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Assessment and treatment of insomnia in adult patients with alcohol use disorders

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ABSTRACT

Insomnia in patients with alcohol dependence has increasingly become a target of treatment due to its prevalence, persistence, and associations with relapse and suicidal thoughts, as well as randomized controlled studies demonstrating efficacy with behavior therapies and non-addictive medications. This article focuses on assessing and treating insomnia that persists despite 4 or more weeks of sobriety in alcohol-dependent adults. Selecting among the various options for treatment follows a comprehensive assessment of insomnia and its multifactorial causes. In addition to chronic, heavy alcohol consumption and its effects on sleep regulatory systems, contributing factors include premorbid insomnia; co-occurring medical, psychiatric, and other sleep disorders; use of other substances and medications; stress; environmental factors; and inadequate sleep hygiene. The assessment makes use of history, rating scales, and sleep diaries as well as physical, mental status, and laboratory examinations to rule out these factors. Polysomnography is indicated when another sleep disorder is suspected, such as sleep apnea or periodic limb movement disorder, or when insomnia is resistant to treatment. Sobriety remains a necessary, first-line treatment for insomnia, and most patients will have some improvement. If insomnia-specific treatment is needed, then brief behavioral therapies are the treatment of choice, because they have shown long-lasting benefit without worsening of drinking outcomes. Medications work faster, but they generally work only as long as they are taken. Melatonin agonists; sedating antidepressants, anticonvulsants, and antipsychotics; and benzodiazepine receptor agonists each have their benefits and risks, which must be weighed and monitored to optimize outcomes. Some relapse prevention medications may also have sleep-promoting activity. Although it is assumed that treatment for insomnia will help prevent relapse, this has not been firmly established. Therefore, insomnia and alcohol dependence might be best thought of as co-occurring disorders, each of which requires its own treatment.

Introduction

Insomnia is common, persistent, and associated with both relapse and suicidal thoughts in adult patients with alcohol dependence.[1] Therefore, assessment and treatment of insomnia among patients with an AUD is critical. This article focuses on adult patients, and readers interested in adolescents are referred elsewhere (Bootzin & Stevens, 2005; Britton et al., 2010; Hasler, Martin, Wood, Rosario, & Clark, 2014). Insomnia can refer to a symptom or a diagnosis. Unless otherwise stated, insomnia is defined as a symptom for the purposes of this article and refers to difficulty initiating or maintaining sleep (including early morning awakening) and/or non-restorative or poor quality sleep as reported by the patient. Difficulty falling asleep (DFA) is sometimes referred to as sleep-onset or initial insomnia, while difficulty maintaining sleep can refer to either middle insomnia (awakenings and time awake after sleep onset, followed by more sleep) or terminal insomnia (early morning awakening without being able to fall back asleep). For diagnostic purposes, insomnia symptoms must also 1) be distressing (i.e., a source of dissatisfaction) to the patient or interfere with daytime functioning, and 2) occur despite adequate

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[1] As most of the research reviewed here was conducted between 1994 and 2013, the diagnostic term, alcohol dependence, as characterized by DSM-IV (American Psychiatric Association, 2000) or the International Classification of Diseases (http://www.who.int/substance_abuse/terminology/ICD10ClinicalDiagnosis.pdf?ua=1) is utilized. In 2013, DSM-5 eliminated alcohol dependence and abuse as diagnoses and replaced them with the single diagnosis of alcohol use disorder (AUD), qualified by severity (American Psychiatric Association, 2013). Alcohol dependence in DSM-IV is roughly equivalent to moderate-to-severe AUD in DSM-V.

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opportunity or circumstances for sleep (American Academy of Sleep Medicine, 2014; American Psychiatric Association, 2013).

Rates of insomnia in patients with alcohol dependence

A review of nine studies across 2133 alcohol-dependent (AD) patients revealed a mean prevalence for insomnia of 56% (range: 36–91%) for symptomatic insomnia (Zhabenko, Wojnar, & Brower, 2012). Adding four other studies for a total of 3173 patients brings the average to 58.4% (Kolla et al., 2014; Perney, Lehert, & Mason, 2012; Watanabe, Ogihara-Hashizume, Kobayashi, Mitsushio, & Komiyama, 2001; Zhabenko et al., 2012). The wide variability in range across studies is likely due to differences in sample characteristics (e.g., demographics, drinking severity, duration of abstinence, and comorbidity), as well as definitions of, and methods used to measure, insomnia. Nevertheless, these prevalence studies provide clinicians with an estimate and expectation for their own practices. Independent correlates of insomnia using multivariable analyses that were consistent across studies include 1) measures of drinking severity such as quantity (Baekeland, Lundwall, Shanahan, & Kissin, 1974), frequency (Zhabenko et al., 2012), Michigan Alcoholism Screening Test scores (Zhabenko et al., 2012), and gamma-glutamyltransferase levels (Perney et al., 2012); and 2) general measures of psychiatric severity (Brower, Krentzman, & Robinson, 2011; Zhabenko et al., 2012) as well as specific measures of anxiety and depression (Baekeland et al., 1974; Perney et al., 2012).

Mechanisms of alcohol-related insomnia may include genetic polymorphisms, which have been correlated with insomnia severity in AD patients (Brower, Wojnar, Sliwerska, Armitage, & Burmeister, 2012), depression (Zhabenko, Krentzman, Robinson, & Brower, 2013), and alcohol-associated impairments in sleep regulation processes, including reduced biological drive for sleep (Armitage, Hoffmann, Conroy, Arnedt, & Brower, 2012; Irwin et al., 2002), and dysregulation in circadian rhythms (Conroy et al., 2012; Hasler, Smith, Cousins, & Bootzin, 2012).

