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., 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. 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. 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. found that 31% of 80 abstinent alcoholics 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 and the association of sleep apnea with cardiovascular morbidity and mortality 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.

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 and were undergoing treatment for alcoholism.
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 (mechanical 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 drop in oxygen saturation. An AH1 was calculated as the number of apneas plus hypopneas/hr of sleep. An apnea index (Al) 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, $\chi^2$, and regression analysis (Statgraphics v5, STSC, Inc., Rockville, MD). We used AH1 as the primary measure of severity of sleep-disordered breathing and selected an AH1 of 10 as a cutpoint for defining the presence of sleep-disordered breathing. We also assessed two other commonly used cutpoints: Al of 5 and AH1 of 5.

RESULTS

None of the nine female subjects had sleep-disordered breathing. Of the 66 male subjects, 11 (17%) had an AH1 of $\geq 10$, 16 (24%) had an AH1 $\geq 5$, and 8 (12%) had an Al $\geq 5$. In 7 of the 11 with AH1 $\geq 10$, 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 or over are shown in Fig. 1. Of those age 40 years or over, 28.6% had an AH1 $\geq 10$ compared with 2.5% of those under age 40 ($\chi^2 10.1; p = 0.001$). Increases in the proportion of subjects over age 40 with AH1 $\geq 5$ and Al $\geq 5$ were also highly significant. Of male subjects, 31% of those age 40 or over had an AH1 $\geq 10$ 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 AH1 with body mass index ($r = 0.54; p < 0.0001$). Using multiple linear regression to control for the effects of body mass index on AH1, the effect of age was still significant ($r = 2.75; p = 0.008$). There was a weak negative correlation of duration of abstinence with AH1 that was not statistically significant ($r = -0.21; p = 0.20$).

We compared polysomnographic features of subjects with and without apnea; the results are shown in Table 1. Subjects with AH1 $\geq 10$ 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
but who do not have apnea whenEthanol in
to an increase in the duration of obstructive apneas and
general population but in as many as 60% of the elderly,24
imilar effects observed in animal studies appeared to be
effects of ethanol than are the ventilatory muscles.
moderate doses reduces genioglossal activity, but not min-
snore, and can increase the frequency and severity of
snores occasionally. In susceptible persons, alcohol can lead to airway occlusion during sleep:
for example, it can induce sleep apnea in males who snore,
and the prevalence of obstructive sleep apnea increases
significant in the elderly than it is in young and middle-
old reflects the CNS depressant effects of alcohol and leads
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 thresh-
old 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 asso-
ciated 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 apneaic 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 prevale-
ance rates of sleep-disordered breathing have been re-
ported 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 AH1 ≥ 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 Sjø12 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 mark-
edly from those of another large study of healthy elderly36
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

