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

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**ARTICLE INFO**

Article history:
Received 12 October 2014
Accepted 3 December 2014

Keywords:
Sleep
Alcohol dependence
Alcoholism
Pharmacotherapy
Cognitive-Behavioral therapy
Review

**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.

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**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). Alcoholic dependence in DSM-IV is roughly equivalent to moderate-to-severe AUD in DSM-V.
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 et al., 2001; Zhabenko et al., 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 practice. 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, Arndt, & 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, Ehl, 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, Rinac, & 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) abstinence 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, Hornyk, 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).
Why poor sleep is associated with relapse is unknown. Possible mediators include impaired executive functioning (e.g., impulse control, judgment, decision making), negative affect, enhanced sensitivity to stress, and self-medication. While self-medication is commonly endorsed by patients, it has been poorly studied as a mechanism for relapse and one study failed to find an association between self-medication and relapse (Brower et al., 2001).

Sleep and suicidal behavior

The relationship between sleep disturbances and suicidal behaviors, including thoughts, across populations has recently been reviewed (Pigeon, Pinquart, & Conner, 2012). This relationship was recently extended to include a sample of alcohol-dependent patients (Klimkiewicz et al., 2012) and veterans who misuse alcohol (Chakravorty, Grandner, et al., 2014).

Assessment

When conducting a history from alcohol-dependent patients with a complaint of insomnia, the following questions will help to determine the nature, severity, and potential causes of the symptoms:

- Is there difficulty falling asleep (sleep-onset or initial insomnia), staying asleep (sleep maintenance or middle insomnia), waking too early in the morning and being unable to fall asleep again (late insomnia), or some combination of these symptoms? Initial and middle insomnia are the most common in AD patients (Currie et al., 2003; Zablenko et al., 2012).
- How frequently do these symptoms occur and for how long? Both DSM-5 (American Psychiatric Association, 2013) and ICSD-3 (American Academy of Sleep Medicine, 2014) specify criteria that insomnia symptoms should occur at least 3 nights per week for at least 3 months to make a diagnosis of chronic insomnia (ICSD-3) or persistent insomnia (DSM-5). However, symptoms that occur less frequently or for shorter durations may still be clinically significant.
- On nights when insomnia symptoms occur, a) how long does it take to fall asleep, b) how many awakenings occur and result in how much time awake, and c) how many total hours of sleep does the patient get? In general, more than 30 min to fall asleep, more than 30 min of awake time after falling asleep, and/or less than 6.5 h total sleep time are problematic.
- When are usual bedtimes and wake times? Are these consistent or variable across nights? Do they suggest the patient goes to sleep earlier than most people do, but also awakens early (“sleep phase advance” commonly seen in older adults); or goes to sleep later than most people and sleeps in later (“sleep phase delay” somewhat typical of adolescents). These variations in phase shifts suggest a circadian component to a patient’s complaint of insomnia.
- Do insomnia symptoms either cause the patient significant distress or impair daytime functioning (e.g., work or academic performance, cognitive abilities, emotional regulation, or interpersonal relationships)?
- Do the symptoms occur despite an adequate opportunity and environment conducive for sleep? Deliberately staying up late either to accomplish work or engage in pleasurable activities when one has to get up early does not provide an adequate opportunity for sleep and differs from insomnia.
- What is the relationship between insomnia symptoms and drinking alcohol? 1) Does the patient use alcohol to fall sleep? While self-medication of insomnia with alcohol is usually ineffective, it is common (Brower et al., 2001) and will need to be addressed when initiating and maintaining sobriety. 2) Did insomnia precede the onset of alcohol dependence? The answer will help determine if insomnia has been independent of drinking. If so, it may persist despite abstinence and require its own treatment. 3) Has insomnia persisted during prior sober periods? If true for periods between 1 and 3 months, then insomnia may be independent of continued drinking and other causes will need to be ruled out.

The clinician’s main concern when taking a history is: What is causing insomnia in this particular patient? One should assume that alcohol is always one contributing factor, but not necessarily the only one, because insomnia is frequently multifactorial. As a general rule, if dependent drinking patterns are the main cause of insomnia, then one may expect some improvement usually within 1–3 months of abstinence-based treatment.

Reasons for persistent insomnia despite abstinence from alcohol include:

1. Premorbid insomnia. In clinical samples, more than 50% of alcohol-dependent patients reported premorbid insomnia (Currie et al., 2003). Prospective studies indicate that insomnia is a risk factor for developing alcohol-use disorders (Crum, Storr, Chan, & Ford, 2004; Wong, Brower, Nigg, & Zucker, 2010).
2. Co-occurring or comorbid disorders, which generally fall into three groups: medical, psychiatric, and other sleep disorders.
   - Common medical disorders that can cause insomnia include but are not limited to chronic pain, cardiac dysrhythmias, congestive heart failure, hypothyroidism, gastroesophageal reflux disease, and chronic obstructive pulmonary disease (Reite, Weissberg, & Ruddy, 2009).
   - Mental disorders associated with insomnia such as mood disorders, anxiety disorders, and trauma-related disorders are more likely to occur in those with than without alcohol dependence (Hasin, Stinson, Ogburn, & Grant, 2007; McCarthy & Petrakis, 2010). Diagnostic criteria for post-traumatic stress disorder include distressing dreams or nightmares about the trauma as well as insomnia due to increased arousal. In addition, insomnia may be associated with trauma that occurred temporally close to, or after bedtime; for example, in cases of childhood sexual trauma in which the perpetrator awoke the victim from sleep. In one study of 302 AD patients, a history of childhood abuse was two times more common in those with than without insomnia (40% vs. 21%, p = .001), and significantly predicted insomnia (OR = 2.4, p = .01) after controlling for other variables, including medical and psychiatric severity (Zablenko et al., 2012).
   - Alcohol-dependent patients may also have higher rates of other sleep disorders, including obstructive sleep apnea (OSA) and periodic limb movement disorder (PLMD) (Aldrich, Brower, & Hall, 1999; Cann et al., 2002). Although these two disorders can only be diagnosed with polysomnography, a sleep history can provide clues if any of the following are reported by the patient or a bed partner: loud snoring, breathing cessation or gasping for air during sleep, kicking or other disruptive behaviors during sleep, restless legs due to unpleasant sensations in them around bedtime, and daytime sleepiness. Patients may be unaware of OSA or PLMD, so bed partners are important to interview when available. Both disorders are associated with multiple mini-arousals at night, which are frequent enough to disrupt sleep but not long enough to be remembered. Consequently, patients may not feel rested in the morning or be sleepy during the day. Restless legs syndrome (RLS), which can
interfere with falling asleep, is highly comorbid with PLMD. Therefore, RLS generally signals that PSG is indicated. Nocturnal wandering, including sleepwalking, is also more common in those with than without alcohol use disorders (Ohayon, Mahowald, Daumilliers, Krystal, & Léger, 2012). Reite et al. (2009) recommended the following three questions to screen for sleep disorders, including insomnia:

