Variables Associated With Alcohol, Drug, and Daily Smoking Cessation in Patients With Severe Mental Illnesses

Jose de Leon, M.D.; Margaret T. Susce, R.N., M.L.T.; Francisco J. Diaz, Ph.D.; Diego M. Rendon, B.S.; and Diana M. Velásquez, B.S.

Background: Co-occurrence of substance use disorders and severe mental illnesses (SMIs) is a major U.S. public health issue, although the role of tobacco is usually neglected. This study explored variables associated with alcohol, drug, and smoking cessation in a naturalistic setting.

Method: Logistic regression was used to study variables associated with cessation of alcohol and drug use disorder and daily smoking in 560 SMI inpatients and outpatients from central Kentucky facilities. Patients with a lifetime history of alcohol or drug use disorder were considered to be in cessation if they had not suffered from abuse or dependence during the last year. Alcohol and drug use disorder diagnoses were determined using the Clinician Rating of Alcohol and Drug Use Disorder. Patients were recruited from July 2000 to March 2003.

Results: The cessation rates for alcohol and drug use disorders were, respectively, 44% (95% CI = 39% to 49%) and 46% (CI = 40% to 51%); these were higher than the daily cigarette smoking cessation rate of 10% (CI = 7% to 13%). Drug use disorders ($p \leq .02$), outpatient status ($p < .001$), and having a medical complication of obesity (diabetes mellitus, hypertension, or hyperlipidemia; $p < .001$) were significantly associated with alcohol cessation. Alcohol use disorder ($p < .001$), starting treatment with psychiatric medications after 33 years of age ($p < .001$), taking these medications for 14 years or more ($p = .02$), schizophrenia diagnosis ($p < .001$), outpatient status ($p = .03$), and obesity ($p = .04$) were significantly associated with drug cessation. Cessation of daily smoking was associated with hypertension ($p = .02$), late start of treatment with psychiatric medications (> 33 years old; $p = .01$), and lack of lifetime drug abuse ($p < .001$).

Conclusions: These results are limited by the cross-sectional and naturalistic design but suggest that public health experts, researchers, and clinicians need to mindfully address smoking cessation in patients with SMIs. Clinicians may want to consider that medical illnesses may motivate patients with SMIs to stop substance abuse and that patients with SMIs who abuse both alcohol and drugs rarely stop abusing just one of them.

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Corresponding author and reprints: Jose de Leon, M.D., University of Kentucky Mental Health Research Center at Eastern State Hospital, 627 West Fourth St., Lexington, KY 40508 (e-mail: jdeleon@uky.edu).

Co-occurrence of substance use disorders and severe mental illnesses (SMIs) is a major public health problem in the United States. U.S. review articles have reported that histories of alcohol or drug abuse disorders are present in more than half of schizophrenia and bipolar patients[1,2] and that more than three quarters of people with alcohol dependence have a history of a mental disorder.[1,3] An epidemiologic study that included general and institutionalized populations suggested that schizophrenia, bipolar disorder, and major depression are associated with alcohol and drug use disorders.[4]

Despite the fact that nicotine is probably the most abused drug among people with SMIs, the above studies did not consider nicotine as a comorbid drug. Major depressive disorder[5,6] and bipolar disorder[5,7] appear to be associated with increased levels of current daily smoking and with difficulty in quitting smoking.[5] Studies focusing on current smokers show that nicotine dependence is strongly associated with SMIs and that social campaigns for decreasing smoking in the general population have very limited influence on people with SMIs.[8] Although schizophrenia patients are not included in general popula-

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tion surveys,[5,9] worldwide case-control studies suggest that schizophrenia is associated with current smoking when compared to the general population[10] and after controlling for confounding variables.[11] Increased current smoking in people with schizophrenia may be explained by decreased smoking cessation and/or increased smoking initiation.[10,12] Worldwide studies confirm that, compared with the general population, schizophrenia is associated with increased lifetime daily smoking[10] and with an increased risk of daily smoking initiation after controlling for confounding factors.[11,12] Daily smoking is considered a sign of nicotine addiction. Worldwide studies also confirm that schizophrenia is associated with decreased smoking cessation when compared with the general population.[10] Since the prevalences of current smoking[10,12–16] and lifetime daily smoking[10] in schizophrenia patients are usually higher than those in patients with other SMIs, tobacco smoking appears to be more strongly associated with schizophrenia than with other SMIs.