Persistence of insomnia

Insomnia may begin prior to or during alcohol withdrawal and is among its diagnostic criteria (American Psychiatric Association, 2013). In the general population, 32% of individuals with a lifetime diagnosis of alcohol dependence reported withdrawal-related insomnia (Brower & Perron, 2010). Among those who also met DSM-IV criteria for alcohol withdrawal (American Psychiatric Association, 2000) the rate was 50%. Acute alcohol withdrawal generally lasts no more than 1 week, although protracted withdrawal syndromes that include sleep disturbance have been described as lasting from weeks to several months (Heilig, Egli, Crabbe, & Becker, 2010). The persistence of insomnia despite several months or more of abstinence or treatment for alcohol dependence has been demonstrated in several clinical studies (Brower, Krentzman, et al., 2011; Cohn, Foster, & Peters, 2003; Currie, Clark, Rimac, & Malhotra, 2003; Kolla et al., 2014; Perney et al., 2012). Brower, Krentzman, et al. (2011) studied 225 alcohol-dependent patients entering inpatient and outpatient programs and found that 103 (46%) had baseline insomnia based on a questionnaire. At 6-month follow-up, 25% (26 of 103) had persistent insomnia at 6 months despite abstinence for the previous 3 months. Unfortunately, this study did not determine the etiology of insomnia, which could have included co-occurring disorders as well as long-term effects of alcohol on brain regions regulating sleep. Nevertheless, clinicians may expect approximately one-quarter of their alcohol-dependent patients to have persistent insomnia despite abstinence from alcohol.

Parallel findings for persistent sleep abnormalities as measured by polysomnography (PSG) despite 3–27 months of abstinence have been reported and previously reviewed (Brower, 2001). Sleep architecture can be disrupted for 21–27 months, including an increase in the percentage of Stage 1 sleep (N1 or light sleep), a decrease in the percentage of N3 or slow-wave sleep (deep sleep), an increase in rapid eye movement (REM) sleep percentage (REM%), and a decrease in REM sleep latency (REM-L: time to first REM sleep period after falling asleep). These alterations in REM sleep (increased REM% and decreased REM-L) are characteristics of increased REM pressure (Gann et al., 2001; Gillin et al., 1994) and may possibly be experienced by patients as increased and/or vivid dreaming. A more recent, albeit small cross-sectional, study of 42 AD individuals with a mean (range) duration of 196 (30–719) abstinent days revealed increased N1% and REM%, and decreased N3% and slow-wave activity during non-REM (NREM) sleep, when compared to control subjects (Colrain, Turlington, & Baker, 2009). Total estimated lifetime alcohol consumption, but not duration of sobriety prior to PSG, predicted these results. This suggests that chronic, heavy alcohol intake contributes to objectively measured sleep disturbances that persist despite length of sobriety. In terms of PSG-measured sleep continuity parameters, it can take 5–9 months for sleep onset latency (time to fall asleep) and sleep efficiency (percentage of time in bed spent sleeping) to normalize (Drummond, Gillin, Smith, & DeModena, 1998; Williams & Rundell, 1981), and 14 months for total sleep time to normalize (Drummond et al., 1998), although the sample sizes for these studies are small. Altogether, sleep PSG parameters can remain abnormal for 2 or more years of abstinence (Drummond et al., 1998).

Sleep predicts relapse

At least 10 published studies using PSG parameters as predictors since 1975 (Allen & Wagman, 1975; Allen, Wagman, & Funderburk, 1977; Brower, Aldrich, & Hall, 1998; Clark et al., 1998, 1999; Drummond et al., 1998; Feige, Scaal, Hornyak, Gann, & Riemann, 2007; Gann et al., 2001, 2002; Gillin et al., 1994) and seven studies since 1979 using subjective reports of sleep (Brower et al., 1998; Brower, Aldrich, Robinson, Zucker, & Greden, 2001; Conroy et al., 2006; Foster, Marshall, & Peters, 1998; Foster & Peters, 1999; Malcolm, Myrick, Veatch, Boyle, & Randall, 2007; Skoloda, Alterman, & Gottheil, 1979) have linked baseline sleep problems with subsequent return to drinking or relapse.

Difficulty falling asleep is the most replicated, subjective marker of relapse (Brower et al., 1998; Conroy et al., 2006; Foster & Peters, 1999; Skoloda et al., 1979). Consistent with subjective reports, at least two studies found that PSG-measured sleep onset latency (i.e., increased time to fall asleep) predicted drinking at follow-up (Brower et al., 1998; Drummond et al., 1998), and one study with actigraphy-measured sleep onset latency did as well (Smith, Hill, Marshall, Keaney, & Wanigaratne, 2013). Alterations in REM sleep parameters (e.g., increased REM%, decreased REM-L, and increased REM density), indicative of increased REM pressure, are also a replicated, prospective marker of relapse (Gann et al., 2001; Gillin et al., 1994). Although a role for dreaming as a marker for relapse has been suggested (Choi, 1973; Christo & Franey, 1996; Flowers & Zweben, 1998), it is not well studied. One study found an association between periodic limb movements during sleep and relapse (Gann et al., 2002). Most studies defined relapse as any self-reported drinking during the follow-up period, but one study (Conroy et al., 2006) found that sleep predictors of relapse may differ depending on how drinking outcomes are defined (e.g., frequency of drinking days vs. heavy drinking days) and when outcomes are measured (e.g., 6 weeks vs. 12 weeks).