Sleep Disturbance and Its Relationship to Alcohol Use

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Abstract

Background: Disturbed sleep is a common complaint in primary care settings and many persons drink alcohol specifically to help them sleep. However, habitual alcohol use may exacerbate sleep disturbance.

Purpose: To review evidence regarding the association between alcohol use and sleep disturbance.

Data Sources: We searched MEDLINE, PSYCHINFO, the National Institute on Alcohol Abuse and Alcoholism ETOH database, BIBLIOSLEEP and the Rutgers Alcohol Studies Database for English-language articles published between January 1966 and August 2002. Search terms included, for example, *alcohol-related disorders, alcohol intoxication, or alcoholism* in combination with *sleep, sleep initiation and maintenance disorders, sleep apnea syndromes, sleep stages, or polysomnography*. We also searched the reference lists of previously published trials, overviews and book chapters for additional studies.

Study Selection: The search strategy produced over 440 citations. After elimination of duplicates, we reviewed 114 relevant articles, of which 19 were primary studies with measurements of alcohol use and sleep.

Data Extraction: One reviewer read each article and constructed tables. A second reviewer checked the tables for accuracy. Consensus resolved discrepancies.

Results: In general, scientific consensus exists that alcohol, in low to moderate doses, initially promotes sleep, but that chronic use ultimately disrupts sleep-related physiology. Evidence suggests a relationship between alcohol use and chronic insomnia. The preponderance of cross-sectional studies makes it difficult to establish a causal direction, and great variability in

definition and measurement both alcohol use and insomnia across studies renders the magnitude of the association uncertain. Sleep disturbance is more prevalent among patients with alcohol abuse or dependence than the general population, and may persist for months into abstinence. Some evidence suggests that such sleep pathology among alcoholic patients may predict relapse.

Conclusions: Insomnia is associated with alcohol use, and highly prevalent among patients with alcohol problems. Clinical alertness to insomnia as a symptom of nascent, current or past alcohol problems might facilitate timely intervention and lead primary care clinicians to evaluate sleep complaints more thoroughly. Consideration of sleep disturbance in alcohol treatment or aftercare plans could help patients anticipate sleep problems and reduce relapse risk.

Alcohol and Insomnia

Disturbed sleep is a common complaint in primary care settings. For example, in the Medical Outcomes Study, 16% of persons had severe insomnia and 34% had mild insomnia over the prior 4 weeks, and a substantial proportion of the remaining 50% of the sample had some symptoms of sleep disturbance (1). At 2-year follow-up, 59% of persons with mild insomnia and 83% of patients with severe insomnia still had sleep problems. Insomnia has been associated with subsequent health and mortality, in addition to causing or worsening somatic symptoms that contribute to quality-of-life decline (1, 2, 3,).

Insomnia, generally defined as difficulty initiating or maintaining sleep, lasting longer than three weeks is considered chronic. Chronic insomnia usually has different causes than transient insomnia, which is most often stress-related or due to acute illness (4). Insomnia frequently has a complex mix of contributing causes, and clinicians need to assess psychological (e.g. depression and anxiety), medical (e.g. pain and obstructive sleep apnea), and lifestyle-related (e.g. caffeine consumption) risk factors (5, 6). Substance abuse problems underlie approximately 10-15% of chronic insomnia cases (7). Of adult Americans, as many as 70% drink alcohol, and half of these experience at least a temporary alcohol-induced problem at least once in their lives. These problems are likely more prevalent in the 10% of Americans who drink alcohol daily (8, 9).

Historically, alcohol has been used as a sedative (7). However, recognition of the more subtle and complex relationship of alcohol and insomnia is important for a variety of reasons. Sleep disturbance may be an early sign of inappropriate alcohol use or the sole manifestation of current alcohol abuse or dependence. As such, clinical alertness to insomnia as a symptom of nascent or current alcohol problems might facilitate timely intervention. Sleep disturbance is

also common among patients in recovery from alcohol use disorders, and understanding of this relationship may increase recognition of recovering patients in primary care. Relatedly, recognition of nascent, current or past alcohol problems among insomniacs might lead primary care clinicians to alter their treatment of sleep complaints, limiting, for example, their use of sedative-hypnotic agents. Therefore, this review examines the relationship between alcohol problems and insomnia, both highly prevalent among persons seeking medical care.

Methods

Selection of studies

Studies that examined the relationship between alcohol consumption and sleep distribution were identified by searching the following databases: MEDLINE (through PUBMED January 1966 to August 2002); PSYCHINFO (1967 through 2002); National Institute on Alcohol Abuse and Alcoholism (10) ETOH database (1981-2002), BIBLIOSLEEP (1990-2001) and the Rutgers Alcohol Studies Database (1989-2001). The PUBMED search used the keywords *alcohol-related disorders, alcohol intoxication, or alcoholism* in combination with *sleep, sleep initiation and maintenance disorders, sleep apnea syndromes, sleep stages, or polysomnography,* limited to the following study types: *randomized controlled trials, meta-analysis, or epidemiologic studies*; this strategy yielded 54 articles. The PSYCHINFO search used the keywords *alcohol abuse, alcoholism, alcohol intoxication (acute or chronic), alcohol withdrawal, alcohol drinking attitudes, alcoholic beverages, alcoholic psychosis, sobriety or alcohol rehabilitation,* in combination with *sleep, sleep disorders, insomnia, sleep apnea, sleep onset, REM sleep, NREM sleep, sleep wake cycle, sleep treatment or hypnotic drugs,* limited to the following study types: *randomized clinical trials, meta-analysis, cohort studies, case-control studies, review or guideline*, this strategy yielded 41 articles. The NIAAA ETOH search used

the keywords *sleep or sleep disorders,* limited to the following study types: *randomized controlled trials, case-control studies, meta-analysis, prospective studies or literature reviews and guidelines*; this strategy yielded 89 articles. The BIBLIOSLEEP search used the keywords *alcohol, alcoholic, or alcoholism, limited* to the following study types: *randomized, case-control, cohort or prospective studies*; this strategy yielded 79 articles. The Rutgers Alcohol Studies Database search used the keywords *sleep, insomnia, dyssomnia, polysomnograph, dream, circadian, or somnolence,* limited to this strategy yielded 177 articles. All searches were limited to human subjects and English language. We searched the reference lists of previously published trials, overviews and book chapters for additional studies. After elimination of duplicates, we reviewed 114 relevant articles. Of these articles, 19 were primary studies with measurement of alcohol use and sleep. One reviewer read each article and constructed tables. A second reviewer checked the tables for accuracy. Consensus resolved discrepancies.