The association between substance use disorders and SMIs is very complex.[17–19] When both are present, greater severity and persistence of both mental and drug use disorders occur.[18] In the United States, SMIs may be associated with an increased risk of secondary alcohol and illegal drug abuse.[19] However, nicotine addiction tends to start at a young age (in most cases before the SMI onset). Therefore, in most cases nicotine addiction cannot be secondary to the mental illness. Nicotine addiction may be a risk marker for SMIs. Shared genetic factors possibly influence a simultaneous propensity for smoking and mood disorders,[7,20] as well as for smoking and schizophrenia.[21,22]

Current guidelines favor integrating treatments for alcohol/drug abuse with treatments for schizophrenia and mood disorders.[23–28] They recommend combining pharmacologic and psychological interventions for substance abuse that have been studied in controlled and uncontrolled trials in patients with SMIs.[23–28] Although some data demonstrate that current pharmacologic and psychological smoking cessation treatments have some success in the general population, these treatments are unfortunately rather unsuccessful in people with SMIs, particularly those with schizophrenia.[29]

The main objective of this study was to explore the association of a number of clinical and demographic variables with alcohol, drug, and smoking cessation in a naturalistic setting. Variables associated with lifetime alcohol and drug use disorders and lifetime daily smoking were also investigated. A relatively large sample of patients with SMIs was used. This sample probably accurately represents patients treated in public facilities in central and northern Kentucky, which offer relatively well-integrated treatments for SMIs and alcohol/drug abuse but neglect nicotine dependence.

METHOD

Sample

A sample of 560 inpatients and outpatients from central Kentucky facilities was recruited during a risperidone pharmacogenetics investigation.[30–32] Institutional review board approval was obtained, and patients with past or current risperidone treatment who were willing to sign a written informed consent statement to participate in a study that included a blood collection were included in the sample. From July 2000 to March 2003, inpatients were recruited from 2 state hospitals: Lexington's Eastern State Hospital (ESH), the primary psychiatric hospital for acute admissions in one third of Kentucky, with approximately 1600 admissions per year, and Louisville's Central State Hospital, covering a different catchment area with approximately 900 admissions per year. Outpatients were recruited from the Bluegrass Community Mental Health Centers (providing outpatient services for the ESH catchment area) and from the University of Kentucky Outpatient Clinic in Lexington.

Table 1 describes the most frequent diagnostic groups using DSM-IV clinical diagnoses made by treating physicians and other clinical characteristics. Numerical variables such as age at SMI onset and duration of psychiatric medication were divided according to their quartiles in an exploratory way. When the 75th percentile of onset age (33 years) was used to dichotomize this variable, the resulting dichotomous variable was significant in several analyses. Similarly, the median of duration of psychiatric treatment was used to dichotomize this variable (Table 1).

Two research nurses with at least 5 years of experience with these state hospitals' patients collected alcohol and drug use disorder information through interviews and chart reviews. Each patient was classified as having or not having a lifetime alcohol or drug use disorder by 1 of the research nurses using the Clinician Rating of Alcohol and Drug Use Disorder.[33] A score of 3 on this scale was considered positive for lifetime disorder. The principal investigator initially trained the 2 research nurses and later found that they were proficient in the rating, which required a relatively simple clinical decision based on all available information. Therefore, no further training was provided and no interrater reliability was formally conducted. This rating differed from medication side effects scales, on which the first author rated approximately three quarters of the patients. Moreover, the research nurses did not assess medication side effects independently until 1 year of coratings with the principal investigator was completed and formal interrater assessments were conducted. The reason for the difference in training focus and interrater assessment between substance use and medication side effects assessments was that the study was more specifically focused on side effects; also,

Table 1. Demographic and Clinical Characteristics of 560 Patients With Severe Mental Illnesses

Characteristic	Mean	SD
Age, y	42.6	12.9
Age at start of psychiatric medications, y	26.8	11.7
Duration of psychiatric medications, y	15.9	11.5
Education, y	11.3	3.1
	%	N
Age > 45 y	42	237
Education level of high school or lower	71	397
Gender		
Male	54	303
Female	46	257
Race		
Caucasian	81	457
African American	17	93
Other	2	10
Inpatients	77	430
Marital status		
Single	45	254
Divorced	28	158
Married	17	92
Other	10	56
Lifetime alcohol use disorder (abuse/dependence)	64	360
Lifetime drug use disorder (abuse/dependence)	52	291
Lifetime daily smoking[a]	77	424
DSM-IV diagnoses[b]		
Schizophrenia	28	157
Schizoaffective disorder	19	108
Bipolar disorder	18	99
Major depressive disorder	12	67
Drug- or alcohol-induced psychotic disorder	6	33
Personality disorders	6	33
Other psychotic disorders	5	31
Other	6	32
Psychiatric medications		
Late start (age > 33 y)	25	139
Long duration (≥ 14 y)	51	288
Antipsychotics[c]		
None	4	23
Risperidone	64	357
Olanzapine	16	91
Quetiapine	13	74
At least 1 typical	13	72
Mood stabilizers		
Lithium	10	54
Valproate	27	153
Carbamazepine	4	21
Obesity (body mass index ≥ 30 kg/m^2)	46	257
Diabetes mellitus	18	101
Hypertension	27	151
Hyperlipidemia	13	74
Any medical complication[d]	39	220