- Are you satisfied with your sleep? (Screens for insomnia.)
- Are you excessively sleepy during the day? (Screens for sleep apnea, periodic limb movement disorder, narcolepsy.)
- Does your bed partner complain about your sleep? (Screens for snoring, kicking, and parasomnias such as sleepwalking, sleep terrors, and REM sleep behavior disorder during which patients can dangerously act out their dreams.)

3. Use of other substances and medications that can induce insomnia. In addition to drinking, other substances known to cause or worsen insomnia include overuse of caffeine or stimulant intoxication, cannabis withdrawal, opioid withdrawal, sedative-hypnotic withdrawal, and tobacco withdrawal (Conroy & Arnedt, 2014). Use of opioids and sedative-hypnotics can also worsen sleep apnea. Many non-addictive medications are also associated with insomnia such as stimulating antidepressants (e.g., bupropion), thyroid medication, and bronchodilators (Conroy & Brower, 2011). Serotonin-selective reuptake inhibitors (SSRIs), used to treat depressive and anxiety disorders, may improve sleep to the degree insomnia is related to those disorders, but they can also disrupt sleep parameters and increase periodic limb movements during sleep as measured by PSG (Armitage, 2000; Yang, White, & Winkelman, 2005).

4. Stress. AD patients generally seek treatment because of one of more stressful events, such as family conflicts, occupational problems, legal trouble (e.g., drunk driving arrest), and/or exacerbations of psychiatric symptoms or medical disorders. These stressors, which can interfere with sleep, do not necessarily resolve simply because one stops drinking. Neurophysiologically correlates of stress, including hypothalamic-pituitary-axis (HPA) dysregulation, are associated with hyperarousal that can contribute to insomnia (Roehrs, Gumenyuk, Drake, & Roth, 2014).

5. Environmental factors & inadequate sleep hygiene. Some sleep environments and sleep habits will compromise sleep. Alcohol-dependent patients can have poor sleep habits, such as bedtime routines and irregular sleep schedules (Currie et al., 2003). A disruptive bed partner (who snores or kicks), children, or pets; noise; room temperature (too hot or too cold); melatonin-suppressive lighting (including televisions and computer screens); stimulating bedtime activities; and/or an uncomfortable mattress or pillows may all compromise the environment for sleep.

Beyond history: rating scales and objective sleep measures

Self-administered rating scales are useful to assess the severity of insomnia symptoms at baseline and then track change over time after treatment is started. A few are highlighted here. The Sleep Problems Questionnaire (Jenkins, Stanton, Niemcyr, & Rose, 1988) has four questions keyed to the past 1 month, yielding a score ranging from 0 to 20 with higher scores indicating greater severity, and measures change over time (Brower, Krentzman, et al., 2011). Three items ask about initial, middle, and late insomnia, and the fourth asks about feeling tired and worn out upon awakening in the morning. Advantages include brevity and ease of scoring. Disadvantages include lack of a cut-off score for insomnia and no questions about daytime impairment. The Athens Insomnia Scale with eight items keyed to the past month has been internationally validated and used with alcohol-dependent patients (Zhabenko et al., 2012). In addition to asking about initial, middle, and late insomnia, it includes questions about daytime functioning and a cut-off score to screen for a diagnosis of insomnia. The Insomnia Severity Index is a 7-item questionnaire that asks about types of insomnia and daytime impairment. It is keyed to the past 1-2 weeks for more frequent measurements with interpretable cut-off scores (Bastien, Vallières, & Morin, 2001). The Pittsburgh Sleep Quality Index (PSQI) is a longer form with 19 items and a more complicated scoring algorithm than the ones above. It is not limited to insomnia questions, but has evolved into a gold standard among sleep specialists with a cut-off score (>5) to screen for sleep disturbance (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989). Daytime sleepiness is commonly measured by the Epworth Sleepiness Scale (Johns, 1991).

Sleep diaries provide a meaningful view of night-to-night sleep patterns, such as bedtimes, final awake times, time spent in bed, number and duration of nighttime awakenings, total sleep time, and quality of sleep (Carney et al., 2012). Patients fill in the form both in the morning after they wake up and at night before bedtime for 1-2 weeks. For patients seeking sleeping pills, sleep diaries help to delay premature prescribing, until the physician has obtained enough data to analyze actual sleep patterns. As sleep diaries also amount to daily homework assignments, which patients may or may not complete, they allow the clinician to assess a patient's current (and perhaps future) adherence and motivation for active involvement in the assessment and treatment process.