How common is insomnia and is it related to alcohol use? What level of alcohol use?

The prevalence of insomnia across community samples varies according to its definition and measurement. Differences in screening questions and their time frame (e.g. past month vs. last 12 months) explain much of this variability. Persons with insomnia have high night-to-night variability in the quality of their sleep (11), yet few surveys consider frequency of insomnia. Moreover, the magnitude of differences between persons with insomnia and controls is often minimal, and many persons with self-reported insomnia do not demonstrate objective sleep abnormalities on polysomnography (12). Some self-report measures (e.g. amount) tend to underestimate sleep disturbance and other measures (e.g. time to get to sleep) tend to overestimate insomnia in comparison to sleep laboratory data (13, 14).

Although many studies suggest a relationship between alcohol use disorders and chronic insomnia exists **(Table 1)**, the direction of association is uncertain because the use and misuse of alcohol is both a cause and an effect of chronic insomnia. In the Epidemiological Catchment Area study, the prevalence of chronic insomnia was 10.2% (6). Alcohol abuse disorders were significantly increased among those with insomnia (OR 2.4; 95% CI 1.0-6.1), although these figures were likely underestimates because the definition of insomnia required that it not be solely related to alcohol use. In the six other community insomnia surveys presented in Table 1 that included alcohol use as a covariate in their analyses, the prevalence of insomnia was 13-53%. Several of these studies were not able to detect a significant relationship between alcohol use and insomnia (1, 2, 15). For instance, in an analysis of the Michael Orton study data, Katz & McHorney reported no significant trends of association between alcohol use and insomnia, although the measure of alcohol use was limited to no history of use, past or current use (1). Indeed, measures of alcohol use vary significantly across studies. Ford, et al. used abuse/dependence diagnoses to characterize alcohol use; Tachibana, et al. reported on days of alcohol use per week; Harma, et al. reported on annual consumption; and Janson, et al. assessed drinking with the CAGE questionnaire. (6, 16-18).

Among patients with diagnosed alcohol abuse or dependence, the rate of sleep disturbance is higher than that found in the general population. Six studies of patients in alcohol treatment have reported insomnia rates of 25-72% (19-24) (**Table 2**). Comparison of these studies is difficult due to different insomnia definitions and time frames, as well as different drinking severities, demographics and diagnostic comorbidities among varied samples. This variability is a natural result of a lack of an accepted gold standard for insomnia that has face, concurrent, external and predictive validity (12).

Normal Sleep Architecture and Alcohol's Polysomnographic Effects

Sleep consists of two states; rapid eye movement (REM) sleep and non-REM sleep (NREM) (12). Non-REM sleep is divided into four stages. Stage 1 is the lightest stage, from which it is easiest to arouse the sleeper, stage 2 is intermediate and characterized by sleep spindles and K-complexes on electroencephalogram (EEG). Stages 3 and 4 are referred to as slow wave sleep or delta sleep per the EEG. Sleep typically begins with stage 1 sleep, and progresses to deeper stages of NREM sleep when entry into the first period of REM sleep occurs. REM and NREM sleep then alternate in approximately 90-minute cycles. The states of sleep are homeostatically regulated such that deprivation of REM sleep leads to pressure to enter REM and is accompanied by a rebound increase in REM once begun. Similar effects are observed after slow wave sleep deprivation.

The relationship between overuse of alcohol and sleep disturbance has been related to the common use of alcohol as a sleep aid. Alcohol consumed in the evening has generally predictable effects on REM sleep, slow wave sleep, and sleep time and continuity, but effects on sleep latency (time to fall asleep) are more variable. Sleep laboratory researchers have performed experiments with healthy non-alcoholic subjects using alcohol doses ranging from 0.16 to 1.0 g/kg (one to three ounces), yielding breath alcohol concentrations as high as 105 mg% (25). Inhibition of REM sleep has been observed since the 1960's (26) in normal subjects who ingested high doses of alcohol (1g/kg), although effects are less consistent with lower doses. REM reduction becomes less pronounced with continued alcohol use, but there is often a REM rebound when alcohol use halts. Slow wave sleep increases after moderate to high bedtime alcohol use, but the effect of lower doses on SWS are again less certain. Slow wave sleep effects diminish with repeated nights of alcohol consumption (27). The effect of alcohol on sleep

continuity and total sleep are quite variable but appear to be dose related. Lower doses may increase total sleep time, whereas higher doses may lead to short-term withdrawal, increasing sympathetic activity and sleep disruption, particularly during the second half of the night, thereby decreasing total sleep time.

Alcohol can have either a stimulating effect that increases sleep latency (time to fall asleep) or a sedating effect that reduces sleep latency, depending on dose and the interval from drinking to bedtime. Stimulating effects are noted at low doses and as blood alcohol levels rise, usually in the first hour after use; sedating effects occur at high doses and as blood levels fall (28-31). Interestingly, few studies have focused on the subjective stimulant properties of alcohol, which may not only relate to insomnia but to the vulnerability to alcohol use problems over time. Late afternoon ("happy hour") drinking, as much as six hours before bedtime, also disrupts sleep, although alcohol is no longer present in the brain at bedtime (32). This phenomenon suggests a relatively long-lasting change in sleep regulation. Other studies suggest that alcohol consumption contributes to insomnia among university students (55).