[a]Ten subjects who had used other nicotine products were excluded.
[b]Main clinical diagnoses that explain the treatment with antipsychotics. Other psychotic disorders include those described in the DSM-IV "Schizophrenia and Other Psychotic Disorders" section.
[c]Only the most frequently prescribed antipsychotics (> 10%) are listed. Two antipsychotics were prescribed in 108 patients, and 3 were prescribed in 9 patients.
[d]Diagnosis of diabetes mellitus, hypertension, or hyperlipidemia.

the principal investigator found that the research nurses were well trained in substance use assessments but not in complex decisions about medication side effects.

A patient with lifetime alcohol or drug use disorder was considered as being in cessation if he/she did not suffer from abuse or dependence during the last year, based on patient report and hospital chart information (including progress notes from substance abuse counselors who usually know repeatedly admitted patients and urine drug screen results for patients who had a drug abuse history). Cessation rate for alcohol use disorder was defined as the proportion of patients with lifetime alcohol use disorder who were in alcohol cessation. Cessation rates for drug use disorder and lifetime daily smoking were defined analogously.

History of use of cigarettes and other tobacco products was established for all subjects. Lifetime daily smoking was defined as smoking cigarettes on a daily basis during some period in life. Only 550 subjects were included in the clinical analysis of lifetime daily smoking after excluding 10 subjects who had used other tobacco products. Of the 550 subjects, 424 (77%) were lifetime daily smokers, and 126 (23%) had never smoked cigarettes daily. A lifetime daily smoker was considered as being in smoking cessation if he/she did not use cigarettes during the last year.

One state hospital has a substance abuse education program and works closely with a detoxification program not affiliated with the hospital but located on its grounds. The other hospital has a dual-diagnosis unit. None of the hospitals or outpatient facilities has smoking cessation programs. Patients with privileges smoked outside hospital units. Some physicians prescribed nicotine replacement gum for patients who could not smoke, but long-term nicotine replacement was not prescribed after discharge since it is not available in the community. Therefore, smoking cessation probably occurred in the absence of any formal behavioral or pharmacologic intervention.

Statistics

The association of clinical and demographic variables with lifetime drug use disorder was initially explored by means of 2-way cross-tabulations for univariate analyses.[34] Odds ratios (ORs) were used as a measure of association, and their 95% confidence intervals (CIs) were computed. An OR > 1, particularly when high and significant, indicates that the associated factor increases the risk; an OR < 1, particularly when low and significant, indicates that the associated factor decreases the risk and may be considered protective if it is verified by intervention studies (referred to in this article as "potentially protective"). An OR that is not significantly different from 1 indicates lack of association. A 95% CI is a range of highly plausible OR values, and, in 95% of similar studies, the CI will include the "true" OR.

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Table 2. Variables Associated With Lifetime Alcohol Use Disorder and Alcohol Cessation in 560 Patients With Severe Mental Illnesses

Variable	OR	95% CI	p Value[a]
Lifetime alcohol use disorder[b]			
Lifetime drug use disorder	8.7	5.5 to 13.6	< .001
Lifetime daily smoking	3.3	2.0 to 5.3	< .001
Male gender	2.4	1.6 to 3.7	< .001
Alcohol cessation in patients with lifetime alcohol use disorder[c]			
Drug use disorder			
Stopped using drugs vs never had a drug use disorder	2.0	1.1 to 3.7	.02
Never had a drug use disorder vs current drug use disorder	10.0	5.0 to 20.2	< .001
Outpatient status	4.0	2.0 to 8.0	< .001
Any medical complication[d]	2.8	1.6 to 4.8	< .001

[a]Wald χ^2 test.
[b]Hosmer-Lemeshow goodness-of-fit test: $\chi^2 = 1.8$, df = 5, p = .88. The analysis included 360 patients with and 200 without a lifetime alcohol use disorder.
[c]Hosmer-Lemeshow goodness-of-fit test: $\chi^2 = 0.7$, df = 6, p = .99. The analysis included 159 patients who did and 201 who did not stop having an alcohol use disorder for more than 1 year.
[d]Diagnosis of diabetes mellitus, hypertension, or hyperlipidemia.
Abbreviations: CI = confidence interval, OR = odds ratio.

