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Sleep-Disordered Breathing in Alcoholics: Association with Age

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Sleep apnea and related disorders are not uncommon in abstinent alcoholics. We assessed the relationship between age and the presence and severity of sleep-disordered breathing in alcoholism by performing one night of polysomnography on 75 abstinent alcoholic subjects undergoing treatment for alcoholism. Sleep-disordered breathing (defined as 10 or more apneas plus hypopneas/hr of sleep) was present in 17% of 66 men aged 22–76 and in 0 of 9 women aged 28–63 years. Three percent of men under age 40 years had sleep-disordered breathing compared with 25% of men between ages 40–59 and 75% of those above age 60. Although alcoholics with sleep-disordered breathing had a higher body mass index than those without, the increased frequency over age 40 was statistically significant after controlling for the effects of body mass index. Sleep in subjects with sleep-disordered breathing was significantly more disturbed than in subjects without sleep-disordered breathing. Our findings suggest that sleep-disordered breathing in older male alcoholics is more prevalent than has been reported in most studies of normal men and that the increase in sleep-disordered breathing that occurs with age in alcoholics is greater than the age-related increase in sleep-disordered breathing that occurs in healthy elderly men. Furthermore, sleep-disordered breathing is a significant contributor to sleep disturbance in a substantial proportion of male alcoholics above the age of 40 years. Sleep-disordered breathing, when combined with existing cardiovascular risk factors and alcohol use, may contribute to the increased risk of stroke and mortality that occurs in alcohol users. Although none of the women alcoholics in this study had sleep-disordered breathing, a reliable estimate of the prevalence of sleep-disordered breathing in women alcoholics will require additional studies.

Key Words: Alcohol, Alcoholism, Sleep, Sleep disorders, Sleep apnea.

ALTHOUGH SLEEP COMPLAINTS and sleep disruption are common in alcoholics, the causes of disordered sleep are not well understood. In some alcoholics, sleep apnea is a significant factor, and there is some evidence that sleep-related breathing disorders are more common in alcoholics than in the general population. Vitiello et al.,[1] using overnight pulse oximetry, found increased nocturnal hypoxemia in 19 older abstinent male alcoholics compared with controls; however, 58% of the alcoholics and none of the control group were smokers. Among the alcoholics, severity of hypoxemia correlated significantly with duration of alcohol use but not with smoking history or age. In a subsequent study, Vitiello et al.[2] again found increased nocturnal hypoxemia in abstinent male alcoholics compared with controls, but the incidence of smoking was again much higher in the alcoholic group than in the control group. It is likely that sleep apnea contributed to the nocturnal hypoxemia observed in these subjects, but as the investigators recorded only oxygenation data and not direct measures of apnea, the possibility that hypoxemia was due to chronic lung disease cannot be excluded.

Two studies have assessed apnea in abstinent alcoholics. Tan et al.[3] found increased numbers of central and obstructive apneas and hypopneas in 16 abstinent male alcoholics compared with controls. Central apneas and hypopneas were associated with the presence of nervous system damage. The number of apneas plus hypopneas/hr of sleep, referred to as the apnea-hypopnea index (AHI), is a measure of apnea severity; an AHI of 5 is a commonly used cutpoint to distinguish sleep apnea (AHI > 5) from normal sleep-related respiration (AHI < 5). Mamdani et al.[4] found that 31% of 80 abstinent alcoholic men had an AHI > 5 and that those with sleep apnea were older and had a longer drinking history than those without apnea.

The exacerbation of sleep apnea by alcohol consumed within a few hours of sleep onset[5–9] and the association of sleep apnea with cardiovascular morbidity and mortality[10–13] suggest that the occurrence of sleep apnea in heavy alcohol users, i.e. alcoholics, is an important clinical problem and that its occurrence in older abstinent alcoholics is of particular concern because of the potential for exacerbation of apnea severity, hypoxemia, and ventricular ectopy following heavy alcohol use just before sleep. We therefore investigated the relation of age to the frequency and severity of sleep-disordered breathing in a series of rigorously diagnosed alcoholics. Portions of this work have been presented in abstract form.[14]