The sedating effects are dose dependent for moderate levels of alcohol consumption (0.4-0.8g/kg; 2-3 drinks; a standard drink is considered 12 ounces of beer, 5 ounces of wine, or 1.5 ounces of distilled spirits, each contains approximately 0.5 ounces of alcohol) and last for several hours (30, 33). With increasing amounts of alcohol, up to six drinks, sleep latency decreases. As with other short-acting sedatives, rebound occurs and arousal is heightened 2-3 hours after blood alcohol concentrations fall to near zero. Clinically, there is an increase in the number of arousals, associated with increased catecholamine concentration later in the night and increased light or stage 1 sleep ensues. Metabolized at a rate of approximately one glass of wine per hour, after 5 drinks at 10 p.m., the alcohol level will be near zero at 3 a.m., with an increase in arousal from

this time onwards. REM sleep rebound occurs in the second half of the night associated with intensive dreaming or nightmares. These effects can contribute to worsening in sleep continuity. Tolerance to alcohol's effect on sleep architecture develops and can be demonstrated by the normalization of EEG changes after 3-9 nights of use in normal subjects (34, 27). Tolerance to the sedative effects occurs after 3 to 7 days of exposure as well (7). However, little is known about the chronic effects of moderate alcohol consumption on sleep in persons without a history of alcohol dependence.

Polysomnographic Findings among Alcoholic Persons

Acute intoxication induces sleep onset, albeit with disruptions in the latter half of the night. As alcohol dependence develops, patients often complain of inability to fall asleep without first consuming alcohol. Sleep becomes more severely disturbed during alcohol withdrawal. During acute withdrawal, patients take a long time to fall asleep and show small amounts of delta or slow wave (stage 3 and 4) sleep and poor sleep efficiency (35, 36). Pronounced insomnia and marked sleep fragmentation is common during the first days of withdrawal (37). Slow wave sleep remains reduced and severe REM deprivation leads to REM rebound. This REM rebound may contribute to hallucinations. While insomnia is an almost universal feature of alcohol withdrawal, it may stem from psychological as well as physiological factors. Sleep disturbance may represent a manifestation of anger, sadness or grief that surfaces during detoxification and early recovery. The expression and tolerance of these emergent affects may be important to recovery.

Sleep in patients with delirium tremens may be entirely REM sleep interrupted by numerous awakenings (38). Sleep may be virtually absent with delirium tremens; conversely, alcohol withdrawal may end with a period of extended sleep (39). Sleep disturbance, with sleep

architecture similar to that seen during acute withdrawal, continues for weeks, with or without DTs, but is less severe.

The sleep of persons with alcohol disorders who are not acutely intoxicated or in withdrawal is characterized by decreased slow wave sleep, disrupted REM sleep, greater fragmentation of sleep (more sleep stage changes), more awakenings, and decreased sleep efficiency, that is, less time in bed is spent asleep (36). Nonetheless, a substantial proportion of persons, once abstinent describe having been aware that alcohol kept them awake, but that they nonetheless continued to drink when they awoke at night (40).

Alcoholics when they are not drinking, tend to sleep poorly with decreased slow wave sleep, increased stage 1 sleep and delayed sleep onset. Cross-sectional reports have found that insomnia persists for months after last use in nearly half of patients, (41, 42) and can last up to 2 years of longer after last alcohol intake (43, 44). Sleep symptoms also manifest during periods of active alcohol intake. Without longitudinal assessment, it is not clear whether insomnia has its onset after the cessation of alcohol or whether this insomnia is a "reactivation" of a sleep pathology that predated and perhaps led to alcohol use. Most reports suggest that the sleep of recently abstinent alcoholics is short and fragmented, but that this sleep improves slowly over time (45, 46). The cause and significance of reduced slow wave sleep (SWS) that occurs in some abstinent alcoholics is uncertain. SWS appears to be generated in the frontal lobes; it is possible that frontal lobe dysfunction caused by toxic effects of long-term high-dose alcohol leads to reduced SWS. Abstinent alcoholics with low SWS appear to develop functional tolerance and reacquire physical dependence more quickly than those with normal SWS suggesting permanent frontal lobe alterations (35). Whether sleep pattern changes are permanent in some alcoholics is unclear. Limitations in most studies with alcoholics include incomplete diagnosis of other

psychiatric disorders, lack of measurements of the use of pharmacological sleep aids, and inadequate assessment of other sleep disorders (e.g. apnea).

Effect of Alcohol on Insomniacs

Sleep studies of a healthy, non-alcoholic population are not adequate to assess the hypnotic effects of alcohol because sleep latency and efficiency are likely to be adequate in this group. Yet we know that insomniacs commonly use alcohol to promote sleep. Some insomniacs develop conditioned associations, believing they cannot sleep without alcohol use. Anxiety and symptoms of withdrawal may contribute to this behavior. While experts suggest that over time chronic bedtime use has reduced sleep-inducing effects, and may lead to greater late night sleep disturbance, only one study has characterized the effects of alcohol on the sleep of persons with insomnia (25). This report included twenty subjects, 11 with disturbed sleep for at least a year, and 9 controls, who were moderate social drinkers (<14 drinks/week) and reported no other drug use. Subjects completed assessments of sleep and mood after controlled ethanol drinking over multiple nights. Persons who reported previous use of ethanol as a hypnotic also had higher nightly laboratory self-administration. Low ethanol doses (0.45g/kg) suppressed REM in both controls and insomniacs. However, no consistent changes in sleep latency or sleep time (expected to reduce latency and increase time in insomniacs) were detected, although there were some improvements in sleep structure (increased stages 3 and 4, and decreased stage 1) for insomniacs. There was no second half of the night disruption of sleep in normals as had been reported with higher doses of ethanol in other studies, nor was there disturbances in insomniacs' sleep. Insomniacs did report that consuming alcohol before sleep improved their mood; this affective response may reinforce alcohol's use.