Objective measures of sleep include wrist actigraphy and PSG. Wrist actigraphy, which records movement activity, collects information about sleep patterns without requiring the patient to do anything except wear the device like a wrist watch (Morgenthaler et al., 2007). Due to its cost, it is mostly limited to research with AD participants and to verify sleep diary data (Brower, Conroy, Kurth, Anderson, & Stein, 2011; Currie, Malhotra, & Clark, 2004). Actigraphy may find greater use as lower-priced, but higher quality consumer-oriented products become available. PSG is indicated when (1) there is a suspicion of a sleep disorder such as sleep apnea or PLMD, or (2) the patient has treatment-resistant insomnia. When self-report and objective sleep measures are compared, alcohol-dependent patients tend to overestimate how long it takes them to fall asleep and/or underestimate the duration of time they spend awake during the night after falling asleep (Brooks, Krumlauf, Whiting, Clark, & Wallen, 2012; Conroy et al., 2006; Currie, Malhotra, et al., 2004).

Treatment

There is a growing but limited evidence base for treating insomnia in patients with alcohol dependence. The goals of treatment are to improve sleep and daytime functioning, and to reduce relapse. Even though sleep disturbances are a marker for relapse, treating them does not necessarily reduce relapse to drinking (Roth, 2009). Indeed, randomized controlled trials have demonstrated that treatments which improve sleep in alcohol-dependent patients may have no effect on drinking (Arnedt, Conroy, Armitage, & Brower, 2011; Currie, Clark, Hodgins, & El-Guebaly, 2004; Litten et al., 2012) or even increase it (Friedmann et al., 2008). Thus, treatment needs to target alcohol dependence as well as insomnia and its contributing factors. Furthermore, sleep disturbances across patients improve at least to some extent with sobriety (Brower, Krentzman, et al., 2011). Therefore, treatment for alcohol dependence is always first-line treatment for alcohol-related insomnia, even though it may be insufficient by itself. Insomnia-specific
treatments can be divided into educational approaches, behavior therapies, and medications.

Education

Sleep hygiene is a commonly used educational approach for insomnia (Stepanski & Wyatt, 2003). Sleep hygiene alone is rarely sufficient treatment for insomnia, and is more effective when combined with other insomnia-specific therapies (Kaku et al., 2012; Taylor, Schmidt-Nowara, Jessop, & Ahearn, 2010). Some patients may report that they have tried sleep hygiene techniques and they were not successful. Such patients can be asked how long they practiced them. Sleep hygiene is optimal only if practiced consistently over several weeks to become habits. Essentials of sleep hygiene are listed in Table 1.

Behavioral therapy

Behavioral therapies are generally the first-line treatment for insomnia for several reasons. First, they are effective and longer lasting than medications, which typically stop working when they are discontinued (Friedmann et al., 2008). Second, patients with substance-use disorders are accustomed to using external chemicals to manage their distress (the so-called "pill for every ill" mentality), and behavioral therapy does not reinforce this mindset. Especially during early recovery, alcohol-dependent patients are encouraged to focus on developing non-chemical alternatives to manage their stress and prevent relapse. This is not to say that medications should be avoided altogether. For example, cognitive-behavioral therapy for insomnia (CBT-I) may take several weeks before benefits are achieved and medications might help during that time. Rather, medications should be used judiciously when indicated and with awareness of AD patients' dynamics regarding medication. Behavioral therapies for AD individuals with insomnia have recently been reviewed (Brooks & Wallen, 2014). Two of them, progressive relaxation therapy and CBT-I, have been investigated using randomized controlled trials (RCTs), and are discussed below (see also Table 2).

One study of progressive relaxation therapy randomized 22 AD patients to waitlist control (Greeff & Conradie, 1998). Sleep quality, as assessed by a single question at 2 weeks, was significantly improved in the active group but not the control group. Drinking outcomes were not studied.

Cognitive-behavioral therapy for insomnia (CBT-I) consists of four components: sleep hygiene, stimulus control, sleep restriction, and cognitive therapy; which are detailed elsewhere (Arnedt, Conroy, & Brower, 2007; Curley, Clark, et al., 2004). It is the best studied of behavioral therapies for insomnia across patient populations. Nevertheless, only two randomized controlled trials involving just 77 AD patients have been published to date. In both of these studies, AD patients were selected for insomnia. Some improvements in sleep persisted for 3–6 months. Likewise, Arnedt et al. (Arnedt et al., 2011) randomized 17 AD outpatients to eight weekly sessions of either CBT-I or behavioral placebo treatment, including four in-person and four telephone call sessions. Subjective reports of sleep improved significantly more in the CBT-I group than in the placebo group, and effects were stabilized after five sessions, consistent with the study by Currie, Clark, et al. (2004). Also consistent with the previous study, no difference in relapse rates between groups was found despite improved sleep in the CBT-I group. Potential barriers to implementing CBT-I in clinical practice are limited availability of trained therapists and delayed improvement, usually evident only after several weeks of treatment. Alternative delivery systems including the Internet, smart phone applications, and telephone-delivered CBT-I sessions combined with a self-help manual may increase availability in the future (Brooks & Wallen, 2014; Currie, Clark, et al., 2004). Paradoxically, dysfunctional beliefs about sleep, targeted in CBT-I, were protective of relapse in one study (Smith et al., 2013).

