Minimal Effect of Alcohol Ingestion on Breathing during the Sleep of Postmenopausal Women*

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Eighteen asymptomatic postmenopausal women volunteered to ingest 2 ml of 100-proof vodka per kg of body weight in orange juice on one night and a placebo on another. Overnight sleep monitoring was performed immediately thereafter. Alcohol ingestion caused reduction in total sleep time from 329 to 251 minutes and a decrease in rapid eye movement sleep. There was no difference from placebo in the number of episodes of apnea or hypopnea, or in the frequency, length, or severity of oxygen desaturation. In contrast to the effects of alcohol ingestion in men, the effects on breathing and oxygenation are minimal during the sleep of women if this amount of alcohol is ingested.

Studies of asymptomatic male volunteers showed that ingestion of 2 ml/kg of alcohol before bedtime increased the frequency and severity of oxygen desaturation and breathing disorders during sleep. Worsening of snoring and sleep apnea by alcohol ingestion was thereafter reported to occur in patients with sleep apnea syndrome, in heavy snorers, and in patients with chronic obstructive lung disease. These studies have recently been summarized in editorial form by Remmers. The mechanism by which alcohol ingestion may worsen obstructive sleep apnea may relate to its depressant effect on the upper airway musculature in cats and in humans. Contraction of the upper airway muscles normally functions to splint the pharynx and to oppose the collapsing force produced by the negative inspiratory intrapharyngeal pressure. Depression of this activity would produce a tendency toward suction collapse of the pharynx, particularly during sleep. Of particular interest is the observation that the loss in muscle tone after alcohol ingestion was more pronounced in men than in women.

Early studies by our group demonstrated that asymptomatic men volunteers had much more sleep apnea and nocturnal oxygen desaturation than did premenopausal women volunteers. We have recently published similar findings with reference to the effect of alcohol ingestion before bedtime. Whereas ingestion of 2 ml/kg of 100-proof vodka accentuated sleep apnea and oxygen desaturation in 20 men, no effect was seen during the sleep of 20 young women. Postmenopausal women have been shown to have breathing and oxygenation patterns during sleep that are similar to those of men. The current study attempted to assess the effect of ingestion of alcohol before bedtime on the breathing and oxygenation of postmenopausal women.

METHODS

Eighteen postmenopausal women, ages 51 to 66 years (mean 58 years), participated in the study. Their postmenopausal status was verified by a historical account of past cessation of menses and symptoms of "change of life." Several subjects had participated in earlier studies in which hormonal analysis verified the lack of circulating progesterin. The study was approved by the institutional review boards of the University of Florida and Veterans Administration Medical Center. Subjects were recruited by a newspaper advertisement, were paid $25.00 for participating, and were accepted for study after questioning disclosed the absence of acute or chronic illness. No subject had daytime sleepiness or known alcoholism. All claimed to be social drinkers. Subjects who snored were included in the study, but no quantitation of snoring was done during polysomnography. On two successive nights after a baseline blood alcohol measurement by Intoximeter test, they ingested either 2 ml/kg of 100-proof vodka in orange juice or an identical placebo. The order of ingestion was random. The subjects were not blinded and were allowed one and a half hours to ingest the drink. They repeated the Intoximeter test and then slept. Polysomnography was performed as previously described. Oxygen saturation was measured with an ear oximeter; oral and nasal airflow were sensed with thermistors clipped to one nostril and lip; chest movement was sensed by impedance plethysmography; and electroencephalography, electro-oculography, and electrocardiography were recorded. Apnea was noted if flow ceased in the nose and mouth for ten seconds or longer. With this system of polysomnographic monitoring, central and obstructive sleep apnea cannot be accurately differentiated. For this study, all apneic episodes were counted together. Hypopnea was noted as flows and chest movement decreased and desaturation occurred. Desaturation was thought to be clinically significant when a decrease of greater or equal to 4 percent from the preceding baseline occurred. Differences between the two nights were analyzed using the Wilcoxon signed-ranks test.

RESULTS

Table 1 depicts the demographic characteristics of the 18 women. One woman could be considered obese.
Table 1—Demographic Characteristics of 18 Women

<table>
<thead>
<tr>
<th></th>
<th>Mean (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>58 (51-66)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>159.7 (142.5-167.5)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>62.6 (50-84)</td>
</tr>
<tr>
<td>FVC (liter)</td>
<td>2.74 (1.68-3.86)</td>
</tr>
<tr>
<td>FEV₁ (liter)</td>
<td>1.29 (1.34-2.94)</td>
</tr>
<tr>
<td>FEV₁/FVC (%)</td>
<td>83 (66-97)</td>
</tr>
<tr>
<td>Medication (No. subjects)</td>
<td>3*</td>
</tr>
<tr>
<td>Smoke (No. subjects)</td>
<td>5</td>
</tr>
</tbody>
</table>

One subject, antihistamine; 2 subjects, mild antihypertensive drug.