METHODS

The study sample consisted of 75 adult alcoholics (66 men, 9 women) with an age range of 22–76 years recruited from alcohol treatment programs at the University of Michigan Hospitals, the Ann Arbor Veterans Administration Medical Center, and Chelsea Community Hospital. All subjects had alcoholism diagnosed by clinical evaluation and Diagnostic Interview Schedule[15] and were undergoing treatment for alcohol-

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ism. Mean years of heavy drinking was 11.8 (range 1–51 years). Mean score for the Michigan Alcoholism Screening Test (MAST) was 41 and for the CAGE was 3.25. Potential subjects were excluded if they had a history of major depressive illness, or if they had advanced cirrhosis with jaundice, a portocaval shunt, or a prothrombin time greater than 19 sec. Other exclusionary criteria included dementia (alcoholic or otherwise), aphasia, major stroke, or schizophrenia. All subjects had been free of alcohol for at least 2 weeks at the time of sleep recordings, with an average duration of abstinence of 32 days (range 14–88 days).

After giving informed consent, subjects were studied for one night of polysomnography. During polysomnography the following were recorded using standard techniques: EEG (C3, C4, O1, O2 by International 10–20 system), chin electromyogram (EMG), electrooculogram, electrocardiogram, respiratory effort (mercury strain gauges or piezoelectric belts over the chest and abdomen), airflow at the nose and mouth (thermistors), and bilateral anterior tibialis EMG with surface electrodes. Continuous monitoring was performed by experienced polysomnographic technologists. Oxygen saturation was monitored by pulse oximetry (Biox 3700, Ohmeda Corporation).

All studies were recorded on paper at 10 mm/sec paper speed using 16 channel polygraphs (Grass Instruments, Quincy, MA). Recordings were scored manually for sleep stages by experienced polysomnographic technologists using standard techniques.[16] Apneas were defined as absence of airflow for 10 sec or more. Hypopneas were defined as a decrease in nasal-oral airflow with a parallel reduction in respiratory effort lasting 10 sec or longer and associated with a 3% or greater drop in oxygen saturation. An AHI was calculated as the number of apneas plus hypopneas/hr of sleep. An apnea index (AI) was computed as the number of apneas/hr of sleep. Periodic leg movements were scored according to the criteria of Coleman.[17] A periodic limb movement index (PLMI) was calculated as the number of periodic leg movements occurring during sleep divided by the number of hours of sleep.

Statistical analysis was performed using ANOVA, χ^2, and regression analysis (Statgraphics v5, STSC, Inc., Rockville, MD). We used AHI as the primary measure of severity of sleep-disordered breathing and selected an AHI of 10 as a cutpoint for defining the presence of sleep-disordered breathing. We also assessed two other commonly used cutpoints: AI of 5 and AHI of 5.

RESULTS

None of the nine female subjects had sleep-disordered breathing. Of the 66 male subjects, 11 (17%) had an AHI of ≥ 10, 16 (24%) had an AHI ≥ 5, and 8 (12%) had an AI ≥ 5. In 7 of the 11 with AHI ≥ 10, sleep apnea was predominantly obstructive.

The proportions of male alcoholics with sleep-disordered breathing for age groups 20–29 years, 30–39 years, 40–49 years, 50–59 years, and age 60 years or over are shown in Fig. 1. Of those age 40 years or over, 28.6% had an AHI ≥ 10 compared with 2.5% of those under age 40 (χ^2 10.1; $p = 0.001$). Increases in the proportion of subjects over age 40 with AHI ≥ 5 and AI ≥ 5 were also highly significant. Of male subjects, 31% of those age 40 or over had an AHI ≥ 10 compared with 3% of those under age 40. The increased proportion of subjects over the age of 40 with sleep-disordered breathing remained significant after exclusion of the nine women subjects.

There was a significantly positive correlation between normalized apnea-hypopnea scores and age as demonstrated in Fig. 2. There was also a strong correlation of AHI with body mass index ($r = 0.54$; $p < 0.0001$). Using multiple linear regression to control for the effects of body mass index on AHI, the effect of age was still significant ($t = 2.75$; $p = 0.008$). There was a weak negative correlation of duration of abstinence with AHI that was not statistically significant ($r = -0.21$; $p = 0.20$).