Pharmacotherapy

Pharmacotherapy of insomnia in AD patients has been reviewed previously (Kolla, Mansukhani, & Schneekloth, 2011), including RCTs published before 2010 as well as open-label studies, and studies limited to the withdrawal period (during and up to 15 days after withdrawal). What follows below for the most part are summaries of randomized, double-blind placebo-controlled trials that included sleep outcomes for up to 4 weeks after completing acute

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**Table 1**

<table>
<thead>
<tr>
<th>Sleep hygiene guidelines.</th>
</tr>
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<tbody>
<tr>
<td>1. Make the sleep room as comfortable and conducive as possible (dark and quiet, moderate temperature, good bed and pillows). Use earplugs or eye masks if helpful.</td>
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<tr>
<td>2. Set and keep regular bedtimes and wake times, within 1 h daily, including weekends.</td>
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<tr>
<td>3. Do not nap during the day, as it will reduce sleep drive at night, although brief naps (10–20 min) may be helpful to reduce daytime sleepiness.</td>
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<tr>
<td>4. Create a bedtime routine to wind down and prepare yourself for sleep.</td>
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<tr>
<td>5. Avoid stimulating or anxiety-provoking activities within an hour of bedtime and avoid exercise within 3 h of bedtime.</td>
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<tr>
<td>6. Avoid bright lights and television or computer screens before bedtime, which can suppress melatonin secretion.</td>
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<tr>
<td>7. Do not drink alcohol prior to bedtime. (Abstain completely for alcohol-dependent patients.)</td>
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<tr>
<td>8. Use of drugs and tobacco dependence can disrupt your sleep.</td>
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<tr>
<td>9. Do not ingest caffeine-containing drinks or foods in the evening.</td>
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<tr>
<td>10. Limit other beverages and heavy meals prior to bedtime. A light snack is acceptable.</td>
</tr>
</tbody>
</table>

**Table 2**

<table>
<thead>
<tr>
<th>Authors, year</th>
<th>N</th>
<th>Selected for insomnia</th>
<th>Setting</th>
<th>PSG</th>
<th>Treatment intensity</th>
<th>Effect on insomnia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Greeff and Conradie (1988)</td>
<td>22</td>
<td>Yes</td>
<td>IP</td>
<td>No</td>
<td>10 sessions in 2 weeks</td>
<td>↓</td>
</tr>
<tr>
<td>CBT-I</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Currie, Clark, et al. (2004)</td>
<td>60</td>
<td>Yes</td>
<td>OP</td>
<td>No</td>
<td>5 sessions in 7 weeks</td>
<td>↓</td>
</tr>
<tr>
<td>Arnedt et al. (2011)</td>
<td>17</td>
<td>Yes</td>
<td>OP</td>
<td>Yes</td>
<td>8 sessions in 8 weeks</td>
<td>↓</td>
</tr>
</tbody>
</table>

ns = no significant difference from control group; IP = inpatient; OP = outpatient; PSG = polysomnography to rule out other sleep disorders. * See text for details.
detoxification and withdrawal, given the focus on treatment of persistent insomnia (Table 3). In the United States, medications for sleep can be classified as non-prescription sedatives-hypnotics, medications specifically approved by the Food and Drug Administration (FDA) for insomnia, and so-called “off-label” prescription medications that are approved by the FDA, but not for insomnia (McCall & McCall, 2012; Roehrs & Roth, 2012). Prescriptions available in parts of Europe but not the U.S. include prolonged-release melatonin and agomelatine.

**Melatonin agonists (melatonin, ramelteon, agomelatine)**

Current evidence suggests that melatonin levels are decreased and/or delayed in abstinent AD individuals and during withdrawal (Conroy et al., 2012; Kühlein, Hauger, & Irwin, 2003; Schmitz, Sepandj, Pichler, & Rudas, 1996). No controlled studies of melatonin or melatonin agonists for alcohol-associated insomnia have been published to date. Melatonin, a naturally occurring hormone, is both 1) a chronobiotic that in small doses can advance or delay the circadian phase of the sleep cycle, depending on the timing of its administration; and 2) a sleep-inducing medication with modest effects in larger doses when administered before one’s usual bedtime (Ferraccioli-Oda, Qawasmi, & Bloch, 2013). It has not been studied as an aid to sleep in AD patients. Ramelteon is a prescription melatonin agonist approved by the FDA to treat sleep-onset insomnia. One open-label study of five AD patients treated with 8 mg nightly taken 30 min before bedtime for 4 weeks showed improvements in insomnia as measured by the Insomnia Severity Index and sleep diary (Brower, Conroy, et al., 2011). In a similar open-label study of 9 AD outpatients with insomnia, another melatonin agonist, agomelatine, in doses of 25–50 mg also improved sleep in AD patients over a 6-week period (Grosshans, Mutschler, Luderer, Mann, & Kiefer, 2014). Hepatotoxicity may be a limiting factor for agomelatine in AD patients.

**Sedating antidepressants (trazodone, doxepin, mirtazapine)**

There are two randomized double-blind, placebo-controlled studies of trazodone to treat sleep problems in AD patients. These are reviewed in detail due to 1) its historical status as the most commonly prescribed medication for sleep in alcohol-dependent patients (Friedmann et al., 2003), and 2) controversy over its use. The first study involved 18 AD patients with insomnia who, 2 weeks after completing pharmacological detoxification, received study medication 1 h prior to bedtime for 4 weeks. Trazodone was titrated from 50 to 200 mg over the first week of treatment and lowered to 150 mg between days 10 and 20 if not tolerated well. (Five of eight trazodone-treated patients had their dose reduced due to dizziness or hangover.) Polysomnography was performed at baseline when all patients took placebo, on the first night after randomization to study medication (trazodone vs. placebo), and at 4 weeks only if absent (n = 16 of 18) (Le Bon et al., 2003). The trazodone group showed significant improvements in PSG-measured sleep (increased sleep efficiency and decreased wake time after sleep onset) when compared to placebo on both night 1 and night 28 after randomization. On post-randomization night 1, percentage of NREM sleep was also significantly improved in the trazodone vs. placebo group. No differential improvement in sleep onset latency was found. Drinking outcomes were not reported.