Table 3. Variables Associated With Lifetime Drug Use Disorder and Drug Cessation in 560 Patients With Severe Mental Illnesses

Variable	OR	95% CI	p Value[a]
Lifetime drug use disorder[b]			
Lifetime alcohol use disorder	9.3	5.6 to 15.1	< .001
Lifetime daily smoking	3.5	2.1 to 6.1	< .001
Male gender	1.8	1.2 to 2.8	.007
Age > 45 y	0.21	0.13 to 0.32	< .001
Drug cessation in patients with lifetime drug use disorder[c]			
Alcohol use disorder			
Stopped using alcohol vs never had an alcohol use disorder	7.1	2.8 to 18.6	< .001
Never had an alcohol use disorder vs current alcohol use disorder	3.3	1.4 to 8.1	< .001
Started treatment with psychiatric medications after 33 y of age	6.8	2.7 to 17.0	< .001
Schizophrenia	4.1	2.0 to 8.1	< .001
Outpatient status	2.5	1.1 to 5.9	.03
Duration of treatment with psychiatric medications ≥ 14 y	2.4	1.2 to 4.7	.02
Obesity	2.0	1.0 to 3.8	.04

[a]Wald χ^2 test.
[b]Hosmer-Lemeshow goodness-of-fit test: $\chi^2 = 2.6$, df = 6, p = .85. The analysis included 291 patients with and 269 without a lifetime drug use disorder.
[c]Hosmer-Lemeshow goodness-of-fit test: $\chi^2 = 7.6$, df = 8, p = .48. The analysis included 133 patients who did and 158 who did not stop having a drug use disorder for more than 1 year.
Abbreviations: CI = confidence interval, OR = odds ratio.

Table 4. Variables Associated With Lifetime Daily Cigarette Smoking and Smoking Cessation in 550 Patients With Severe Mental Illnesses

Variable	OR	95% CI	p Value[a]
Lifetime daily smoking[b]			
Lifetime alcohol use disorder	3.6	2.2 to 6.0	< .001
Lifetime drug use disorder	3.1	1.8 to 5.4	< .001
Education level of high school or lower	2.1	1.3 to 3.3	.003
Schizophrenia	2.0	1.3 to 3.2	.003
Obesity	0.61	0.39 to 0.96	.03
Smoking cessation in lifetime daily smokers[c]			
Started treatment with psychiatric medications after 33 y of age	2.5	1.2 to 4.8	.01
Hypertension	2.3	1.2 to 4.5	.02
Lifetime drug use disorder	0.24	0.12 to 0.49	< .001

[a]Wald χ^2 test.
[b]Hosmer-Lemeshow goodness-of-fit test: $\chi^2 = 9.3$, df = 8, p = .31. The analysis included 424 lifetime daily smokers and 126 never daily smokers.
[c]Hosmer-Lemeshow goodness-of-fit test: $\chi^2 = 4.5$, df = 4, p = .34. The analysis included 44 patients who quit smoking for more than 1 year and 380 who continued daily smoking.
Abbreviations: CI = confidence interval, OR = odds ratio.

Those variables with a p value < .25[35] were then included as independent variables in a multivariate logistic regression that used lifetime alcohol use disorder as the dichotomous dependent variable. The regression provided adjusted ORs for the independent variables (Table 2). A similar methodology was used to explore the association of clinical and demographic variables with lifetime drug use disorder (Table 3), lifetime daily smoking (Table 4), alcohol cessation among patients with lifetime alcohol use disorder (Table 2), drug cessation among patients with lifetime drug use disorder (Table 3), and smoking cessation among lifetime daily smokers (Table 4). The Hosmer-Lemeshow goodness-of-fit test was used to examine the fitness of the logistic models. All models fit well.[34,35]

The above analyses were repeated using only male and female subsamples because genders may have different patterns.[36] They were also repeated within patients with schizophrenia disorders (defined as those having a DSM-IV clinical diagnosis of schizophrenia or schizoaffective disorder) and patients with mood disorders (DSM-IV bipolar or major depressive disorder).

RESULTS

Cessation Rates

Cessation rates were 44% for alcohol use disorder (159/360, 95% CI = 39% to 49%) and 46% for drug use disorder (133/291, 95% CI = 40% to 51%). The cessation rate for daily cigarette smoking was relatively smaller, 10% (44/424, 95% CI = 7% to 13%).