The effects of repeated nightly alcohol use both on sleep and continued ethanol self-administration among insomniacs is not known. Why do insomniacs view alcohol as an effective hypnotic? What properties of alcohol are associated with its reinforcing effects as a hypnotic? The mood-altering effect of alcohol before sleep may be the prominent mechanism. This relaxant effect occurs when the level of alertness is high for insomniacs, just before trying to sleep. Alcohol's sedating and anxiolytic effects probably occur in part through a GABA-benzodiazapine receptor mechanism (47). Continued alcohol use however remains of concern given past data on the development of tolerance within a week of repeated ingestion. However published tolerance studies involved normal subjects, using high doses of alcohol (34, 27). The effect of low doses of alcohol in insomniacs is uncertain. In the community, if tolerance develops, is alcohol use abandoned or is dose increased in search of improved sleep? Are other treatment options sought? These questions warrant further research.

The intensity of insomnia will dictate whether an individual seeks treatment with either prescription or over-the-counter medications, or self-treatment. The majority of persons with sleep difficulties do not consult their physician regarding their insomnia, (6) which raises the question as to how frequently alternative substances are used to facilitate sleep. Alcohol is perceived to be a convenient, cost-effective and low risk hypnotic, and two studies have addressed such self-treatment in general population samples (48, 49). In these studies 15-28% used alcohol specifically to help them sleep. Among persons who complained of insomnia and reported using alcohol to help them sleep, 67% felt it was effective (50). Two-thirds of those who use alcohol for sleep do so for less than a week at a time, but 15% used alcohol for more than 4 weeks (48). Males are 1.37 times as likely as females to use alcohol as sleep aid. Each higher quartile in level of difficulty falling asleep was increasingly associated with alcohol use

for sleep although the causal direction of this association cannot be determined (48). Those who used alcohol as a sleep aid had a higher mean daytime sleepiness after adjusting for level of insomnia, total sleep time and sociodemographic factors. This finding is consistent with laboratory studies that report alcohol quickly loses its effectiveness as a hypnotic, while retaining its sleep disturbant properties.

No study has examined data on the efficacy of alcohol as a sleep aid over time among moderate or heavy drinkers. Nonetheless, 44% of alcoholics report frequent alcohol use for sleep (24). Alcoholics with insomnia are more likely to report using alcohol often for sleep than were those without insomnia (24). If insomnia is a withdrawal symptom, then relief drinking seems a reasonable and reinforcing strategy, although counterproductive. As individuals become desperate for sleep, alcohol makes it easier to fall asleep at least initially, until sleep disruption develops. Alcohol use perpetuating sleep disturbance, in turn provoking greater alcohol use, is a cycle that might lead to an alcohol-dependent sleep disorder.

When the elderly report sleep problems, it is important not to assume that they are associated with normal process of aging. Elderly persons who drink any alcohol frequently report drinking before bedtime, and in one report of 155 older women (85 and over) with symptomatic insomnia, 70% used alcohol for sleep (51). Effects of alcohol on the elderly may be more profound as one drink is considered moderate consumption, and the central nervous system may be more sensitive to effects of alcohol. Both insomnia and sleeping pill use increase with age, and alcohol is often used in conjunction with over-the-counter sleep medications (51). Many elderly persons report falling asleep more quickly after alcohol use (52). The normal changes in sleep patterns as one ages (increase in stage 1 sleep (light sleep), may be exaggerated due to alcohol use. More frequent awakenings during the second half of the night (often due to thirst

and polyuria) may lead to unsteadiness during nighttime trips to the bathroom, increasing the risk of falls.

Not only the elderly suffer serious impairment from alcohol use. The body's response to alcohol varies according to the intensity and frequency of ethanol consumption as well as age, circadian rhythm, and basal level of sleepiness. Individual differences in the subjectively assessed sedating effects of ethanol have been found. In studies of the biological sons of alcoholic men, rating of intoxication and fatigue are lower than such ratings in control groups (53). In general, persons who are partially sleep-deprived (e.g. insomniacs) prior to consumption of alcohol show greater sedation soon after dosing compared to those without sleep deficits. Well-rested subjects show no increase in physiologic sleepiness after a moderate ethanol dose (30). However even among the well-rested, reduction in alertness enough to impair performance occurs in the early morning hours after evening drinking (54). Therefore, the marked reduction in alertness and related performance deficits that normally occur at night are worsened by ethanol. Impairment in reaction time and performance persist after several hours after blood levels drop to zero (55). Those who use alcohol as a sleep aid are more tired and show greater impairment in their daytime alertness compared with people who abstain from alcohol at night (33).

The consequence of daytime sleepiness may affect functioning at work and in social life. In addition, a sleepy individual is at greater risk to have accidents on the road, at work- and at home (56). The addition of ethanol to sleepiness due to insomnia may be a particularly dangerous combination (54). Alcohol intake prior to sleep was associated with a 2 times higher risk of having severe daytime sleepiness (OR 2.1; 95% CI 1.4-3.0) (57). Thus sleep deprivation and even low-dose alcohol can impair driving performance (56, 33). Most problematic is moderate risk alcohol use in chronically sleep-deprived populations such as shift workers and

teenagers who show greatly increased rates of traffic accidents due to falling sleep at the wheel especially during the early morning and late afternoon when circadian rhythms cue for sleep. Indeed, alcohol consumption is a common cause of insomnia among university students (55). As little as one ounce of alcohol increases sleepiness in sleep-deprived persons increasing the risk of accidents (30). Drinkers may not recognize the decline in sleep quality, increasing the danger that sleepiness and alcohol consumption will co-occur.

Alcohol Affects Sleep Through Other Mechanisms

Sleep-disordered breathing may be an important contributor to sleep complaints and sleep disruption in alcoholics. Alcohol affects breathing during sleep in normal persons and persons with obstructive sleep apnea (OSA) through two major mechanisms. Alcohol relaxes upper airway dilator muscles (decreasing airway patency), and it prolongs the time required to arouse or awaken after an apnea occurs (58). When blood alcohol is highest, nasal and pharyngeal resistance can increase up to 50% in normal males (59, 60). Men appear more susceptible to the effects of alcohol on breathing perhaps due to narrower pharyngeal airways (61). Alcohol also selectively depresses hypoglossal nerve activity, and alters carotid body chemoreceptor function. Bedtime consumption of alcohol has been suggested as a provocative test for diagnosing breathing disturbance during sleep (7). Indeed, alcohol has more profound effect on breathing during sleep than benzodiazapines.