### Table 1. Subject Characteristics

<table>
<thead>
<tr>
<th></th>
<th>All subjects (mean ± SE)</th>
<th>Apnea absent (mean ± SE)</th>
<th>Apnea present (mean ± SE)</th>
<th>F</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of subjects</td>
<td>75</td>
<td>64</td>
<td>11</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>40.3 ± 1.3</td>
<td>36.3 ± 1.2</td>
<td>52.3 ± 5.4</td>
<td>17.8</td>
<td>0.0001</td>
</tr>
<tr>
<td>Sex ratio</td>
<td>M/F</td>
<td>M/F</td>
<td>M/F</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body mass index</td>
<td>25.5 ± 0.6</td>
<td>24.7 ± 0.6</td>
<td>29.7 ± 5.3</td>
<td>11.0</td>
<td>0.0014</td>
</tr>
<tr>
<td>% Smokers</td>
<td>86</td>
<td>85</td>
<td>89</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking pack-years</td>
<td>25.1 ± 2.3</td>
<td>24.0 ± 2.5</td>
<td>32.8 ± 5.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of yr of heavy drinking</td>
<td>10.6 ± 1.1</td>
<td>10.0 ± 1.1</td>
<td>13.8 ± 3.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MAST</td>
<td>41.0 ± 1.6</td>
<td>42.4 ± 1.7</td>
<td>33.1 ± 6.1</td>
<td>4.03</td>
<td>0.049</td>
</tr>
<tr>
<td>CAGE</td>
<td>3.3 ± 0.1</td>
<td>3.3 ± 0.1</td>
<td>3.2 ± 5.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total recording time (min)</td>
<td>368.5 ± 3.6</td>
<td>368.4 ± 4.0</td>
<td>369.3 ± 46.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total wake time (min)</td>
<td>59.2 ± 4.8</td>
<td>56.3 ± 5.2</td>
<td>63.9 ± 11.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total sleep time (min)</td>
<td>291.6 ± 5.7</td>
<td>295.6 ± 6.2</td>
<td>269.0 ± 40.2</td>
<td>2.77</td>
<td>0.10</td>
</tr>
<tr>
<td>Sleep latency (min)</td>
<td>42.9 ± 4.2</td>
<td>39.6 ± 4.6</td>
<td>61.5 ± 50.3</td>
<td>3.46</td>
<td>0.07</td>
</tr>
<tr>
<td>Latency to REM sleep (min)</td>
<td>70.3 ± 6.2</td>
<td>74.7 ± 6.4</td>
<td>45.5 ± 13.5</td>
<td>2.83</td>
<td>0.10</td>
</tr>
<tr>
<td>Sleep efficiency (%)</td>
<td>79.2 ± 1.5</td>
<td>80.4 ± 1.5</td>
<td>73.0 ± 11.4</td>
<td>3.30</td>
<td>0.07</td>
</tr>
<tr>
<td>% Stage 1 sleep</td>
<td>25.1 ± 1.8</td>
<td>21.6 ± 1.4</td>
<td>44.5 ± 10.5</td>
<td>27.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>% Stage 2 sleep</td>
<td>46.6 ± 1.7</td>
<td>51.4 ± 1.4</td>
<td>32.3 ± 4.0</td>
<td>21.0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>% Stage REM sleep</td>
<td>21.2 ± 0.8</td>
<td>21.5 ± 0.8</td>
<td>19.0 ± 3.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>% Stage 3–4 sleep</td>
<td>5.2 ± 0.9</td>
<td>5.4 ± 1.0</td>
<td>4.2 ± 3.2</td>
<td></td>
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</tr>
<tr>
<td>AHI</td>
<td>5.2 ± 1.6</td>
<td>1.3 ± 0.3</td>
<td>28.0 ± 6.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline oxygen saturation (%)</td>
<td>95.1 ± 0.2</td>
<td>95.3 ± 0.3</td>
<td>94.7 ± 0.4</td>
<td></td>
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</tr>
<tr>
<td>Minimum oxygen saturation (%)</td>
<td>86.4 ± 1.1</td>
<td>86.4 ± 0.6</td>
<td>81.4 ± 2.9</td>
<td>9.30</td>
<td>0.004</td>
</tr>
<tr>
<td>% with PLMI &gt; 10</td>
<td>11.8</td>
<td>6.2</td>
<td>45.5</td>
<td>13.2</td>
<td>0.0005</td>
</tr>
</tbody>
</table>
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. 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. On the other hand, data from our laboratory and from others 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. 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. 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., body weight was lower in the apneic group than in the nonapneic group. In our sample of alcoholics, whose 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 found no first-night effect on apnea in 100 seniors evaluated for sleep apnea and periodic leg movements. Bliwise et al. 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 ≥ 10 on night 1, whereas 12 of 66 (18%) had an AHI ≥ 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 ventilricular ectopy. Snoring or obstructive sleep apnea or both have been associated with hypertension, stroke, myocardial infarction, and increased risk of cardiovascular death during sleep. 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. Furthermore, the mortality and cardiovascular morbidity in patients with obstructive sleep apnea is greater in untreated patients than in treated patients. 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.

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