Variables Associated With Lifetime Alcohol Use Disorder and Alcohol Cessation

Male gender, lifetime drug use disorder, and lifetime daily smoking were significantly associated with lifetime alcohol use disorder in the logistic regression (Table 2).

Among patients with a lifetime alcohol use disorder, alcohol cessation was significantly associated with outpatient status and having at least 1 medical complication (diabetes mellitus, hypertension, or hyperlipidemia). Drug

abuse variables were also significantly associated with alcohol cessation and showed a stepwise association, with the highest alcohol cessation rate for those who stopped abusing drugs, an intermediate rate for those who never abused drugs, and the lowest for those who were currently abusing drugs. When alcohol cessation was compared in patients who stopped abusing drugs versus patients with no lifetime drug use disorder, the OR was 2.0. When patients with no lifetime drug use disorder were compared with patients currently abusing drugs, the OR was 10.0. Therefore, when alcohol cessation was compared in those who stopped abusing drugs versus those who were currently abusing drugs, the OR was very high, 20.0 ($2.0 \times 10.0 = 20.0$).

In females, outpatient status, the above drug abuse variables, and hypertension were significantly associated with alcohol cessation in the logistic regression. In males, the drug abuse variables, diabetes mellitus, and bipolar disorder were significantly associated with alcohol cessation. The drug abuse variables and diabetes mellitus were significant in schizophrenia patients, while the drug abuse variables, hypertension, and outpatient status were significant in patients with mood disorders.

Variables Associated With Lifetime Drug Use Disorder and Drug Cessation

Lifetime drug use disorder was significantly associated with male gender, lifetime alcohol use disorder, and lifetime daily smoking in the logistic regression model (Table 3). Age older than 45 years was also significant and had a potentially protective effect (OR = 0.21).

Among patients who had a lifetime drug use disorder, drug cessation was significantly associated with starting treatment with psychiatric medications after 33 years of age, having a schizophrenia diagnosis, outpatient status, taking psychiatric medications for 14 years or more, and obesity. The OR for drug cessation comparing patients who stopped alcohol versus those who never abused alcohol was 7.1, and the OR comparing patients who never abused alcohol versus those who were currently abusing it was 3.3. Therefore, the OR for drug cessation comparing patients who stopped alcohol versus those who were currently abusing it was 23.4 ($7.1 \times 3.3 = 23.4$).

In females, only the 2 alcohol abuse variables listed above were significantly associated with drug cessation in the logistic regression. In males, the above alcohol abuse variables, age older than 45 years (potentially protective), having a schizophrenia diagnosis, starting treatment with psychiatric medications after 33 years of age, and outpatient status were significantly associated with drug cessation. In schizophrenia patients, the variables that were significantly associated with drug cessation were the alcohol abuse variables and age older than 45 years (potentially protective). In patients with mood disorders, the alcohol abuse variables were the only significant variables.

Variables Associated With Lifetime Daily Smoking and Smoking Cessation

Lifetime alcohol and drug use disorders, schizophrenia, and having a level of education of high school or lower were associated with lifetime daily smoking in the logistic regression (Table 4). Obesity was associated with an OR < 1, so it was potentially protective.

A cessation of daily smoking longer than 1 year was associated with hypertension and a late start of treatment with psychiatric medication (> 33 years old). Lifetime drug abuse was "potentially protective" against smoking cessation; that is, it increased the risk that a daily smoker continued smoking.

In the females' logistic regression, smoking cessation was associated with a late start of treatment with psychiatric medication and outpatient status, while in males it was only associated with lifetime drug abuse disorder. Smoking cessation was associated with hypertension and lifetime drug abuse disorder in schizophrenia patients, but it was associated with late start of treatment with psychiatric medication, hyperlipidemia, and lifetime alcohol use disorder in patients with mood disorders.

Current Treatment With Risperidone or Olanzapine

Risperidone and olanzapine were the most frequently used antipsychotics. Cessation rates were not associated with risperidone (alcohol OR = 0.88, CI = 0.58 to 1.3; drug OR = 0.75, CI = 0.47 to 1.2; and smoking OR = 1.1, CI = 0.60 to 2.1) or olanzapine treatment (alcohol OR = 1.4, CI = 0.81 to 2.6; drug OR = 1.4, CI = 0.75 to 2.8; and smoking OR = 0.93, CI = 0.40 to 2.2).