Normal sleepers consuming a single large drink can develop snoring and even obstructive sleep apnea (OSA) resulting in oxygen desaturations (7, 62). Persons with moderate alcohol use have double the number of respiratory events and lower nocturnal oxygen saturation compared to those who do not drink (63). Alcohol exacerbates sleep-related breathing disorders, and the two

to four percent of Americans with OSA are particularly susceptible. Those with OSA who consume even modest amounts of alcohol greatly increase the frequency and severity of apneas, especially in the first hours of sleep when blood alcohol levels are highest (64-66). Nocturnal hypoxemia, observed in some studies of alcoholics, may be due in part to smoking, although age, body mass index, and duration of alcohol use are also correlated (67, 68). Alcohol can also worsen the oxygen saturation during sleep of patients with COPD, which may result in increased ventricular ectopy (69, 70). The combination of OSA, snoring and alcohol increases a person's risk of heart attack, stroke and sudden death (71). Alcohol thus has a pernicious cyclic effect on OSA. First, it may increase the frequency of apneic events, increasing sleep disruption which leads to daytime fatigue. This sleepiness, in turn adds to the sedative effects of alcohol.

OSA itself is associated with impaired driving and increased rates of motor vehicle accidents. Among OSA subjects who consumed 14 or more drinks per week, self-reports of sleep-related accidents are fivefold higher compared to those who drink lesser amounts (72). Sleep apnea and heavy alcohol use are independent contributors to increased accident risk.

While the acute effects of alcohol on respiration during sleep have been studied, the effects of chronic alcohol use are less well described. Those with alcoholism appear to be at increased risk for sleep apnea, especially if they snore (73). One study suggests abstinent alcoholics do not have a markedly increased prevalence of sleep disordered breathing (episodes of apnea) compared to the general population (68) suggesting that long term alcohol abuse does not permanently compromise upper airway motor function or respiratory drive. But this finding has not been consistently reported (67).

Alcohol affects sleep through other mechanisms as well. Alcohol may increase movement disorders that disturb sleep. Men and women who consume two or more drinks per

day had two- to threefold increase in periodic leg movements that fragment sleep (73). Alcohol may also provoke sleepwalking, especially when taken in combination with methylphenidate, diphenhydramine or amitryptiline (74). In normal volunteers, low to moderate alcohol ingested 4 hours before bedtime inhibits nocturnal melatonin secretion. While the effect of the suppression of melatonin is unclear, it may play a role in regulation of circadian rhythm (75). Finally gastritis, esophageal reflux and polyuria that alcohol consumption may induce can disrupt sleep.

Insomnia As A Risk For Relapse of Alcohol Problems

Inpatients with a history of alcohol dependence, insomnia during early recovery has been linked to alcohol relapse. Both subjective and objective measures of difficulty sleeping may be associated with relapse to drinking (6) (**Table 3**). Brower, et al. reported that subjectively reported insomnia remains a predictor of relapse even after controlling for severity of alcohol dependence and depressive symptoms in a sample of alcoholics undergoing treatment (24). A history of self-medicating insomnia with alcohol was not associated with relapse. Brower, et al. noted that patients who report symptoms of insomnia do not necessarily think of themselves as having insomnia, just as alcoholics often do not accept labeling (24). Waking up often, getting too little sleep, and have trouble getting to sleep are more often endorsed. The optimal screening questions to capture insomnia among alcoholic patients is worthy of study. Foster, et al. also found that subjectively measured difficulty falling asleep predicted relapse 3-5 months later (22).

Using objective polysomnographic measures, (**Table 3**) five studies have demonstrated a significant effect of impaired sleep on relapse to drinking among alcoholics undergoing treatment (45, 76-79). Gillin, et al. reported that shortened REM latency (time until REM sleep begins), and increased REM % (percentage of total sleep time in REM) predicted relapse over a

3-month follow-up in non-depressed patients following inpatient alcohol treatment discharge (76). Brower, et al. also reported that prolonged sleep latency was associated with relapse in nondepressed patients (78). In alcoholic patients with secondary depression, increased REM density was associated with relapse at three months (77).

Other polysomnographic studies have implicated reduced slow wave sleep as a marker for alcoholic relapse, although this evidence is equivocal (35). Contradictory findings regarding the predictive value of SWS have been reported (45, 76-78) after controlling for other sleep variables. Two studies reported a relationship between prolonged sleep latency and subsequent relapse (45, 78), but two other studies found no such relationship (76, 77).

The worsening of already poor sleep in abstinence may be one factor that leads to relapse. Resumption of drinking reduces stage 1 sleep and wakefulness, and increases SWS and reduces REM as in other drinkers, at least for a few days, leaving to the subjective impression among alcoholics that drinking has impaired their sleep. But return to heavy alcohol use eventually worsens sleep. Limitations in this research include the absence of biological or personal corroboration of abstinence; limited and varied definitions of relapse; small sample sizes; lack of comorbid diagnostic assessments and measures or craving; and lack of control for confounding clinical variables such as age and dependence severity.

Overlap of alcohol-related insomnia with other psychiatric disorders

Just as evidence suggests the association between alcohol use and insomnia, clear evidence supports the observation that depression and anxiety disorders are associated with insomnia (6, 80-83). The consistency of the association mitigates the possibility that sleep disturbance, as one of the criteria for diagnosis of major depression, is a measurement artifact. Sleep difficulties are among the most common symptoms experienced with anxiety and

depression (84). Diagnoses of major depression, anxiety disorder, panic disorder and social phobia are also more common among problem drinkers than in the general population (8). Alcoholic patients studied in sleep laboratories have shown marked variation in the rates of psychiatric disorders, but these studies have serious selection bias compared to community-based studies. Still, the finding that alcohol use interacts with various neurotransmitters implicated in the pathophysiology of mood and anxiety disorders is consistent with epidemiological reports (85, 86). However, it is not known to what extent comorbidity reflects a causal relationship or a common underlying etiology (87).

