The Association Between Moderate Alcohol Use and Illness Severity in Bipolar Disorder: A Preliminary Report

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Objective: To examine the association of alcohol consumption with symptoms, illness course, and health care utilization among non-alcoholic patients with bipolar disorder.

Method: Subjects were 148 patients with bipolar I or II disorder enrolled in a longitudinal study of cognitive-behavioral therapy versus psychoeducation. Subjects were 18 to 60 years old, in full or partial remission, and non-heavy drinkers with no history of substance use disorders. At least 4 weeks of consistent naturalistic treatment with mood stabilizer was required for enrollment. Measures included the Structured Clinical Interview for DSM-IV, the Hamilton Rating Scale for Depression, the Clinician-Administered Rating Scale for Mania, and the Khavari Alcohol Test. Data were gathered from July 2002 to December 2004.

Results: Mean weekly alcoholic beverage consumption was minimal among both men (3.8 standard drinks, SD = 8.9) and women (1.2 standard drinks, SD = 1.9). Nonetheless, total alcohol consumption among men was associated with lifetime manic episodes ($F = 10.2$, $df = 1$, $p = .003$) and emergency department visits ($F = 4.3$, $df = 1$, $p = .046$). Spirits consumption among men was strongly associated with lifetime manic episodes ($F = 81.8$, $df = 1$, $p < .001$) and emergency department visits ($F = 14.0$, $df = 1$, $p < .001$). Among women, the frequency of alcohol consumption was associated with lifetime episodes of depression ($F = 15.5$, $df = 1$, $p < .001$) and hypomania ($F = 4.8$, $df = 1$, $p < .03$). Wine consumption among women was associated with lifetime hypomanic episodes ($F = 13.6$, $df = 1$, $p < .001$) and current manic symptoms ($F = 4.0$, $df = 1$, $p < .05$).

Conclusion: Despite low volumes of consumption, alcohol was associated with measures of illness severity in bipolar disorder among both men and women. The adverse effects of alcohol on bipolar disorder may occur over a range of consumption, rather than being confined to heavy drinkers.

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Nearly a century ago, Kraepelin[1] observed a high prevalence of alcoholism among his manic-depressive patients. Despite growing clinical and public-health interest in mitigating the effect of alcohol on bipolar disorder, comorbid alcohol use disorders (AUDs) remain common among individuals with bipolar disorder, with lifetime prevalence rates approaching 50%.[2] Recent data from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) show that bipolar disorder has the strongest association with AUDs of all mood and anxiety disorders,[3] replicating findings from the Epidemiologic Catchment Area study.[4] Data from community samples[3] and clinical samples[5] alike show that alcohol is the most commonly abused drug among both bipolar I and II subjects.

The deleterious effect of AUDs on the course, treatment, and outcome in bipolar disorder has been shown repeatedly.[2,6–8] When AUDs occur in bipolar disorder, recovery is delayed, relapse is hastened, symptoms are greater in number and persist between episodes, and disability and mortality are increased.[6] Hospitalizations[2] and suicidal ideation and suicide attempts[9] are also more frequent among bipolar individuals with comorbid AUDs.

Two previous studies[10,11] provide a signal that moderate alcohol use may have an adverse impact on mood disorders. Castaneda and colleagues[10] reviewed the potential theoretical mechanisms by which moderate alcohol use could exacerbate mood and anxiety disorders, including its effects on neurotransmitter systems, sleep, pharmacokinetics, and pharmacodynamics, and concluded that ab-

stinence from alcohol should be recommended to patients with mood and anxiety disorders. Worthington and colleagues[11] examined alcohol consumption among 94 outpatients with major depressive disorder who received 8 weeks of open treatment with fluoxetine. They found that even with a mean alcohol consumption of less than 1 ounce per day, baseline alcohol consumption was a significant negative predictor of treatment response.

Despite the clear exacerbating effects of AUDs on bipolar disorder, and the possible negative effect of moderate alcohol consumption on treatment response in unipolar depression, to our knowledge there are no data regarding the association of alcohol consumption and bipolar disorder among patients with no history of AUDs. Such a study is needed to better understand the impact of alcohol consumption on bipolar disorder among nonalcoholic individuals, as the majority of those with bipolar disorder do not suffer from AUDs. In order to mitigate the potential confounding effect of heavy drinkers who do not meet AUD criteria, only subjects who consumed less than the recommended weekly maximum identified in national low-risk drinking guidelines[12] were included. Our a priori hypothesis was that adverse effects of alcohol consumption on bipolar disorder occur even at levels consistent with low-risk drinking guidelines.

