprasidone. No data were available for the 11 remaining patients. The most commonly prescribed concomitant medications for the study group were benzodiazepines (24.5%, 107 patients), divalproex sodium (23.6%, 103 patients), selective serotonin reuptake inhibitors (21.1%, 92 patients), and anticholinergics (13.8%, 60 patients).

Prevalence of diabetes mellitus for the entire study group was 14.2% (N = 62 of 436). A trend was noted for higher prevalence rates of diabetes among patients receiving atypical antipsychotic drugs (15.2%; N = 59 of 388) compared with those receiving decanoate medications (6.3%; N = 3 of 48) ($\chi^2 = 2.984$, p = .078). No significant difference was found between the prevalence rate of diabetes among patients with schizophrenia (13.8%; N = 27 of 196 patients) and the prevalence rate found in the rest of the study group (14.6%; N = 35 of 240 patients) ($\chi^2 = 0.673$, p = .41). In addition, no association was found between divalproex sodium treatment and diabetes diagnosis ($\chi^2 = 2.615$, 2-sided Fisher exact test for significance = 0.118).

An analysis was performed to examine the relationship between duration of antipsychotic drug exposure and presence of diabetes. A Cox regression of the effect of length of time on antipsychotic drugs controlling for age, both for total years on all antipsychotics and years on current antipsychotic, was conducted using SAS PROC PHREG (SAS Institute, Cary, N.C.). Age showed little impact on length of time on antipsychotic drugs and the development of diabetes (SE = 0.02, $\chi^2 = 0.094$, p = .76, hazard ratio = 0.99). Separate general linear model analyses (univariate analysis of variance) were then conducted on the effect of total years taking antipsychotics and years taking current antipsychotic on developing diabetes. Both variables showed a strong trend toward statistical significance (total years taking antipsychotics: F = 3.90, SE = 0.108, standard error of the mean (SEM) = .002, p = .053; years taking current antipsychotic: F = 3.87, SE = 0.112, SEM = .002, p = .054).

Table 2. Prevalence of Diabetes Mellitus by Age, Gender, Family History, and Race (N = 436)

Characteristic	Diabetes in Study Group, N/N	Prevalence %
Age, y		
18–39	16/185	8.6
40–49	21/138	15.2
50–59	24/88	27.3
60+	1/25	4.0
Gender		
Male	22/250	8.8
Female	40/186	21.5
Family history		
Positive	25/75	33.3
Negative/unknown	37/361	10.3
Race		
White	35/268	13.1
Black, Hispanic, other	27/168	16.1

Table 2 presents the prevalence rates of diabetes in the entire study group by age, gender, family history of diabetes, and race/ethnicity. Chi-square analysis revealed significant effects of age ($\chi^2 = 16.514$, p < .001), family history of diabetes ($\chi^2 = 27.128$, p < .001), and gender ($\chi^2 = 14.114$, p < .001). Odds ratios for race/ethnicity (white/nonwhite), age (over/under 42 years), gender (male/female), and family history of diabetes (positive/negative) were 1.32, 2.06, 2.69, and 4.06, respectively.

DISCUSSION

This study provides an estimate of the point prevalence of diagnosed diabetes among patients with schizophrenia and other severe mental disorders receiving antipsychotic drugs within a community mental health center setting. The 14.2% prevalence rate of diabetes found in this study is approximately twice the estimated 7.3% prev-

alence rate of diabetes mellitus found among the general adult population in the year 2000 across comparable age groups.[23] These results are consistent with recent reports suggesting that patients with severe mental disorders receiving antipsychotic drugs are at high risk for developing diabetes.[20,21,24–32] Results also indicate that age, family history, gender, and race/ethnicity should be considered in assessing the risk of diabetes for an individual patient.

Among demographic variables examined, increased age and family history of diabetes were associated with the greatest risk for developing diabetes. The 17% prevalence rate of family history of diabetes in this study is consistent with previous reports of an 18% to 30% rate of type 2 diabetes among family members of patients with schizophrenia.[33] These rates are high in comparison with the 1.2% to 6.3% rates of diabetes found in the general population,[2] providing further evidence of vulnerability to diabetes among the severely mentally ill. While the prevalence of diabetes is slightly higher in women than in men within the general population,[23] the 21.5% prevalence rate of diabetes among women noted in this study is a somewhat unexpected finding. This high rate may be due to gender differences in body mass index, adiposity, or other potentially confounding variables.