The other study randomized 173 AD inpatients to either placebo or trazodone 50–150 mg as tolerated, taken 1 h nightly before bedtime for 12 weeks. Patients were discharged after 3–5 days of detoxification. Follow-up assessments occurred both during treatment (at 4 and 12 weeks) and 12 weeks after treatment ended (week 24) (Friedmann et al., 2008). The follow-up rate was 81.5%. As measured by the PSQI, a large effect size (Cohen’s d: −0.93) favoring trazodone for improved sleep quality was reported at week 12. This may help to explain its popularity among prescribers. After stopping medication, however, sleep worsened in the trazodone group and no differences in sleep quality were observed at week 24. There was no significant difference between the trazodone and placebo groups for continuous abstinence at 24 weeks (9.1% vs. 14.1%, respectively), which is a high standard for measuring drinking outcomes. Unexpectedly, the placebo group had better drinking outcomes with medium effect sizes (Cohen’s d > 0.50) with an increased percentage of abstinent days at 12 and 24 weeks and decreased percentage of heavy drinking days through the first 12 weeks. In addition, a small effect size favored

### Table 3

<table>
<thead>
<tr>
<th>Authors, year</th>
<th>N</th>
<th>Daily dose</th>
<th>Selected for insomnia</th>
<th>PSG</th>
<th>Treatment duration</th>
<th>Effect on insomnia</th>
<th>Effect on drinking</th>
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<tr>
<td>Gabapentin</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Brower et al. (2008)</td>
<td>21</td>
<td>1500 mg qhs</td>
<td>Yes</td>
<td>Yes</td>
<td>6 weeks</td>
<td>ns</td>
<td>↓</td>
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<tr>
<td>Trevisan et al. (2008)</td>
<td>57</td>
<td>400 mg TID</td>
<td>No</td>
<td>No</td>
<td>4 weeks</td>
<td>ns</td>
<td>ns</td>
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<tr>
<td>Anton et al. (2009)</td>
<td>60</td>
<td>1200 mg qhs</td>
<td>No</td>
<td>No</td>
<td>39 days</td>
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<td>↓</td>
</tr>
<tr>
<td>Anton et al. (2011)</td>
<td>150</td>
<td>300-300-600 mg</td>
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<td>No</td>
<td>6 weeks</td>
<td>↓</td>
<td>↓</td>
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<td>300 or 600 TID</td>
<td>No</td>
<td>No</td>
<td>12 weeks</td>
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<td>↓</td>
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<td>Trazodone</td>
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<td>Le Bon et al. (2003)</td>
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<td>Yes</td>
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<td>No</td>
<td>12 weeks</td>
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<td>↑</td>
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<td>Litten et al. (2012)</td>
<td>224</td>
<td>400 mg (XR)</td>
<td>No</td>
<td>No</td>
<td>12 weeks</td>
<td>↓</td>
<td>ns</td>
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<td>Chakravorty, Hanlon, et al. (2014)</td>
<td>20</td>
<td>400 mg</td>
<td>Yes</td>
<td>Yes</td>
<td>8 weeks</td>
<td>↓</td>
<td>not studied</td>
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<td>Acamprosate</td>
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<td>Staner et al. (2006)</td>
<td>24</td>
<td>666 mg TID</td>
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<td>Yes</td>
<td>23 days</td>
<td>ns</td>
<td>ns</td>
</tr>
<tr>
<td>Perney et al. (2012)</td>
<td>592</td>
<td>2 or 3 g</td>
<td>No</td>
<td>No</td>
<td>24 weeks</td>
<td>↓</td>
<td>ns</td>
</tr>
<tr>
<td>Topiramate</td>
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<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Johnson et al. (2008)</td>
<td>371</td>
<td>100-200 mg</td>
<td>No</td>
<td>No</td>
<td>14 weeks</td>
<td>↓</td>
<td>↓</td>
</tr>
</tbody>
</table>

ns — no significant difference from placebo; PSG — polysomnography; TID — three times daily; qhs — at bedtime.

* These are target doses. Manufacturers’ recommendations should be followed for titration to reach the target dose.

† Treatment duration ≥4 weeks in all studies listed for relevance to persistent insomnia.

* Drinking improved only for patients who had lower than study threshold withdrawal scores during detoxification.

* All gabapentin-treated patients also received naltrexone, and were compared to naltrexone + placebo, and double placebo.

* Patients drank during 1st 8 days of study and were sober for last 15 days. PSG data for days 2 and 14 of abstinence favored the acamprosate group, but the time × group interaction was not significant.

* Drinking outcomes presented in an earlier publication, cited in text.
placebo recipients for fewer drinks per drinking day at 24 weeks. No drinking outcomes favored the trazodone group. Thus, overall findings included superior sleep outcomes by self-report while taking trazodone, no lasting benefit to sleep after trazodone was stopped, and worse drinking outcomes for trazodone both during and after the medication phase. The data did not allow the study authors to explain worse drinking outcomes in the trazodone group during treatment, but they offered two hypotheses. First, an active metabolite of trazodone is n-chlorophenylpiperazine, which has been shown to increase craving, anxiety, and cortisol levels in alcohol-dependent individuals under controlled laboratory conditions (Umhau et al., 2011). Second, some practitioners and treatment programs advise against the use of all sedative-hypnotic medications during early recovery, because they may trigger relapse. Presumably, their sedative effects mimic alcohol’s desired effect such that it provides an internal cue to resume drinking. Indeed, 79.0% of the trazodone group (vs. 48.5% of the placebo group) believed they received active medication, presumably due to its sedative-hypnotic effects.