Ford, in one of the few epidemiological studies of insomnia that considered both psychiatric disorders and alcohol abuse in a large community sample, reported that 7% of persons with insomnia had alcohol abuse compared to 3.8% of persons with no sleep complaint; 40.4% of persons with any psychiatric disorder had insomnia compared to 16.4% of persons with no sleep complaint (6). Comparing incidence rates of psychiatric disorders in those with and without insomnia, insomnia was most strongly related to major depression, followed by anxiety disorders and alcohol abuse. Sleep disturbance of at least two weeks of duration was a significant risk factor for developing alcohol abuse disorders (OR 2.7; 95% CI 1.4-5.2) over a year of follow-up. This study did not answer the question of whether alcohol abuse has an independent association with insomnia after controlling for depression. Only one study has reported that severity of both alcohol dependence and depressive symptoms were significantly associated with insomnia among alcohol treatment patients (24).

Alcoholics may suffer from depression and/or anxiety independently of their drinking or may experience depression during or after periods of heavy drinking (8, 40, 88). Alcoholics without depression are as likely to report drinking in response to depressive symptoms as

depressed alcoholics (89). Less studied is the relationship between moderate drinking and alcohol's putative depression-inducing effects (9). In a large Finnish study, Sexton et al., reported that there was a modest inter-relationship between alcohol consumption and emotional distress over a 7-year time span (90). Among moderate drinking men (those reporting drunkenness less than once a month), drinking was an antecedent of depressed mood, whereas for women, dysphoria was associated with less drinking at follow-up. One possible explanation for this finding is that women treat dyphoria with drinking but later curtail their alcohol use due to negative effects. Unfortunately, standardized measures of mood and alcohol consumption were not available in this study.

The consequences of disrupted sleep from alcohol use may be difficult to differentiate from many of the signs and symptoms of psychiatric disorders. Difficulty falling asleep, early morning awakening, fatigue, and decreased concentration resulting from insnomnia, complicate the assessment of affective symptoms. Moreover sleep problems often exacerbate primary psychiatric symptoms (91). Alcohol use, even when it conforms to normal drinking patterns complicates the clinical course of these psychiatric disorders. Even small amounts of alcohol have been associated with the development of anxiety and mood symptoms among asymptomatic persons (92). These alcohol effects influence next-day behaviors, demonstrating that mood changes outlast blood ethanol levels (9, 93). Ethanol-induced cognitive disruption may also impair previously successful coping mechanisms. Alterations in alertness, judgement, impulse control, decision-making and mood, could be interpreted by patients and clinicians as symptoms of relapse of primary psychiatric disorders.

Multiple studies indicate that depressive symptoms dissipate with abstinence from alcohol, and often these changes can occur dramatically during the first month of abstinence,

although normalization may also occur slowly (94, 97). Anxiety symptoms often decrease during and following alcoholism treatment. As with depression, investigation continues as to whether lifetime anxiety symptoms precede or follow the onset of heavy drinking and withdrawal (98). Nonetheless, insomnia has been found to be a risk factor for depression as well as alcohol relapse in other studies (99, 100).

The sleep of individuals with depressive and/or anxiety disorders resembles the sleep of persons with alcoholism (84). Similar REM sleep changes occur during withdrawal in alcoholics with and without secondary depression (77). The sleep of depressed as well as anxious persons also shows increased sleep latency and number of awakenings, and decreased total sleep time (although some persons with depression have hypersomnia). Anxious patients show similar findings. Sleep profiles are not helpful in differentiating among these disorders. Moeller et al. reported that patients who develop major depressive disorder (MDD) secondary to alcoholism share many sleep abnormalities with patients who have primary MDD. Secondary MDD patients did have less total sleep times and less non-REM sleep than that reported in patients with alcoholism alone (101). This finding suggests an additive effect of these two disorders known to affect sleep.

Distinctions between patients with different disorders on the basis of EEG findings have been difficult to generalize. While there may be group differences in EEG findings in individual studies with small samples, there has been no acceptance of any polysomnographic criteria for evaluating the sensitivity and specificity of specific distinguishing parameters. The polysomnographic should not be considered a primary diagnostic instrument for evaluating patients with psychiatric disorders and sleep complaints. EEG information has not helped elucidate pathophysiology or treatment course. Due to the differential effects of dose and timing

and the question of persistence of effects, the PSG has not proved helpful in diagnosing insomnia due to substance abuse. However within specific groups, for instance alcoholics in the early stage of treatment, PSG findings may provide important prognostic information, as seen in studies of relapse prediction. Overall, an accurate clinical history is a better indicator of alcohol-related insomnia. PSG may be useful to verify or quantify sleep difficulties, or to diagnose another sleep pathology such as sleep apnea.

The interactions between alcoholism, depression, anxiety—using strict diagnostic criteria-- and sleep remain understudied, but it is clear that insomnia in substance-using patients often has more than one cause. Longitudinal studies from childhood could perhaps disentangle whether sleep disturbance is a non-causal indicator of an underlying process, an epiphenomenon, that predisposes individuals to major depression, anxiety disorders and/or alcoholism, or whether early sleep disturbance has a causal role in a process that leads to one or more of these disorders. Psychological evaluation of patients who complain of insomnia is unquestionably important. It is unclear whether chronic insomnia causes depression, anxiety, or other psychological disturbances, or whether such disorders cause insomnia. At best, we can say that in certain patients, psychological disorders and insomnia often co-exist.

Treatment

An estimated 10 million people consult health care practitioners for sleep disorders and of these, half receive prescriptions for sleep medications (102). For those patients with chronic insomnia who have an underlying problem of substance abuse, providers need to prescribe particularly carefully (103). It is important to recognize and treat the underlying disorder primarily, rather than treating insomnia exclusively as a symptom. Patients may be told to focus on abstinence and that sleep improvement will follow. This approach will be unacceptable to

many patients because sleep abnormalities can persist despite prolonged abstinence. Moreover, disturbed sleep might predispose some patients to relapse. Therefore sleep disturbances during early recovery should be monitored closely with careful consideration of both behavioral and pharmacological treatments. Alcoholic patients at risk for relapse are easily identifiable by routine questions about sleep (24). The potential for improving drinking outcomes by treating insomnia is being investigated (103-105).