Antipsychotic medications appear to be a significant risk factor in the development of diabetes mellitus, but the relative level of risk associated with each type of antipsychotic medication cannot be clearly determined using data from this study. Decanoate medications were associated with the lowest prevalence rates of diabetes in the study despite high mean durations of treatment, although the trend did not reach statistical significance. This finding is similar to the results from the only previously published study comparing decanoate antipsychotic drugs with an atypical antipsychotic drug by Hagg and colleagues.[34] The study found a trend toward lower prevalence rates of diabetes among 67 patients receiving decanoate drugs compared with 63 patients receiving clozapine.[34]

Among the atypical antipsychotic drugs, several studies have found that clozapine and olanzapine may confer a particularly high level of risk for diabetes,[24–30,32,35] but this finding has not been confirmed by other studies.[36–40] Although the present study found no significant differences in prevalence rates of diabetes among patients receiving clozapine, olanzapine, risperidone, and quetiapine, it is critical to note that this study was not designed to assess relative risk associated with each medication. For example, 8 of 9 patients with diabetes taking quetiapine received the diagnosis of diabetes before the initiation of quetiapine. While this finding could suggest that quetiapine is associated with a low rate of diabetes, it also might be explained by clinicians' choosing quetiapine for patients who had developed diabetes while taking older medications. Such switching would alter the prevalence rates found with quetiapine and other medications by moving cases of diabetes from one medication group to another. In addition, the study did not control for mean duration of antipsychotic drug exposure, a variable that showed a strong trend toward being associated with increased risk of diabetes. The study also did not control for medication nonadherence, a common occurrence among persons with severe mental disorders. In a recent review of 39 published studies, the mean ± SD rate of medication nonadherence among patients with schizophrenia was 40.5% ± 18.5%.[41] By reducing the total duration of exposure to antipsychotic medications, it is possible that nonadherence could result in a reduced risk for development of diabetes mellitus.

Several additional study limitations should be considered. One potentially important limitation is the overrepresentation of patients taking clozapine in this non–random study sample. If clozapine does impose a higher risk for diabetes than other antipsychotic drugs, then the large number of clozapine patients in this study could have inflated the overall prevalence rate. This study also did not control for the effects of concomitant medications, although analysis of data on divalproex sodium did not reveal an increased prevalence of diabetes. Another limitation is the retrospective methodology of this study, an approach that is likely to have underestimated the actual prevalence by failing to detect undiagnosed cases. Controlled studies are needed to further define the relative risk of diabetes associated with different antipsychotic medications, as well as the risk associated with clinical and demographic factors.

CONCLUSION

Patients with severe mental disorders receiving antipsychotic drugs are at an increased risk for developing diabetes mellitus compared with the general population. Clinicians should regularly monitor all such patients for diabetes, particularly those patients with established demographic risk factors, including family history of diabetes, increased age, female gender, and minority race/ethnicity.

Management strategies are needed to address the high prevalence of diabetes within the severely mentally ill population, with the goal of preventing long-term adverse health outcomes.

Drug names: chlorpromazine (Thorazine and others), clozapine (Clozaril and others), divalproex sodium (Depakote), fluphenazine (Prolixin and others), haloperidol (Haldol and others), olanzapine (Zyprexa), quetiapine (Seroquel), risperidone (Risperdal), ziprasidone (Geodon).

REFERENCES

1. Dixon L, Weiden P, Delahanty J, et al. Prevalence and correlates of diabetes in national schizophrenia samples. Schizophr Bull 2000;26:903–912