When generalizing to one’s own clinical practice, one should consider the following: this was a predominantly male sample (48.5%) recruited from a single inpatient detoxification unit in a Veterans Affairs hospital, of which one-third were unemployed and one-fifth were homeless. At baseline, patients reported drinking approximately 80% of days in the past 3 months and averaged 22 drinks per day. In addition, post-discharge treatment interventions after detoxification were not standardized between groups and not well-specified, but only 25% had formal treatment after completing inpatient detoxification. To date, no replication studies have been published.

Two retrospective controlled studies of alcohol-dependent patients may also help add perspective to these findings. The first study was also conducted with a U.S. veterans population, involving 14,443 episodes of hospitalization for alcohol dependence without psychosis (Monnelly, Locastro, Gagnon, Young, & Fiore, 2008). Of these, 2248 received at least 2 pills of trazodone alone within 45 days of discharge and 9243 had 2 pills of trazodone in combination with other psychiatric/addiction medications (antidepressants, antipsychotics, anticonvulsants, or naltrexone/disulfiram). Two other comparison groups received either quetiapine alone (n = 505) or in combination (n = 2437). The trazodone-in-combination group was used as the reference group, and the outcome was time to rehospitalization for alcohol dependence (unadjusted medians for trazodone alone and in combination were 10.1 and 10.3 weeks respectively vs. 6.1 and 7.1 weeks, respectively, for quetiapine alone and in combination). After adjusting for age, sex, ethnicity, previous hospitalizations, and comorbid psychiatric diagnoses, the trazodone-alone and quetiapine-alone groups were rehospitalized significantly sooner than the trazodone-in-combination group. The second study included 283 residential-treated AD patients from an academic medical center, of which 30% took trazodone at the time of discharge and 60% were followed for 6 months (Kolla, Schneekloth, et al., 2011). No differences between groups were found with nearly 50% in the intent-to-follow analysis and 22% in the followed sample reporting any use of alcohol. The authors conceded that their study was not comparable to the RCT by Friedmann et al. (2008). Aside from study design, the sample and treatment characteristics differed widely with the latter study having more women (31%), more comorbid drug and mental disorders, more sleep problems in the trazodone group, more formal treatment (4 weeks of residential treatment), and 50% of patients taking relapse prevention medication for alcohol dependence. Taken together, these retrospective studies are suggestive that supplementing trazodone with other medications as indicated may help delay relapse and/or hospitalization.

In conclusion, these studies should be considered when weighing the benefits and risks of prescribing trazodone for sleep in AD patients. Patients having trouble staying sober while taking trazodone may need to either stop it and receive other sleep therapy or supplement it with other medications, such as relapse prevention medications.

Two other sedating medications are worth mentioning. Doxepin (in doses of 3 and 6 mg at bedtime) has antihistaminic effects and is approved in the U.S. to treat sleep-maintenance insomnia. There are no specific studies of its use in AD patients. Mirtazapine has not been studied specifically for its sleep-promoting effects in AD patients, but it has positive effects on PSG variables in depressed patients (Schmid et al., 2006; Shen et al., 2006), which is frequently comorbid with alcohol dependence. In one randomized trial of 60 AD patients both during and 4–5 weeks after alcohol withdrawal, those assigned to psychotherapy + mirtazapine had significant improvement in anxiety and depressive symptoms compared to either psychotherapy alone or psychotherapy + venlafaxine (Liapas, Paparrigopoulos, Tzavellas, & Rabwivlis, 2005). In two open-label trials of AD patients with comorbid major depressive disorder, it improved depression and decreased craving in one study (Yoon et al., 2006) and drinking in the other (Cornelius et al., 2012). Finally, it does not worsen obstructive sleep apnea (Carley, Olopade, Ruigt, & Rudulovacki, 2007).

**Sedating antipsychotics (quetiapine)**

A 12-week, randomized, placebo-controlled, double-blind study in 224 AD patients (not selected for insomnia) showed significantly improved, subjectively reported sleep in the quetiapine group (400 mg) with no benefit on drinking outcomes (Litten et al., 2012). An 8-week randomized, placebo-controlled double-blind study in 20 AD patients reported decreased wake time after sleep onset with quetiapine (400 mg nightly) compared to placebo as measured by PSG, but no difference in craving scores (Chakravorty, Hanlon, et al., 2014). The limited evidence to date suggests that quetiapine in mid-range doses may improve sleep without improving drinking outcomes. Even at smaller doses, however, side effects such as weight gain and abuse potential may limit its use as first choice therapy for insomnia in AD patients (Coe & Hong, 2012). Thus, doses should start at 25–50 mg at bedtime. They usually do not need to exceed 100–150 mg nightly in the absence of indicated psychiatric comorbidity, such as a major mood disorder or psychosis.