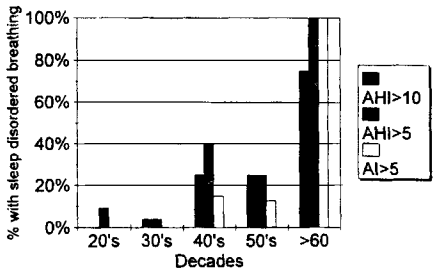

Fig. 1. Proportions of alcoholics with sleep-disordered breathing for age groups 20–29 years ($n = 13$), 30–39 years ($n = 27$), 40–49 years ($n = 22$), 50–59 years ($n = 8$), and age 60 or over ($n = 5$) using three different cutpoints to define sleep-disordered breathing: AHI ≥ 10 (AHI ≥ 10), AHI ≥ 5, and AI ≥ 5 (AI ≥ 5). Increases in the proportion of subjects over age 40 with AHI ≥ 10, AHI ≥ 5, and AI ≥ 5 were all significant (χ^2 10.1; $p = 0.001$ for AHI ≥ 10; χ^2 13.6, $p = 0.0002$ for AHI > 5; χ^2 10.2, $p = 0.001$ for AI > 5). The increases remained significant at $p < 0.002$ for AHI > 10, AHI > 5, and AI > 5 after exclusion of the nine women subjects.

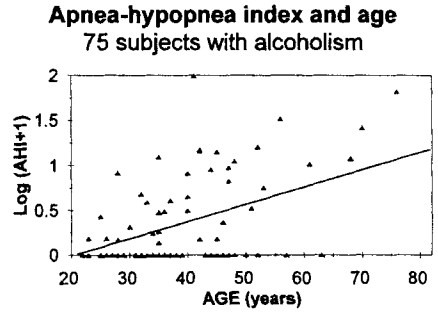

Fig. 2. Age is plotted against log-transformed AHI, log (AHI + 1). There is a strong correlation of age with apnea severity ($r = 0.45$; $p = 0.0004$). For the 66 male subjects, the correlation was even stronger ($r = 0.49$; $p = 0.00003$).

We compared polysomnographic features of subjects with and without apnea; the results are shown in Table 1. Subjects with AHI ≥ 10 had more stage 1 sleep, less stage 2 sleep, and more periodic leg movements. In addition, these subjects showed a trend toward lower amounts of sleep, longer sleep latency, lower sleep efficiency, and shorter rapid eye movement (REM) sleep latency. All statistically significant differences remained significant when men only were analyzed. The increase in sleep latency in subjects with sleep-disordered breathing is somewhat surprising, because sleep-disordered breathing is usually associated with increased somnolence and shorter sleep latencies both during daytime naps and at night.

DISCUSSION

Alcohol, even in modest quantities, has striking effects on nocturnal breathing in patients with sleep apnea and in those, such as chronic snorers, who are at risk for sleep apnea. In normal subjects, alcohol produces narrowing of the upper airway with an increase in pharyngeal and nasal resistance,[18] and when ingested within a few hours of sleep it can induce snoring in persons who do not habitually

Table 1. Subject Characteristics

	All subjects (mean ± SE)	Apnea absent (mean ± SE)	Apnea present (mean ± SE)	*F*	*p*
No. of subjects	75	64	11		
Age	40.3 ± 1.3	38.3 ± 1.2	52.3 ± 5.4	17.8	0.0001
Sex ratio	66M/9F	55M/9F	11M		
Body mass index	25.5 ± 0.6	24.7 ± 0.6	29.7 ± 5.3	11.0	0.0014
% Smokers	86	85	89		
Smoking pack-years	25.1 ± 2.3	24.0 ± 2.5	32.8 ± 5.8		
No. of yr of heavy drinking	10.6 ± 1.1	10.0 ± 1.1	13.8 ± 3.2		
MAST	41.0 ± 1.6	42.4 ± 1.7	33.1 ± 6.1	4.03	0.049
CAGE	3.3 ± 0.1	3.3 ± 0.1	3.2 ± 5.7		
Total recording time (min)	368.5 ± 3.6	368.4 ± 4.0	369.3 ± 46.6		
Total wake time (min)	59.2 ± 4.8	58.3 ± 5.2	63.9 ± 11.3		
Total sleep time (min)	291.6 ± 5.7	295.6 ± 6.2	269.0 ± 40.2	2.77	0.10
Sleep latency (min)	42.9 ± 4.2	39.6 ± 4.6	61.5 ± 50.3	3.46	0.07
Latency to REM sleep (min)	70.3 ± 6.2	74.7 ± 6.4	45.5 ± 13.5	2.83	0.10
Sleep efficiency (%)	79.2 ± 1.5	80.4 ± 1.5	73.0 ± 11.4	3.30	0.07
% Stage 1 sleep	25.1 ± 1.8	21.6 ± 1.4	44.5 ± 10.5	27.5	<0.0001
% Stage 2 sleep	48.6 ± 1.7	51.4 ± 1.4	32.3 ± 8.0	21.0	<0.0001
% Stage REM sleep	21.2 ± 0.8	21.5 ± 0.8	19.0 ± 3.1		
% Stage 3–4 sleep	5.2 ± 0.9	5.4 ± 1.0	4.2 ± 3.2		
AHI	5.2 ± 1.6	1.3 ± 0.3	28.0 ± 6.2		
Baseline oxygen saturation (%)	95.1 ± 0.2	95.3 ± 0.3	94.7 ± 0.4		
Minimum oxygen saturation (%)	86.4 ± 1.1	88.4 ± 0.8	81.4 ± 2.9	9.30	0.004
% with PLMI > 10	11.8	6.2	45.5	13.2	0.0005