For alcohol dependent persons undergoing detoxification, sleep quality may be an important mediating outcome. During the first two weeks after detoxification, five days of carbamazapine was superior to lorazepam in improving sleep for patients with mild to moderate alcohol withdrawal (106). In this trial with limited follow-up, improvement in sleep parameters might have been a pharmacokinetic effect resulting from lorazepam's short action. Patients treated with lorazepam may have experienced benzodiazepine withdrawal in the post-detoxification period, affecting sleep. Tests of longer-acting benzodiapzepines for alcohol detoxification versus carbamazapine (or other medications used for detoxification such as Valproate) are needed, particularly in the outpatient setting where self-medication of sleep problems often occurs. No controlled studies targeting sleep disturbance during alcohol withdrawal have demonstrated improved alcohol outcomes.

Ritanserin, a specific 5-hydroxytyramine antagonist was tested at three doses against placebo over 6 months in a randomized trial with 493 detoxified alcohol-dependent individuals (107). None of the three dosages revealed significantly impaired sleep problems compared to effects against placebo in sleep quality in persons without psychiatric disorders. Gabapentin, an anticonvulsant, in an open label, uncontrolled study, showed promise as a safe and effective treatment for alcohol-dependent patients with insomnia during early recovery (103).

Certain agents previously used for insomnia have fallen out of favor because of their interaction with alcohol. Barbiturates and chloral hydrate are markedly potentiated by alcohol and are almost never clinically indicated for insomnia among alcoholics. Benzodiazepines should only be considered after safer alternatives have proven ineffective due to their cross-tolerant with alcohol (108).

All benzodiazepines can produce tolerance and most agents lose their sleep-promoting properties within 2 weeks. Alprazolam and diazepam demonstrate greater rewarding effects of single challenge doses in abstinent alcoholic subject compared to groups without alcohol dependence (109). But not all alcoholics have a reinforcing euphoric response, and clinicians cannot predict who may abuse benzodiazepines. Differences in the rewarding properties of various benzodiazepines in alcoholics have not been extensively studied. Many believe that rapid onset-rapid offset medications present the greatest risk for misuse (110). The finding regarding abuse liability of benzodiazepines in persons with alcohol dependence suffer from the selection bias of only studying alcoholics seeking treatment. Some have argued that misuse of this class of medications is most common in severely dependent patients, and uncommon in less dependent patients (111, 112). The safety and effectiveness of benzodiazepines for short-term management of insomnia thus remains uncertain. However, it is for persistent insomnia, which can lead to alcohol relapse, that better and safer treatments are needed. Physical dependence and withdrawal can occur with long-term use of all benzodiazepines, and all medications in this class can cause rebound insomnia following discontinuation. No studies have demonstrated the hypnotic efficacy of benzodiazepines beyond 12 weeks.

Mood stabilizers, sedating antidepressants and low-potency neuroleptics are commonly prescribed but have not been rigorously studied (105). Trazodone, a sedating antidepressant, is

the medication most commonly prescribed by addiction experts for insomnia among sleep-disturbed alcoholics (105); an ongoing trial is examining its effect on sleep and alcohol outcomes in early recovery. Many non-pharmacologic therapies have been used including muscle relaxation, biofeedback, cognitive therapy, stimulus control, acupuncture, yoga, meditation, sleep restrictive therapies, and sleep hygiene techniques (4). Removing stimulant use six hours prior to sleep, and avoiding late meals and naps are simple advice that may be helpful. In progressive relaxation therapy, training muscle tension and breathing are used to create a restful state. Greeff, et al. reports that 10 sessions of training in alcoholic men with insomnia showed significant improvement in self-reported quality of sleep using a pre-post design in 11 men compared to controls (103).

Summary

Sleep disturbance is a common symptom related to alcohol and psychiatric disorders that patients and providers might find easier to discuss than other more stigmatized symptoms. Routine inquiry about sleep disturbance in medical and psychiatric settings might lead to greater recognition of alcohol use disorders and/or other psychiatric disorders. However, physician assessment of sleep history is poor compared to that of other health related problems (113, 114). Clinicians may trivialize insomnia despite its serious underlying causes, such as alcohol abuse and affective disorders, and its serious consequences, such as cardiac morbidity. Alcohol use or abuse, major psychiatric disorders, obstructive sleep apnea, diabetes mellitus with nocturia, and other serious conditions may be the source of a patient's sleep complaints. Thus, the assessment and treatment of insomnia merits greater training and clinical consideration.

In low to moderate doses, alcohol initially promotes sleep. However, scientific consensus maintains that chronic use ultimately disrupts sleep-related physiology. These sleep problems

may result from partial tolerance and withdrawal during the night or somatic effects such as headache or gastric irritation. Alcohol should not be used as a sleep aid particularly in those at increased risk for development of sleep-related breathing disorders, such as older persons, obese persons or chronic snorers. The sleep of sober alcoholics is often extremely disturbed -- sleep latency is prolonged, and sleep is fragmented, light and abbreviated -- often for months after abstinence. The initial return to drinking improves the sleep of the alcoholic, but only short-term. Incorporating discussion of sleep hygiene, relaxation techniques and cognitive-behavioral interventions for patients in alcohol treatment or aftercare may help patient avoid or overcome sleep problems and reduce relapse risk. Much uncertainty surrounds the care of patients who do not respond to these behavioral interventions. Ongoing and future studies should examine the safety and effectiveness of pharmacological and behavioral interventions for sleep-disturbed patients with alcohol use disorders.