**Sedating anticonvulsants (gabapentin, topiramate)**

Five double-blind RCTs in AD outpatients investigated gabapentin vs. placebo for periods of 4 weeks or longer. The first and smallest of these (n = 21) was the only one to select for patients with insomnia and to employ PSG (Brower et al., 2008). After 6 weeks of study medication (titrated to 1500 mg at 45 min before bedtime), patients were followed for an additional 6 weeks. No significant differences were found between groups in PSG measures at 3 weeks or in subjective sleep measures at 3 and 6 weeks. After medication was stopped, there was a non-significant trend for rebound insomnia in the gabapentin group. In terms of drinking outcomes, gabapentin significantly delayed onset to relapse to heavy drinking at both 6 and 12 weeks. The second study (Trevissan et al., 2008) randomized 57 male veterans to gabapentin (400 mg three times a day), valproic acid (500 mg three times a day), or placebo for treatment of acute withdrawal (5 days) and protracted alcohol withdrawal (4 weeks). There were no differences between the 3 groups in terms of reduced drinking, relapse rates, or improved sleep, although both anticonvulsants reduced anxiety compared to placebo. Another study (Anton et al., 2009) administered 1200 mg nightly (after titration) of gabapentin vs. placebo to 60 patients for 39 days (including the withdrawal period) with...
follow-up at 4 and 8 weeks post treatment. Patients who received gabapentin also received flumazenil for the first 2 days. The effects of gabapentin on outcomes interacted with pre-treatment withdrawal scores. Those with higher withdrawal scores (n = 16) had better drinking outcomes if they received gabapentin. The opposite was true for insomnia as measured by the ISI. Those with lower withdrawal scores had better sleep if they received gabapentin, whereas those with higher withdrawal scores slept better if they received placebo. The effects of medication on drinking outcomes were not mediated by its effect on sleep. The third study (Anton et al., 2011) randomized 150 outpatients to one of 3 groups: naltrexone + gabapentin in divided doses (300-300-600 mg/d), naltrexone + placebo, or double placebo. Gabapentin was given for the first 6 weeks only, whereas naltrexone and its placebo were given for 16 weeks with a 65% completion rate. During the first 6 weeks, the gabapentin group had the best sleep and drinking outcomes. The fifth study (Mason et al., 2014) randomized 150 outpatients to gabapentin (either 300 or 600 mg TID) or placebo for 12 weeks with a 57% study completion rate. Those receiving gaba- pentin, particularly the 1800 mg daily dose, had better drinking and sleep outcomes. Each of these studies except one found improved drinking outcomes with gabapentin, but sleep effects were more variable with two studies showing a positive effect, another one only finding benefit in those with low withdrawal scores, and two studies—which had the smallest sample sizes—finding no effect on sleep (Table 3). The three studies that found some improvement in sleep did not select for patients with insomnia.

Topiramate

A 14-week, multi-site double-blind RCT of 371 outpatients in which topiramate was titrated over 5 weeks to 300 mg daily in two divided doses (100 & 200 mg) found significantly improved drinking outcomes (Johnson et al., 2007) and sleep (Johnson et al., 2008) in the topiramate vs. placebo group. Patients were not selected for insomnia.

Acamprosate has modest effects in sustaining abstinence and is approved by the FDA as maintenance treatment in AD patients. In a double-blind RCT of 24 AD men, acamprosate (666 mg TID), starting 8 days prior to drinking cessation, was reported to improve sleep as measured by PSG on days 2 and 14 after stopping alcohol. Specifically, the acamprosate group had significantly decreased wake time after sleep onset, increased stage 3 percentage, and reduced REM-L as compared to the placebo group when PSG measures on both days were combined (Staner et al., 2006). However, no significant time by treatment group interactions were found. Both groups stayed sober between days 1 and 14. A large, 26-week double-blind RCT of 592 outpatients with a follow-up rate of 49% (Perney et al., 2012) found that sleep reported during a structured interview improved by 39.1% and 2.6% with acamprosate and placebo, respectively (p = .001). Independent, significant predictors of improvement were baseline sleep score, percent abstinent days, and acamprosate. Acamprosate, however, did not show benefit in drinking outcomes compared to placebo (Mason, Goodman, Chabac, & Lehert, 2006). Thus, the effects of acamprosate on sleep are likely independent of its effects of drinking.

Benzodiazepine receptor agonists

These include structural benzodiazepines, both those FDA-approved for sleep in the U.S. (estazolam, flurazepam, quazepam, temazepam, and triazolam) and those commonly used to treat AWD (chlordiazepoxide, diazepam, oxazepam, and loraze- pam). In addition, they include alpha-1-selective benzodiazepine receptor agonists (eszopiclone, zaleplon, zolpidem, zopiclone). These medications are widely avoided by addiction medicine physicians to treat insomnia after acute withdrawal is complete (3–7 days), because of their abuse potential and risk for overdose when taken with alcohol. The abuse potential of alpha-1-selective benzodiazepine receptor agonists is equivalent to traditional benzodiazepines (Griffiths & Johnson, 2005). Moreover, there are no RCTs to evaluate their safety and efficacy to treat persistent insomnia in abstinent AD patients. Finally, there are other alternatives as discussed above. While their use remains controversial for these and other reasons (Ciraulo & Nace, 2000), long-term use of benzodiazepines does not necessarily increase the risk for relapse (Mueller et al., 2005) and they have known safety and efficacy for insomnia in patients without substance-use disorders (Roehrs & Roth, 2012). Before deciding to use these medications for insomnia in AD patients, the following should be considered: Is there a prior history of a sedative-hypnotic use disorder? Is there a prior history of overdose involving sedative-hypnotics? Is there a physician-patient alliance characterized by mutual trust? Is the patient generally compliant with other treatment recommendations? Have alternative treatments been tried and failed (treatment-resistant insomnia)? Has polysomnography been conducted to rule out other sleep disorders? Is the patient at risk for falls or have memory impairment (e.g., older age)? If a decision is made to use this classification of medication after weighing and discussing their risks and benefits, then a signed controlled substances agreement may be helpful. It should include risks and benefits, safety monitoring options (urine drug screens, pill counts, use of electronic prescription monitoring systems), policies on early refills and refills without a clinical visit, and indications for tapering or discontinuation (e.g., return to drinking).