snore, and can increase the frequency and severity of snoring in those who snore occasionally. In susceptible persons, alcohol can lead to airway occlusion during sleep: for example, it can induce sleep apnea in males who snore, but who do not have apnea when abstinent.[5–9] Ethanol in moderate doses reduces genioglossal activity, but not minute ventilation in normal subjects, suggesting that the muscles of the upper airway are more susceptible to the effects of ethanol than are the ventilatory muscles.[19] Similar effects observed in animal studies appeared to be mediated by alterations in the activity of brainstem neurons involved in the regulation of respiration.[20]

Once apnea occurs, ethanol prolongs the time to arousal by decreasing the rate of rise in inspiratory effort during the apnea and increasing the inspiratory effort required to produce an arousal.[21] This elevation in the arousal threshold reflects the CNS depressant effects of alcohol and leads to an increase in the duration of obstructive apneas and to increased severity of associated hypoxemia.[7] The effects of apnea are more pronounced in REM sleep, probably at least in part because arousal systems are less responsive to respiratory stimuli during this state.[22]

The impact of alcohol use on sleep apnea may be more significant in the elderly than it is in young and middle-aged persons. First, sleep-related breathing disturbances are more common in the elderly.[23] Snoring, closely associated with obstructive sleep apnea, occurs in 20% of the general population but in as many as 60% of the elderly,[24] and the prevalence of obstructive sleep apnea increases with age.[25–28] Second, the duration of obstructive apneas is greater in the elderly,[27] and as alcohol use further prolongs apneas, there is more severe hypoxemia. It is therefore not surprising that even in elderly subjects with minor sleep apneic activity that is considered to be within normal limits (<5 apneas/hr), moderate doses of alcohol lead to increased numbers of apneas,[26,29] to increased numbers of episodes of oxygen desaturation >4%, and to reductions in the minimum oxygen saturation during sleep.[7]

Our findings raise several important questions about the relationship between alcoholism, sleep apnea, and aging. First, is the frequency of sleep-disordered breathing and the increase with age that we observed greater than occurs in nonalcoholic subjects? A wide range of prevalence rates of sleep-disordered breathing have been reported in the middle aged and the elderly (see refs. 30 and 31 for review). Lavie estimated that 3.5% of middle-aged industrial workers had an AI ≥ 5,[31] whereas Cirignotta et al.[33] estimated that 2.7% of men aged 30–69 years had AHI ≥ 10. Two large recent surveys reported higher figures. Young et al.[34] found that 14–18% of men and 5–6% of women aged 40–59 years had AHI ≥ 10, whereas Jennum and Sjøl[28] found that 11% of men and 6.3% of women aged 30–60 years had an AHI > 5. In an extensive study of community-dwelling elderly (age 65–100 years), prevalence rates for AHI ≥ 10 were 70% for men and 56% for women,[35] with similar rates in the subgroup of persons aged 65–69. However, these results differ markedly from those of another large study of healthy elderly[36] in which an AHI ≥ 5 was found in just 2.9% in 60–69 year olds, 33% in 70–79 year olds, and 40% in 80–89 year olds.[36] In a third study, 34% of 100 subjects over age 60 years had AHI > 5.[37] Differences in prevalence rates probably reflect recruitment methods, inclusionary and exclusionary criteria, techniques for measuring respiration during sleep, and definitions of sleep-disordered breathing. Nonetheless, our findings of sleep-disordered breathing (AHI ≥ 10) in 25% of men between ages 40–59 and in