2. Adams PF, Marano MA. Current Estimates From the National Health Interview Survey, 1994. National Center for Health Statistics, Vital Health Stat 10 1995;193:1–520
3. Freed H, Fortunato E, Ludlum SD, et al. Changes in the glucose tolerance test occurring during and after insulin shock therapy for schizophrenia. Am J Med 1938;196:36–44
4. Proctor L, Dewan JG, McNeel BH. Variations in the glucose tolerance observations in schizophrenics before and after shock treatment. Am J Psychiatry 1944;100:652–658
5. Braceland FJ, Meduna LJ, Vaichulis JA. Delayed action of insulin in schizophrenia. Am J Psychiatry 1945;102:108–110
6. Freeman H, Zaborenke RN. Relation of changes in carbohydrate metabolism to psychotic states. Arch Neurol Psychiatry 1949;61:569–576
7. Freeman H, Elmadjian F. Carbohydrate and lymphoid studies in schizophrenia. Am J Psychiatry 1950;106:660–667
8. Henneman DH, Altschule MD, Goncz RM. Carbohydrate metabolism in brain disease, pt 2: glucose metabolism in schizophrenic, manic-depressive, and involutional psychoses. Arch Intern Med 1954;94: 402–416
9. Freeman H, Rodnick EH, Shakow D, et al. The carbohydrate tolerance of mentally disturbed soldiers. Psychosom Med 1944;6:311–317
10. Mukherjee SM, Decina P, Bocola V, et al. Diabetes mellitus in schizophrenic patients. Compr Psychiatry 1996;37:68–73
11. Ryan MCM, Collins P, Thakore J. Impaired fasting glucose tolerance in first episode, drug naïve patients with schizophrenia. Am J Psychiatry 2003;160:284–285
12. Charatan FBE, Bartlett NG. The effect of chlorpromazine (“Largactil”) on glucose tolerance. J Ment Sci 1955;101:351–353
13. Hiles BW. Hyperglycemia and glycosuria following chlorpromazine therapy [letter]. JAMA 1956;162:1651
14. Moraczewski AS, Du Buois KP. The influence of chlorpromazine on intermediary carbohydrate metabolism. Arch Int Pharmacodyn Ther 1959;120:201–221
15. Amdisen A. Diabetes mellitus as a side effect of treatment with tricyclic neuroleptics. Acta Psychiatr Scand 1964;4:411–414
16. Schwarz L, Munoz R. Blood sugar levels in patients treated with chlorpromazine. Am J Psychiatry 1968;125:149–150
17. Korenyi C, Lowenstein B. Chlorpromazine induced diabetes. Dis Nerv Syst 1968;29:827–828
18. Cooperberg AA, Eidlow S. Haemolytic anemia, jaundice and diabetes mellitus following chlorpromazine therapy. Can Med Assoc J 1956;75: 746–749
19. Thonnard-Neumann E. Phenothiazines and diabetes in hospitalized women. Am J Psychiatry 1968;124:138–142
20. 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
21. Henderson DC, Cagliero E, Gray C, et al. Clozapine, diabetes mellitus, weight gain, and lipid abnormalities: a five-year naturalistic study. Am J Psychiatry 2000;157:975–981
22. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition. Washington, DC: American Psychiatric Association; 1994
23. Mokdad AH, Bowman BA, Ford ES, et al. The continuing epidemics of obesity and diabetes in the United States. JAMA 2001;286:1195–1200
24. Meyer JM. A retrospective comparison of weight, lipid, and glucose changes between risperidone- and olanzapine-treated inpatients: metabolic outcomes after 1 year. J Clin Psychiatry 2002;63:425–433
25. Wirshing DA. Adverse effects of atypical antipsychotics. J Clin Psychiatry 2001;62(suppl 21):7–10
26. Wirshing DA, Boyd JA, Meng LR. The effects of novel antipsychotics on glucose and lipid levels. J Clin Psychiatry 2002;63:856–865
27. Newcomer JW, Haupt DW, Fucetola R, et al. Abnormalities in glucose regulation during antipsychotic treatment of schizophrenia. Arch Gen Psychiatry 2002;59:337–345
28. Caro JJ, Ward A, Levinton C, et al. The risk of diabetes during olanzapine use compared with risperidone use: a retrospective database analysis. J Clin Psychiatry 2002;63:1135–1139
29. Liebzeit KA, Markowitz JS, Caley CF. New onset diabetes and atypical antipsychotics. Eur Neuropsychopharmacology 2001;11:25–32
30. Gianfrancesco FD, Grogg AL, Ramy MA, et al. Differential effects of risperidone, olanzapine, clozapine, and conventional antipsychotics on type 2 diabetes: findings from a large health plan database. J Clin Psychiatry 2002;63:920–930
31. Kornegay CJ, Vasilakis-Scaramozza C, Jick H. Incident diabetes associated with antipsychotic use in the united kingdom general practice research database. J Clin Psychiatry 2002;63:758–762
32. Lindenmayer JP, Czobor P, Volavka P, 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
33. Mukherjee S, Schnur DB, Reddy R. Family history of type 2 diabetes in schizophrenia patients [letter]. Lancet 1989;1:495
34. Hagg S, Joelsson L, Mjorndal T, et al. Prevalence of diabetes and impaired glucose tolerance in patients treated with clozapine compared with patients treated with conventional depot neuroleptic medications. J Clin Psychiatry 1998;59:294–299
35. 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
36. Wang PS, Glynn RJ, Ganz DA, et al. Clozapine use and risk of diabetes mellitus. J Clin Psychopharmacol 2002;22:236–243
37. Lund BC, Perry PJ, Brooks JM, et al. Clozapine use in patients with schizophrenia and the risk of diabetes, hyperlipidemia, and hypertension. Arch Gen Psychiatry 2001;58:1172–1176
38. Lindenmayer J, Smith RC, Singh A, et al. Hyperglycemia in patients with schizophrenia who are treated with olanzapine. J Clin Psychopharmacol 2001;21:351–353
39. Smith RC, Lindenmayer J, Khandat A, et al. Hyperglycemia in schizophrenic patients treated with olanzapine and clozapine. In: New Research Program and Abstracts of the 154th Annual Meeting of the American Psychiatric Association; May 8, 2001; New Orleans, La. Abstract NR321:87
40. Buse JB, Cavazonni P, Hornbuckle K, et al. A retrospective cohort study of diabetes mellitus and antipsychotic treatment in the United States. J Clin Epidemiol 2003;56:164–170
41. Lacro JP, Dunn LB, Dolder CR, et al. Prevalence of and risk factors for medication nonadherence in patients with schizophrenia: a comprehensive review of recent literature. J Clin Psychiatry 2002;63:892–909