In addition, future research into the relationship between alcohol use and insomnia should consider: 1) whether subjective or objective measures of sleep quality are better predictors of outcomes; 2) whether polysomnography increases our ability to predict relapse beyond subjective measures; 3) the clinical meaning of disturbed sleep architecture and whether disturbances in sleep staging relate to subjective ratings of sleep quality; 4) the stimulant-like effects from acute doses of alcohol, their relationship to sleep and the risk of developing alcohol problems; 5) the relative efficacy of behavioral or pharmacological interventions, and the most favorable phase of abstinence to institute sleep treatment; and 6) gender differences in the relationship between alcohol use and sleep. Because patients can provide more detailed descriptions of sleep on a night-to-night basis than in periodic research interviews, more fine-grained longitudinal assessment of the relationship between different levels of alcohol

consumption and insomnia are also needed to improve the advice primary care providers offer to patients who complain of sleep disturbance.

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Table 1. Association Between Alcohol Use and Insomnia.

Authors/Year	Country	Sample / N	Insomnia Definition	Insomnia Prevalence	Alcohol Definition	Alcohol-Insomnia Association
Bixler et al. 1979	U.S.A.	Los Angeles household survey, N=1006	Trouble falling asleep, waking up during night, waking up too early.	32.2% current	Need for help in past year for problems with alcohol	N.S.
Kales et al. 1984	U.S.A.	Sleep disorders clinic patients and volunteer controls without sleep complaints, N=200	Difficulty falling asleep or maintaining sleep for one year	100% in sleep disorders clinic	Drinking alcoholic beverages	Unadjusted OR, 5.0
Ford et al. 1989	U.S.A.	Epidemiological Catchment Area study, a 5-site household probability survey, N=7954	Two or more weeks with trouble falling or staying asleep or waking too early in prior 6 months, not always associated with alcohol use.	10.2% overall	DSM-III alcohol abuse or dependence	Adjusted OR 2.4 (95% CI, 1.0-6.1) for insomnia at two interviews 1-year apart
Kuppermann,et al.1995	U.S.A.	Telecommunication firm employee volunteers, N=588	Current “problems with sleep”	29.6%	Daily alcohol use	OR 1.04 (N.S.)
Tachibana et al. 1996	Japan	271 male industrial workers	Difficulty falling asleep, mid-sleep awakenings, early morning awakening in last month.	27.7%	Alcohol use 4 or more days per week	OR, 2.6 (95% CI, 1.2-5.7)
Katz & McHorney, 1998	U.S.A.	Medical Outcomes Study, a 3-city clinical sample, N=3445	Difficulty initiating or maintaining sleep in the last 4 weeks on a 6-point Likert-type scale.	16% severe 34% mild	Alcohol use: no history, current or past use	“No significant trends”
Harma et al. 1998	Finland	3020 employed men aged 45-60 in Helsinki Heart Study	Difficulty falling asleep, waking up too early, disturbed or restless sleep in past 3 months	39-53% depending on shift worked	250 or more grams of alcohol per year	OR, 1.3 (95% CI, 1.08-1.52)
Janson et al, 2001	Sweden	Random population survey of 2606 men from Upsala	Severe or very severe difficulty falling asleep and/or maintaining sleep in the last months.	12.8% in 1994	CAGE score 2 or greater	OR 1.75 (95% CI, 1.2-2.5)

Table 2. Prevalence of Insomnia Among Alcohol Treatment Populations.

Authors/Year	Country	Sample / N	Insomnia Definition	Insomnia Prevalence
Mello & Mendelsohn, 1970	U.S.A.	Inpatient alcohol treatment, N=50	Decreased sleep duration from a baseline abstinent period	25%
Baekeland et al. 1974	U.S.A.	Alcohol dependent outpatients, N=294	Single item, self-rating	36%
Feuerlein 1974	U.S.A.	Alcoholic inpatients and outpatients, N=184	Current sleep disturbance by self-report	Inpatients, 39% Outpatients, 36%
Caetano et al. 1998	U.S.A.	Detoxification and residential alcohol treatment, N=748 Driving-Under-Influence program, N=445	Unable to sleep last 12 months	Detox/residential, 67% DUI, 42%
Foster et al. 1998	London, England	Inpatient alcohol detoxification, DSM-IV alcohol dependent, N=82	Score of 1 to 3 (poor) on the 7-point sleep item of the Life Situation Survey (LSS)	72%
Brower et al. 2001	U.S.A.	Inpatient alcohol treatment, N=172	1 or more positive responses on the Sleep Disorders Questionnaire for the past 6 months	61%

Table 3. Relationship Between Sleep Architecture And Recurrent Alcohol Use Among Recovering Alcoholic Persons.					
Authors/Year	**Country**	**Sample / N**	**Relapse Definition**	**Timing of Polysomnography**	**Polysomnographic Findings Associated with Recurrent Alcohol Use**
Allen & Wagman 1977	U.S.A.	Alcoholic male volunteers admitted to an alcoholism sleep research ward, N=18	Clinically assessed "poor outcome" based on amount of sobriety	First weeks of inpatient treatment	Lower slow wave sleep percentage
Gillin et al. 1994	U.S.A.	Inpatient alcohol treatment, male veterans, N=45	Any alcohol consumption 3 months post-discharge	First and fourth weeks of inpatient treatment	Shortened REM latency Increased REM% Possibly increased REM density
Brower et al. 1998	U.S.A.	Inpatient alcohol treatment, male veterans, N=74	Any alcohol use, average follow-up 5 months post-discharge	At least 2 weeks after admission	Prolonged sleep latency
Clark et al. 1998	U.S.A.	28-day inpatient alcohol treatment, depressed males, N=21	Any alcohol use 3 months post-discharge	First and fourth weeks of inpatient treatment	Increased REM density Decreased total sleep time
Drummond et al. 1998	U.S.A.	Inpatient alcohol treatment, male veterans, N=40 (11 later excluded)	Any alcohol use or elevated hepatic enzymes, 5 to 14 months post-discharge	Intake to treatment, N=29 reported 5-mos. abstinent, N=29 14-mos. abstinent, N=9 27-mos. abstinent, N=4	Prolonged sleep latency Lower sleep efficiency