### Table 4

#### Practice points.

**Assessment**

| 1. | Ask what is causing insomnia in this patient? |
| 2. | Always assume alcohol is a cause (impaired sleep homeostasis and circadian rhythm dysfunction), but not necessarily the only cause. |
| 3. | Insomnia is frequently multifactorial. Patients with alcohol-use disorders have increased rates of co-occurring disorders, increased stress during early recovery, poor sleep habits and sleep environments, and may use other drugs or take sleep-interfering medications. |
| 4. | Therefore, assess for other causes and modifiable factors as patients are achieving sobriety. |
| 5. | Use sleep diaries and rating scales to quantify severity, identify unhealthy sleep patterns, and monitor treatment outcomes. |
| 6. | Refer for polysomnography if another sleep disorder (e.g., sleep apnea, periodic limb movement disorder) is suspected or if patient has treatment-resistant insomnia. |

**Treatment**

| 1. | Abstinence is a necessary and reasonable, first-line treatment for insomnia in patients with alcohol-use disorders, but may not be sufficient. |
| 2. | Target other modifiable causes of persistent insomnia such as co-occurring disorders, use of other substances, stress, environmental factors, and inadequate sleep hygiene. |
| 3. | Treatments aimed at improving sleep do not necessarily lead to better drinking outcomes. Therefore, consider alcohol dependence and persistent insomnia as co-occurring disorders, each of which requires its own treatment. |
| 4. | When selecting insomnia-specific treatment, behavioral therapy is a treatment of choice when available, due to its long-term effectiveness without worsening drinking outcomes. |
| 5. | When selecting medications for insomnia, co-occurring psychiatric disorders may guide choice when a medication treats both disorders (e.g., sedating antidepressants, anticonvulsants, or antipsychotics). |
| 6. | When trazodone is associated with relapse, either discontinue it or switch to other drugs. |

K.J. Brower / Alcohol 49 (2015) 417–427

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Summary

Insomnia is common, persistent, and associated with relapse and suicidal thoughts in AD patients. For these reasons, assessment and treatment of insomnia is important. Guiding principles are listed in Table 4. As with other disorders, treatment follows a comprehensive assessment as well as an understanding of all factors that contribute to insomnia in AD patients. In addition to alcohol, these factors include premonorbid insomnia; co-occurring medical, psychiatric, and other sleep disorders; use of other substances and medications; stress; environmental factors; and inadequate sleep hygiene. In addition to a careful history, use of rating scales and sleep diaries are useful to quantify severity, identify unhealthy sleep patterns, and monitor treatment outcomes. Referral for 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.

Although insomnia and other sleep disturbances can persist for months to years after drinking cessation, abstinence remains the first-line treatment for insomnia in AD patients. Continued drinking will compromise other therapies for insomnia and its causes, while sobriety will facilitate assessment as well as treatment of other contributing factors. Most AD patients will notice some improvement in sleep with sobriety. Because insomnia and objectively measured sleep abnormalities are associated with relapse, it is reasonable to expect treatment for insomnia to help prevent relapse. Nevertheless, the benefit of treating insomnia in order to prevent relapse has not been firmly established. That said, insomnia treatment has its own benefits in terms of symptom relief, quality of life, improved functioning, and even longevity (Krystal, Thakur, & Roth, 2008; Vgontzas et al., 2010). Therefore, insomnia and alcohol dependence might be best thought of as co-occurring disorders, each of which requires its own treatment.

When selecting treatments for insomnia during sobriety, brief behavioral therapies are the treatment of choice, because they have shown long-lasting benefit without worsening of drinking outcomes. Medications work faster, but generally work only as long as they are taken, have side effects, and may even worsen drinking outcomes, as in the case of trazodone. Which medications work best with which patients is a topic for future research. Co-occurring psychiatric disorders may provide some guidance when a medication treats both disorders. When selecting a medication, the principle of “do no harm” is paramount. FDA-approved medications with the least risk of side effects, including abuse potential, are ramelteon and low-dose doxepin. Non-prescription antihistamines may work for some patients as alternatives to doxepin, which is also thought to work through the histamine system. Likewise, melatonin may be a reasonable, lower-cost alternative to ramelteon, but one must be aware of the timing of administration and its effects on circadian rhythms. While these first-line medications may be least harmful, RCTs in AD patients with insomnia have not been conducted.

Gabapentin is the best studied of medications for sleep in AD patients, and should be given next consideration. It may be particularly helpful for patients who have an anxiety component, is used to treat restless legs syndrome, and can improve drinking outcomes. Mirtazapine with its sedative properties may be helpful, especially in depressed patients, although RCTs are lacking for treating insomnia in AD patients. Trazodone is commonly used, but patients who have difficulty maintaining sobriety may do better with a different medication. Quetiapine, due to side effects, is best reserved for patients with major mood disorders or psychosis. Nevertheless, two RCTs support its use for insomnia in AD patients, including those without co-occurring disorders. Topiramate and acamprosate, used for relapse prevention, may help improve sleep, although they have not been specifically tested in AD patients selected for insomnia. Benzodiazepine receptor agonists are generally avoided due to their potential for abuse, cross-dependence, and overdose when combined with alcohol. If they are used, then careful assessment and monitoring precautions are recommended to minimize these risks.

Overall, there are many options for managing insomnia in AD patients. Future studies would benefit from selecting AD patients with insomnia, ruling out other sleep disorders with PSG, measuring both sleep and drinking outcomes, and investigating which treatments work best for which patients.

References