METHOD

Sample

Subjects (N = 148) were recruited from an ongoing multicenter study of cognitive-behavioral therapy (CBT) versus psychoeducation for treatment of bipolar disorder that had recruited these subjects from newspaper advertisements and hospital clinics from 4 sites across Canada. Subjects were included if they met the following conditions: principal diagnosis of bipolar I or II disorder, in partial or complete remission (17-item Hamilton Rating Scale for Depression [HAM-D] score < 14, Clinician-Administered Rating Scale for Mania [CARS-M] score < 12), 18 to 60 years old, taking a consistent dose of a mood-stabilizing medication for at least 4 weeks prior to enrollment, and at least 2 mood episodes or clinically significant subsyndromal periods in the past 3 years. Exclusion criteria were the following: electroconvulsive therapy within 1 month of enrollment, severe personality disorder, active general medical condition that could interfere with treatment, and current psychosis, suicidality, or homicidality. Personality disorder, when present, was characterized as severe if the individual had a history of repeated self-injurious or parasuicidal behavior in the past 6 months, if treatment of the individual's personality disorder required higher priority and intensity than that of the bipolar disorder, or if the individual displayed extreme behavior or affect during the assessment that was deemed likely to interfere with the psychosocial intervention (CBT or psychoeducation). Subjects were excluded from the overall CBT versus psychoeducation study if they endorsed any substance abuse or dependence in the previous 3 months. For the purposes of the present study, subjects were also excluded if they endorsed any lifetime substance use disorder (N = 10). In addition, subjects (N = 8) were excluded from the present study if their alcohol use exceeded the weekly maximum for their gender (14 for men, 9 for women) as per national safe-drinking guidelines.[12] Written informed consent was obtained, and institutional research ethics board approval was granted. Data were gathered from July 2002 to December 2004.

The sample investigated comprised 148 patients, representing 89% of the 166 subjects enrolled in the CBT versus psychoeducation study. Sixty-one percent of subjects were women (N = 90), and 71% (N = 105) had a principal diagnosis of bipolar I disorder (vs. bipolar II disorder). The mean age at the time of the interview was 41.2 (SD = 10.8) years, with a range of 20 to 60 years.

Assessment

The Structured Clinical Interview for DSM-IV (SCID)[13] was administered to all subjects by trained clinical interviewers. In addition to DSM-IV diagnoses, age at onset, duration of bipolar disorder illness, and number of affective episodes were determined from the SCID. Current depressive symptoms were assessed with the HAM-D.[14] The CARS-M[15] was used to assess manic symptomatology. CARS-M is a 15-item semistructured clinician-rated interview. Individual items are scored along a 6-point Likert scale ranging from 0 (absent) to 5 (severe). The scale has sound psychometric properties and is highly correlated (r = 0.94) with Young Mania Rating Scale scores.[15]

The Khavari Alcohol Test (KAT)[16] is a validated 12-item measure that evaluates frequency and volume of overall alcohol consumption, as well as consumption of beer, wine, and spirits. The KAT is a reliable and valid measure[16] that is strongly correlated with the Self-Administered Alcoholism Screening Test (SAAST).[17,18] The KAT is highly similar in structure to the volumetric alcohol measure used in the NESARC.[3]

Statistical Analyses

Owing to the known contribution of gender to variability in the association between alcohol and bipolar disorder,[19] cross-tabulation analyses comparing men and women on categorical measures were conducted. In addition, Pearson correlational matrices for continuous study variables were generated separately based on gender.

Statistical significance was set at $p < .05$.

RESULTS

Descriptive data regarding alcohol consumption are presented in Table 1. Overall alcohol consumption in the

Table 1. Descriptive Data for Men (N = 58) and Women (N = 90) With Bipolar Disorder

Characteristic	Men, N (%)	Women, N (%)	Statistics[a] Test Result	p
Comorbid anxiety	18 (31)	42 (47)	$\chi^2 = 3.6$	.059
Alcohol consumption				
Any alcohol	34 (59)	53 (59)	$\chi^2 = 0.0$	.974
Any beer	29 (50)	28 (31)	$\chi^2 = 5.3$	.021
Any wine	21 (36)	38 (42)	$\chi^2 = 0.5$	.466
Any spirits	11 (19)	20 (22)	$\chi^2 = 0.2$	.635
	Mean (SD)	Mean (SD)		
Age, y	41.1 (10.6)	41.3 (10.9)	t = 0.1	.937
Illness duration, y	19.0 (12.5)	18.9 (15.7)	t = 0.0	.977
No. of standard drinks per week				
Total	3.8 (8.9)	1.2 (1.9)	t = 2.5	.015
Beer	2.7 (7.4)	0.6 (1.3)	t = 2.4	.019
Wine	0.6 (1.3)	0.3 (0.6)	t = 1.4	.17
Spirits	0.9 (5.3)	0.2 (0.7)	F = 1.1	.262
No. of drinking episodes per year	68.9 (104.5)	33.2 (55.3)	t = 2.3	.013