75% of those above age 60 suggest higher prevalences of sleep-disordered breathing than have been reported in most studies of normal men and suggest that the increase in sleep-disordered breathing with age in alcoholics is greater than the age-related increase in sleep-disordered breathing that occurs in the healthy elderly men.

A second issue is whether the apparent increased incidence of apnea with age is limited to male alcoholics. All subjects in the study by Mamdani et al.[4] were male, and in our study, in which subjects were recruited predominantly from the Ann Arbor VA Medical Center, most were male. Male sex is a strong risk factor for obstructive sleep apnea, and the depressant effects of ethanol on genioglossus activity are more pronounced in males than in females.[38] On the other hand, data from our laboratory[39] and from others[28,40,41] indicate that 12–35% of patients with sleep apnea are female and that postmenopausal women have an increased risk of apnea compared with premenopausal women.[42,43] In our study, 0 of 9 women alcoholics had sleep-disordered breathing, but larger numbers of women alcoholics will need to be evaluated before the prevalence of sleep-disordered breathing can be reliably estimated.

A third issue is whether the increase in sleep-disordered breathing with age in alcoholics is attributable solely to the effects of aging and alcoholism. It could be, for example, that the increase is due to toxic effects of alcohol on the nervous system as suggested by Tan et al.[3] Alternatively, obesity, smoking, or other factors related to alcoholism or sleep apnea may be responsible. Obesity is associated with obstructive sleep apnea, and the increase in apnea with age among alcoholics might be at least in part a function of higher body weight. However, alcoholics are generally not obese, and in the studies of Mamdani et al.,[4] body weight was lower in the apneic group than in the nonapneic group. In our sample of alcoholics, those with sleep-disordered breathing were heavier than those without sleep-disordered breathing, but the effect of age on breathing disturbance was apparent even after controlling for body weight. As the proportion of smokers was similar in apneic and nonapneic groups, it is unlikely that smoking contributed to the changes we observed.

In this study, we performed only one night of respiratory monitoring. One may ask whether one night of recording is adequate for assessing sleep-disordered breathing. The "first-night effect" is a well-known sleep laboratory phenomenon that is associated with increased sleep latency, increased REM sleep latency, and reduced amounts of REM sleep. However, respiratory first-night effects appear to be much less than the effects on sleep architecture. Dickel and Mosko[37] found no first-night effect on apnea in 100 seniors evaluated for sleep apnea and periodic leg movements. Bliwise et al.[44] found that measures of disordered breathing were relatively stable across nights of recording, although there was an increase in some subjects on the second night: 8 of 66 subjects (age 44–88, mean 67) had an AHI $\geq$ 10 on night 1, whereas 12 of 66 (18%) had an AHI $\geq$ 10 on night 2. As our subjects were recorded on the first night, our estimate of apnea prevalence may, if anything, be low.

The interaction of alcohol and obstructive sleep apnea in the elderly is potentially devastating. In patients with chronic obstructive pulmonary disease and in some elderly patients with mild sleep apnea, alcohol leads not only to increased numbers of apneas, but also to increased ventricular ectopy.[30,45] Snoring or obstructive sleep apnea or both have been associated with hypertension, stroke, myocardial infarction, and increased risk of cardiovascular death during sleep.[10–13] In the elderly, sleep-related respiratory disturbances are associated with mortality independent of the effects of age, and the increased risk of mortality applies to women as well as to men.[46,47] Furthermore, the mortality and cardiovascular morbidity in patients with obstructive sleep apnea is greater in untreated patients than in treated patients.[12,48,49] Thus, it seems likely that sleep apnea, when combined with existing cardiovascular risk factors and alcohol use, may contribute to myocardial infarction and aspiration pneumonia, and may be a significant factor in the increased risk of stroke and mortality that occurs in alcohol users.[50,51]

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