DISCUSSION

Limitations

This study was not originally designed to investigate alcohol, drug, or smoking cessation. However, it probably well represents central Kentucky's severely mentally ill patients who take antipsychotics, since risperidone is the most frequently used antipsychotic. In fact, it is unusual to find antipsychotic-prescribed patients who have never taken risperidone. Obviously, the need to sign a consent form and be willing to cooperate with a blood collection may have biased the sample somewhat, but the first bias (willingness to sign a consent form) is unavoidable in current times. In the past (20 years ago), institutional review boards and state hospital administrations allowed us to review charts and interview patients who provided verbal consent as long as no other invasive procedures were used. Currently, even a clinical interview requires the patient to sign a consent form, introducing some bias in naturalistic clinical studies.

This sample may not accurately represent U.S. patients with severe mental illness because poor and rural people are overrepresented in Kentucky. However, it may accu-

rately represent Kentucky patients with SMIs in treatment because state hospitals and community mental health centers are the main psychiatric treatment providers in this state. Obviously, recruiting at inpatient or outpatient facilities may introduce some bias, but it is not easy to recruit the most severely mentally ill patients. Large U.S. epidemiologic surveys, such as the National Comorbidity Survey, usually include very few schizophrenia patients. In summary, this sample can be better described as representing patients treated with antipsychotics at outpatient or inpatient facilities in central Kentucky. More inpatients than outpatients were included since it is easier to recruit inpatients; they spend at least 24 hours in the hospital if they are admitted. The potential confounding effect of being an outpatient was considered in the logistic regression models.

This naturalistic study reflected recovery associated with the available treatments and/or spontaneous recoveries. The cross-sectional design reflects only a moment in time. Nevertheless, this study provides a good idea of crucial variables that clinicians need to consider regarding drug cessation. Unfortunately, the Clinician Rating of Drug Use Disorder[33] assesses all drugs together, and the research nurses who performed the ratings did not list all drugs for each patient.

In an ongoing pharmacogenetic inpatient study, the research nurses are assessing each drug separately with the Clinician Rating of Drug Use Disorder. At Eastern State Hospital, the major source of patients for this article, we recruited 946 patients in the first year (October 2003–October 2004). Of these patients, 574 had a history of any lifetime drug use disorder. Of these 574 patients, the prevalences were 50% for marijuana, 34% for cocaine, 20% for opioids, 16% for stimulants, and 11% for hallucinogens. Although data for the patients reported in this article and the above 946 patients were collected at different times, all patients came from the same population. Therefore, it is likely that the above abuse percentages would be similar to those for the lifetime drug abusers this article describes.

Patients tend to underreport alcohol and illegal substance abuse, which may hinder collection of substance abuse data. However, underreporting may not be a major issue in this study, since 2 experienced research nurses assessed current and prior substance abuse histories through patient interviews and chart reviews that considered toxicology screens, substance abuse diagnoses, and patients' reports to treating clinicians. More than three quarters of the patients had been under psychiatric treatment for over 5 years; it is unlikely that treating clinicians had missed ongoing substance abuse problems.

The diagnoses of schizophrenia and mood disorders appeared to have few associations with cessation, but, as in previous studies, schizophrenia was associated with lifetime daily smoking. It cannot be ruled out that research diagnoses made through structured interviews may have provided a different outcome. However, we doubt that the lack of research diagnoses significantly changed the results. To put the lack of research diagnosis in context, it must be remembered that U.S. epidemiologic surveys do not use research or clinical diagnoses, but rather the diagnoses obtained by a lay interviewer.

Lifetime Use

Male gender and lifetime daily smoking were consistently associated with lifetime alcohol and drug use disorders. Moreover, older age had a protective effect against drug use disorders.

Lifetime alcohol and drug use disorders were associated with lifetime daily smoking, but low level of education and schizophrenia were specific to lifetime daily smoking. The association of a low level of education with lifetime daily smoking is also observed in the U.S. general population, and the association of schizophrenia with lifetime daily smoking has been observed in many prior case-control studies using patients with other SMIs and/or normal volunteers as controls.[10–16] Obesity and lifetime daily smoking were inversely associated. Obesity in SMIs is probably multifactorial, but other analyses[31] of this sample suggested that there is a subgroup of obese patients in which nicotine use may decrease appetite.

Cessation

The best predictor of alcohol cessation was drug cessation and vice versa. People who persisted in abusing alcohol were very unlikely to stop abusing drugs, and those who persisted in abusing drugs were very unlikely to stop abusing alcohol. People who had abused either alcohol or drugs, but not both, had an intermediate position regarding their motivation for stopping abuse of the substance.

