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Review

Do alcohol use disorders destabilize the course of bipolar disorder?

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ABSTRACT

Objectives: To determine whether long-term data implicate a negative effect of alcohol-use disorders (AUDs) on time to remission, risk of mood episode recurrence, and risk of mood switch/cycling in patients with bipolar disorder (BD). The short-term temporal sequence between alcohol use and onset of mood episodes was also examined.
Methods: A MEDLINE literature search was conducted for measurement-based reports of alcohol and course of bipolar disorder.
Results: Twenty-three original data publications were identified. Three out of 5 studies addressing the impact of AUDs on recovery from a mood episode demonstrated that alcohol did not prolong index mood episodes of any type. Six out of 11 reports evaluating the relationship between alcohol and the long term risk of mood episode recurrences suggested that high levels of alcohol intake increase the risk of a mood recurrence. Five out of 7 studies evaluating the short-term temporal sequence of AUDs and development of mood episodes among BD patients found that increased alcohol use preceded the development of new mood episodes. Four out of 5 studies examining the association between alcohol and rapid cycling indicated that AUDs were associated with higher rates of rapid-cycling.
Limitations: We limited our review to studies that were large enough to perform statistical testing, which may have led us to overlook informative smaller studies.
Conclusions: Although alcohol does not seem to affect time to mood episode remission, alcohol use destabilizes the course of illness over the long run as evidenced by associations with more rapid cycling and mood episode recurrence.

Contents

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1. Introduction

Bipolar disorder (BD) is a common, disabling condition affecting 2–6% of Western populations (Merikangas et al., 2007; Pini et al., 2005). Alcohol use disorders (AUDs), which include alcohol abuse and alcohol dependence, are also common affecting approximately 13–30% of the US population (Hasin et al., 2007; Kessler et al., 2005; Regier et al., 1990). Community surveys indicate that AUDs are particularly prevalent among BD patients, with rates of comorbidity, ranging from 44–62%, (Merikangas et al., 2007; Oquendo et al., 2010; Regier et al., 1990) making them the most common comorbid axis I disorder among BD patients (Regier et al., 1990), (see Table 1**).** Patients with AUDs have a 6-fold greater risk of experiencing a manic episode than those without an AUD (Helzer and Pryzbeck, 1988). Despite the high prevalence of AUDs among BD patients, the impact of AUDs on BD course of illness has not been an extensive focus of research to date.

Previous observational studies have found alcohol dependence to be associated with a variety of negative outcomes among BD patients, including greater risk of treatment nonadherence, (Baldessarini et al., 2008) and higher rates of suicide attempts, (Feinman and Dunner, 1996; Oquendo et al., 2010) violent behavior (Salloum et al., 2002) and hospitalization (Reich et al., 1974). BD patients with an AUD are also more likely to have comorbid nicotine dependence and drug use disorders, conditions contributing to higher morbidity and early mortality (Oquendo et al., 2010).

Whether AUDs are determintal to mood stability in the long-term course of mood episodes in BD patients is uncertain. Current understanding of the biological impact of chronic, heavy alcohol use on the central nervous system (CNS) in BD patients suggest AUDs should produce harmful consequences for long-term mood stability in BD. Alcohol use affects various brain systems in a dynamic fashion as patients progress from controlled to excessive, compulsive use. These systems include neurotransmitters such as glutamate, GABA, dopamine, serotonin and acetylcholine, as well as neuropeptides, such as cannibinoids, endogenous opioids, corticotropin releasing hormone and neuropeptide Y (Chastain, 2006; Vengeliene et al., 2008). These systems likely play a role in BD pathophysiology as several of them are targets for medications commonly used to treat mood episodes. Examples include the anti-dopaminergic effect of atypical antipsychotics, the anti-glutamatergic effect of lamotrigine and the GABA-enhancing effect of valproate. Disruption in sleep architecture resulting from chronic alcohol use (Brower et al., 2011; Roehrs and Roth, 2001) may also detrimentally affect mood regulation (Harvey, 2008). Excessive alcohol use may set in motion changes in CNS signaling systems that make mood episodes more likely to occur or be more severe, possibly via a kindling process within the brain, leading to more mood episodes over time, and shorter well periods (Sonne et al., 1994).

Neuroimaging research suggests potential biological effects of alcohol that may contribute to poorer outcomes. A history of an AUD is associated with structural and biochemical differences within the CNS of BD patients. Neuroimaging studies demonstrate decreased gray matter volume in the right anterior cingulate and left medial frontal gyri, (Nery et al., 2011) both regions important for mood regulation (Goldin et al., 2008). Furthermore, glutamate levels are reduced in the left dorsolateral prefrontal cortex among BD patients with a history of an AUD compared to those without such history (Nery et al., 2010). Although cause and effect cannot be determined from these studies, they suggest that the neural connectivity necessary for sustained mood regulation may be weakened in BD patients with AUDs versus those without.

The effect of AUDs on episode length and the long-term course of illness has not been established. The few studies that have examined the effects of AUDs on the long-term course of BD report conflicting outcomes and an integrated review on this topic has not previously been published. Because the design and reporting of the published studies are too inconsistent to allow a meta-analysis to be performed, we conducted a narrative review examining the effect of AUDs on BD illness course. The goal of this review was to determine whether long-term data implicate a negative effect of AUDs on time to remission, risk of mood episode recurrence, and risk of mood switch/cycling in patients with BD.

2. Methods

A literature search for all measurement-based reports (observational studies, randomized clinical trials, post-hoc analyses) of alcohol use and course of bipolar disorder was conducted via Ovid MEDLINE computerized database on March 31st, 2012. The search terms used included: 'alcohol,' 'alcoholism,' 'bipolar disorder,' 'remission,' 'recurrence,' 'relapse,' 'episode switch,' and 'cycling.' No limits in language or publication dates were applied. This search produced 133 publications. Possibly eligible studies were identified based on titles and abstracts. These articles were assessed for final inclusion based on the full text. Additionally, the reference lists of all selected articles were searched for other potentially relevant studies.

Studies evaluating alcohol and its relationship to the BD course of illness were examined for course of illness measurements, including time to remission from a mood episode, risk of mood episode recurrence and risk of mood switching or rapid cycling. Mood episode recurrence was further subdivided into those studies that reported the long-term risk of mood recurrence associated with AUDs and those that discussed the temporal sequence between alcohol use and development of mood symptoms in patients with established BD. We excluded review articles, studies that combined BD patients with other psychiatric

Table 1
Lifetime rates of AUDs among community-based samples of subjects with bipolar disorder.

Study	Source	Bipolar disorder			Total population		
		AUDs	Alcohol abuse	Alcohol dependence	AUDs	Alcohol abuse	Alcohol dependence
ECA	Regier et al. (1990)	43.6%	16.1%	27.6%	13.5%	5.6%	7.9%
NCS-R	Merikangas et al. (2007) Kessler et al. (2005)	62.3%[a]	39.1%	23.2%	18.6%[a]	13.2%	5.4%
NESARC	Hasin et al. (2007) Oquendo et al. (2010)	54%	NR	NR	30.3%	17.8%	12.5%

Abbreviations: AUDs=criteria met for either alcohol abuse or dependence; ECA=epidemiologic catchment area study; NCS-R=national comorbidity survey replication; NESARC=national epidemiologic survey on alcohol and related conditions; NR=not reported

[a] Calculated.