[a]For all χ^2 analyses, df = 1.

study sample was minimal: 66% of subjects consumed less than 1 alcoholic beverage per week, 25% consumed 1 to 6 drinks per week, and 9% consumed 7 or more drinks per week. The difference in mean weekly overall alcohol consumption for subjects with bipolar I disorder (mean = 2.4, SD = 6.7 standard drinks) versus bipolar II disorder (mean = 2.0, SD = 3.6 standard drinks) was not statistically significant (t = 0.3, p = .75), and this was true of beer, wine, and spirits consumption as well. Based on the results of correlational analyses (Table 2), multivariate analysis of covariance was conducted for the following variables: number of emergency department (ED) visits at baseline; baseline number of manic, hypomanic, and depressive episodes; and manic symptoms at baseline. Age, duration of illness, and comorbid anxiety disorder were included as covariates.

Among men, overall alcohol consumption and spirits consumption accounted for a significant proportion of the variance in emergency department visits (F = 4.3, df = 1, p = .046 and F = 14.0, df = 1, p < .001, respectively). Number of lifetime manic episodes was associated with overall alcohol consumption (F = 10.2, df = 1, p = .003) and spirits consumption (F = 81.8, df = 1, p < .001). There was no significant association between any form of alcohol consumption and lifetime episodes of hypomania or depression.

Among women, the frequency of alcohol consumption was associated with lifetime episodes of depression (F = 15.5, df = 1, p < .001) and hypomania (F = 4.8, df = 1, p < .03). Wine consumption among women was associated with lifetime hypomanic episodes (F = 13.6, df = 1, p < .001) and current manic symptoms (F = 4.0, df = 1, p < .05). There was a statistical trend toward a negative association between current depressive symptoms and overall alcohol consumption (F = 3.0, df = 1, p = .089) and beer consumption (F = 3.4, df = 1, p = .071).

DISCUSSION

The primary finding of this study is that there is an association between alcohol use and illness variables in bipolar disorder among individuals who have no history of alcoholism and who do not exceed weekly low-risk drinking guideline limits. To our knowledge, this is the first report describing the association of alcohol use with bipolar disorder in this population.

There is a growing emphasis in the unipolar depression literature on the importance of treating depression to remission, as the presence of even a few residual depressive symptoms bodes poorly for relapse.[20] By the same token, alcohol consumption below the threshold of abuse or heavy use may predispose individuals with bipolar disorder to worse outcomes. Although moderate alcohol consumption is not necessarily a specific predictor of later AUDs, it may be the case that even modest alcohol consumption asserts a destabilizing influence on bipolar illness in its own right.

The data showed a striking association between lifetime manic episodes and the frequency and volume of alcohol consumption—particularly spirits—among men but not among women. In addition, the frequency of alcohol consumption was associated with lifetime number of depressive episodes among women but not among men. Frye and colleagues[19] reported similar gender differences in the association of lifetime alcoholism with bipolar disorder characteristics. They found that alcoholism was associated with lifetime depressive episodes among women but not among men, and that the presence of comorbid lifetime alcoholism was associated with a trend toward more manic episodes and more hospitalizations for mania among men but not among women. Salloum and colleagues[21] found that female alcoholics with bipolar disorder were more likely than male alcoholics with bipolar disorder to report depressive symptoms when presenting

Table 2. Correlations of Demographic and Clinical Measures With Alcohol Consumption Among Men (N = 58) and Women (N = 90) With Bipolar Disorder