Having at least 1 of the medical complications (diabetes mellitus, hypertension, and hyperlipidemia) that are part of the so-called metabolic syndrome was associated with alcohol cessation. Drug cessation was associated with obesity and variables indicating psychiatric treatment or illness. Late or long-term psychiatric treatment and late or long-term illness were associated with drug cessation. It is impossible to distinguish treatment versus illness effects in this cross-sectional survey.

Lifetime drug abuse was associated with a lack of smoking cessation, while hypertension and a late start of treatment with psychiatric medication (> 33 years of age) or late illness onset increased the chances of smoking cessation. The association between smoking cessation and late start of treatment with medication was significant in the total sample and in the female and mood-disordered subsamples but did not reach significance in the schizophrenia or the male subsamples. It is possible that lower illness severity in females and patients with mood disorders may be associated with smoking cessation, but

we have no verification with any other illness severity measure.

One of the most important findings of this study of severely mentally ill patients is that the number of patients who had stopped daily smoking was very small (10%) compared with alcohol (44%) or drug (46%) use disorders.

Gender Effects

As expected, male gender was associated with lifetime alcohol and drug use disorders in the logistic regression models. Male gender was also associated with lifetime daily smoking in the univariate analysis; however, the male effect in lifetime daily smoking disappeared when the associations between alcohol and drug use disorders with lifetime daily smoking were taken into account.

No particular gender was associated with alcohol, illegal drugs, or smoking cessation after correcting for confounding factors. Cessation rates were always lower for males than females. They were, respectively, 40% (95% CI = 34% to 46%) versus 52% (CI = 43% to 60%) for alcohol, 40% (CI = 33% to 47%) versus 56% (CI = 46% to 66%) for illegal drugs, and 8% (CI = 5% to 12%) versus 13% (CI = 8% to 18%) for smoking. The respective significance levels from 2-tailed χ^2 tests were $p = .03$, $p = .01$, and $p = .11$ for alcohol, drugs, and smoking. However, these significant or borderline significant differences disappeared after correcting for other factors, including abuse of the other substances. The most reasonable interpretation is that males are more prone to abuse all kinds of substances and less prone to quit abusing them once they get addicted. Studies all over the world suggest that males abuse all kinds of substances more than females,[37] and the U.S. National Comorbidity Survey suggested that men not only abuse more drugs but also are less prone to quit.[38]

Schizophrenia and Mood Disorders

Patients with schizophrenia and mood disorders differed remarkably in the prevalence of lifetime daily smoking, but not in lifetime alcohol or drug abuse. The variables associated with alcohol and smoking cessation were relatively similar in schizophrenia and mood disorders. Schizophrenia diagnosis has a particularly strong association with drug use cessation (OR = 4.1; Table 3). Additional analyses suggested that male schizophrenia patients over 45 years of age are more prone to stop abusing illegal drugs. We have personally seen this pattern in many of our male schizophrenia patients, who usually require several years of serious trouble before learning or deciding that they need to stop abusing illegal drugs.

The clinical literature provides some support for the "self-medication" hypothesis in depression, since some patients with a history of depression get depressed after smoking cessation[39] and nicotine may have antidepressant properties in nonsmoking patients.[40] There are few clinical data supporting the "self-medication" hypothesis in schizophrenia.[41]

Motivation

Recent research on motivational interviewing has expanded to include dual-diagnosis populations; that treatment approach is starting to receive more attention by clinicians working with patients suffering from SMIs.[42–45]

This study suggests that motivation may be particularly important to substance use cessation among patients with SMIs. One of the most interesting findings of this study is that medical problems such as diabetes mellitus, hypertension, and hyperlipidemia may be associated (ORs > 1) with alcohol, illegal drug, or smoking cessation. One interpretation is that diagnosing these medical complications in patients with SMIs, including patients with schizophrenia, may motivate the patients to stop substance abuse. Longitudinal studies will be needed to prove this interpretation. If this interpretation is correct, it would suggest that although motivating patients with SMIs to stop abusing any type of substance may be difficult, serious medical issues may motivate them.

Another interpretation for the association of cessation with medical problems is that motivation is increased by increased contact with health care providers. Therefore, physicians should remind patients with SMIs about the deleterious effects of combining substance abuse with their inherent risk of developing a metabolic syndrome. It may also be important to consider peer intervention through other patients with SMIs and more experience, who could be in an advantageous position for stressing the deleterious effects of adding substance abuse to the combination of SMIs and physical illnesses.

The stepwise association of drug abuse with high rates of alcohol cessation may also suggest a motivation factor. Therefore, a motivation for stopping alcohol abuse appears to be explained partially by a motivation for stopping drug abuse. Patients who stopped abusing drugs appeared to be the most motivated, followed by those who had never had a drug use disorder. Current drug abusers had poor motivation for stopping alcohol abuse. Unless patients with SMIs abusing both alcohol and drugs are highly motivated to give them up, attempts to quit abusing one type of substance will be difficult if both are being abused. This strong association also suggests that current substance abuse programs in hospital and outpatient settings combining alcohol and drug treatments may make sense in this population.

The Need for New Smoking Cessation Treatments for Patients With Severe Mental Illnesses

New smoking cessation treatments need to be developed to help patients with SMIs. These patients appear to be isolated from the major wave of smoking cessation

occurring in the United States the last few years. This isolation is a serious challenge since patients with SMIs appear to have high nicotine dependence levels.[8,9] The new biological findings regarding the possible pathophysiologic links between nicotine addiction and schizophrenia may help to develop better pharmacologic interventions for these patients.[22,46]

Alcohol and drug cessation treatments in patients with SMIs have been a concern for 20 or 30 years, since comorbid alcohol and drug abuse may involve grave risks such as high risk of suicide or serious violence toward others.[47] Neglecting smoking cessation in these patients appears unwise, since smoking is probably associated with a long-term risk of medical illnesses including cardiovascular problems and cancer.[48,49] Public health efforts to reduce smoking must include seriously affected subgroups, including patients with SMIs, who are traditionally neglected by society and research programs. The lack of attention to smoking cessation is not unique to state hospitals, but appears to include psychiatric academic hospitals too.[50] The lack of attention to smoking changes (associated with coming in and out of the hospital) may even be unsafe. Smoking modifies blood psychotropic levels, and smoking changes may be associated with increased risk of side effects.[51,52]

The Need for Understanding the Importance of Drug Access

It is likely that the association between smoking and SMIs, particularly in the case of schizophrenia[10–12,21,22] but also in mood disorders,[7,20] may be explained by genetic factors. It is poorly understood what factors or brain abnormalities may make people with SMIs more prone to abuse alcohol and drugs.[17–19] However, the association between SMIs and the abuse of all of these substances is determined by access to the specific drugs. Cross-cultural comparisons help to understand the role of substance access.

Smoking is strongly associated with schizophrenia all over the world[10]; we believe that this may be explained by common genetic vulnerability factors.[21] However, for this association between schizophrenia and smoking to manifest, people need access to tobacco. In some areas of Colombia, cigarettes are very expensive for the average person; therefore, the prevalence of current smoking among schizophrenia patients is much lower than in the United States (26%), though still higher than in the general population (18%).[53]

In some areas of the world other than the United States, patients with SMIs lack easy access to alcohol and drugs. For example, Spain is a country with closer family ties than the United States, and people with SMIs usually live with their families; thus, access to illegal drugs is more restricted. Consequently, lower prevalences of illegal drug use disorders are observed in people with SMIs in Spain than in the United States.[54] In Turkey, where alcohol and illegal drugs are difficult to obtain, people with SMIs have very low prevalences of alcohol and drug use disorders.[55]

The low cost of cigarettes in Kentucky may have contributed to the high tobacco smoking rates in our patients with SMIs and probably explains why Kentucky has had one of the highest smoking rates in the United States for the last few years.[56]

Future Studies

Obviously, these results are limited by the cross-sectional nature of this study and need to be replicated in other states. Kentucky may be characterized by an overrepresentation of rural population, easy access to cigarettes, and a relative lack of nonpublic facilities providing care for patients with SMIs. Although difficult and expensive, longitudinal studies will provide a better idea of the temporal changes in cessation rates. This and other cross-sectional surveys could provide variables that clinicians may find important to help their patients to stop abusing alcohol or drugs. This study suggests that public health experts, researchers, and clinicians need to pay more attention to smoking cessation in patients with SMIs. Clinicians may want to consider that the presence of medical illnesses may motivate patients with SMIs to stop abusing substances and that patients abusing both alcohol and drugs rarely stop abusing only 1 of them.

Drug names: carbamazepine (Equetro, Carbatrol, and others), lithium (Eskalith, Lithobid, and others), olanzapine (Zyprexa), quetiapine (Seroquel), risperidone (Risperdal).

Disclosure of off-label usage: The authors have determined that, to the best of their knowledge, olanzapine and risperidone are not approved by the U.S. Food and Drug Administration for use in substance cessation programs.

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