Variable	Total[a]	Beer[a]	Wine[a]	Spirits[a]	Frequency[b]
Current age					
Men	–0.33*	–0.28*	–0.18	–0.14	–0.33*
Women	–0.33**	–0.28*	–0.05	–0.34**	–0.19
Bipolar illness duration					
Men	–0.18	–0.23	0.00	0.04	–0.14
Women	–0.48***	–0.56***	–0.04	–0.24*	–0.19
Depressive episodes					
Men	–0.13	–0.12	–0.02	–0.10	–0.18
Women	–0.11	–0.16	0.07	–0.11	0.34**
Hypomanic episodes					
Men	–0.19	–0.21	–0.06	–0.10	–0.26
Women	0.21	–0.01	0.47***	0.13	0.32*
Manic episodes					
Men	0.46**	–0.09	0.28†	0.81***	0.39*
Women	–0.15	–0.14	–0.10	–0.11	–0.13
Depressive symptoms					
Men	–0.04	–0.05	–0.12	0.05	–0.05
Women	–0.26*	–0.28*	–0.08	–0.14	–0.05
Manic symptoms					
Men	–0.08	–0.02	–0.16	–0.01	–0.12
Women	0.05	0.01	0.23*	–0.09	0.08
Hospitalizations					
Men	–0.03	0.01	–0.07	–0.04	–0.04
Women	–0.01	0.01	0.00	–0.04	–0.04
Emergency department visits					
Men	0.34*	0.06	–0.05	0.48***	0.32*
Women	–0.10	–0.12	–0.11	–0.08	–0.07

[a]No. of standard drinks per week.
[b]No. of drinking episodes per year.
*p < .05; **p < .01; ***p < .001; †p < .10.

for initial evaluation to a university psychiatric clinic. Therefore, our findings regarding moderate alcohol use among lifetime non-alcoholic individuals with bipolar disorder converge with those reported previously for individuals with comorbid bipolar disorder and alcoholism.

There were negative associations between alcohol consumption and age, and between alcohol consumption and duration of illness—the latter finding being statistically significant among women only. However, these variables were included as covariates in the multivariate analyses and did not attenuate the association between alcohol use and severity of bipolar illness. Alcohol consumption, particularly spirits, was associated with ED visits among men but not among women. One possible explanation for this gender difference is that, as elaborated above, alcohol consumption is associated with lifetime manic episodes among men and lifetime depressive episodes among women. Although ED visits for mania by individuals with bipolar disorder are approximately equal in number to ED visits for depression,[22] bipolar individuals experience more depressive episodes,[23] such that episodes of mania carry a greater probability of resulting in ED visits. In general, individuals with comorbid psychiatric and substance use disorders are known to utilize ED services significantly more than individuals with psychiatric disorders alone,[24] and previous studies of individuals with bipolar disorder specifically have reported similar trends.[25,26]

Our findings suggest that it may not be sufficient to examine overall alcohol use in isolation; rather, it is important to address consumption of specific types of alcohol, which may share opposite associations with illness-associated outcomes. For example, beer consumption among women was negatively associated with depressive symptoms, while wine consumption among women was positively associated with manic symptoms and lifetime hypomanic episodes. These relevant findings would be missed if only overall alcohol use had been examined. Therefore, it is important both that future studies address subtypes of alcohol and that clinicians consider doing the same in assessing and managing bipolar patients.

This study is subject to several methodological limitations. First, subjects in this study represent a minority of individuals with bipolar disorder in that they are consistently treatment adherent, relatively asymptomatic, not substance abusing, and motivated to participate in a psychosocial intervention for bipolar disorder in addition to pharmacotherapy. Nonetheless, these are individuals with significant bipolar illness as manifested by recent recurrent affective episodes. Another limitation is that analyses addressed cross-sectional associations between alcohol use and illness variables, such that conclusions about causality or direction of these associations cannot

yet be drawn. While one explanation for our findings is that moderate alcohol use asserts a destabilizing influence on bipolar disorder, it is also possible that individuals with histories of numerous affective episodes or ED visits use alcohol, even in moderate amounts, to self-medicate. Finally, alcohol use was quantified using self-report alone and did not incorporate information from collateral informants. However, this is not likely to assert a sizable effect given that collateral information has been shown to correlate highly with self-report among individuals with bipolar disorder and substance use disorders.[27]

Taken together, these findings suggest that even at modest volumes of consumption, alcohol is associated with important measures of illness severity in bipolar disorder, including emergency department visits, number of mood episodes, and current symptoms. These observations emanate from a sample that is self-selected, treatment adherent, and relatively asymptomatic, suggesting that the strength of the association of modest alcohol consumption with bipolar disorder identified in this study most likely understates the association of modest alcohol consumption with illness severity among individuals with bipolar disorder in general.

Implications of these findings include the importance of carefully assessing the extent of alcohol consumption and of encouraging abstinence among individuals with bipolar disorder. Future studies from this sample will examine the ongoing dynamic relationship between alcohol consumption and bipolar disorder over 18 months of follow-up.

Drug name: fluoxetine (Prozac and others).

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