(162.5 cm in height and 84 kg in weight). This woman was not a heavy snorer, did not have daytime sleepiness, and did not show multiple episodes of apnea on oxygen desaturation during sleep. Only three women took medications of any kind—one, an antihistamine; two, a thiazide diuretic. Only five women in this study currently smoked cigarettes. After 2 ml kg⁻¹ of alcohol ingestion, the mean blood alcohol level reached was 88 mgdl⁻¹. Tables 2 and 3 depict the effect of alcohol ingestion on sleep and breathing. Because some changes may be due to the order in which the compound was ingested, Table 2 shows the data from the ten subjects who received alcohol on night 1, and Table 3 shows the eight subjects who received placebo first. The Wilcoxon signed-rank test allows statistical separation of the effects of alcohol ingestion alone, and this analysis was performed on the data from all 18 subjects, irrespective of the order of the nights. The p values listed to the right of each table reflect this analysis on 18 subjects and are identical in the two tables.

Alcohol ingestion reduced total sleep time, sleep period time, and amount of rapid eye movement sleep. In contrast to previous studies of men, alcohol ingestion did not affect the number of episodes of apnea, hypopnea, or desaturation. Similarly, the lowest saturation, number of desaturation events to levels less than 90 percent or less than 80 percent, and the mean duration of desaturation episodes were no different after alcohol or placebo ingestion. The only respiratory variable that was significantly changed after alcohol ingestion was the mean duration of the episodes of apnea, which increased from 11.5 seconds to 15.7 seconds. This increase in duration reflects the fact that only 13 subjects had apnea on the placebo night and 17 did so with alcohol (NS). When correcting for the different numbers of subjects in the denominator in each group, the difference in length of apneic episodes becomes insignificant. As we have previously reported, episodes of disordered breathing and oxygen desaturation were most common in stage 2 and REM sleep on both nights.

By Wilcoxon test, one can also assess the effect of the order of ingestion of placebo vs alcohol on consecutive nights. Thus, changes in sleep and breathing that are produced by a first night effect can be eliminated from the analysis of the effect of alcohol. Similarly, the effects on the second consecutive night caused by the compound ingested on the first night can be eliminated from the analysis. In this study, irrespective of the compound ingested, the second night showed more episodes of desaturation less than 80 percent (p = 0.027), hypopnea (p<0.04), total sleep time (p = 0.006), and stages 3 and 4 sleep (p<0.01). This analysis is obviously essential to all studies done on different nights to determine the effect of any intervention on one of the nights. The changes found are compatible with poor sleep on night 1, with a rebound of longer, deeper sleep on night 2 with an increased opportunity for hypopnea to occur. This difference in

Table 2—Sleep and Breathing Variables of Ten Women Who Received Alcohol on Night 1

<table>
<thead>
<tr>
<th></th>
<th>Placebo (Mean ± SD)</th>
<th>Alcohol (Mean ± SD)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood alcohol level (mg/100 ml)</td>
<td>0 ± 8.49</td>
<td>0 ± 39</td>
<td>.06</td>
</tr>
<tr>
<td>Baseline saturation (%)</td>
<td>94.9 ± 2.08</td>
<td>94.7 ± 1.77</td>
<td>NS</td>
</tr>
<tr>
<td>Sleep period time (min)</td>
<td>384 ± 44.63</td>
<td>313 ± 55.72</td>
<td>.006</td>
</tr>
<tr>
<td>Total sleep time (min)</td>
<td>361 ± 39.24</td>
<td>272 ± 62.77</td>
<td>.011</td>
</tr>
<tr>
<td>Stage 1 (%)</td>
<td>3.8 ± 1.87</td>
<td>3.6 ± 1.50</td>
<td>NS</td>
</tr>
<tr>
<td>Stage 2 (%)</td>
<td>49.9 ± 9.23</td>
<td>49.2 ± 10.46</td>
<td>NS</td>
</tr>
<tr>
<td>Stage 3 (%)</td>
<td>3.8 ± 1.23</td>
<td>3.1 ± 1.52</td>
<td>NS</td>
</tr>
<tr>
<td>Stage 4 (%)</td>
<td>24.7 ± 6.09</td>
<td>20.5 ± 5.68</td>
<td>NS</td>
</tr>
<tr>
<td>REM (%)</td>
<td>17.5 ± 3.2</td>
<td>10.1 ± 6.38</td>
<td>.001</td>
</tr>
<tr>
<td>Desaturations &gt; 4% (No.)</td>
<td>24.8 ± 48.59</td>
<td>29 ± 65.47</td>
<td>NS</td>
</tr>
<tr>
<td>Low saturation (%)</td>
<td>86.9 ± 7.56</td>
<td>89.7 ± 4.34</td>
<td>NS</td>
</tr>
<tr>
<td>Desaturations &lt; 80% (No.)</td>
<td>20.5 ± 4.9</td>
<td>21 ± 5.2</td>
<td>NS</td>
</tr>
<tr>
<td>Desaturations &lt; 80% (No.)</td>
<td>1.1 ± 2.02</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>Apnea (No. episodes)</td>
<td>15.2 ± 18.37</td>
<td>11.1 ± 22.8</td>
<td>NS</td>
</tr>
<tr>
<td>Hypopnea (No. episodes)</td>
<td>14 ± 32.57</td>
<td>22 ± 63</td>
<td>NS</td>
</tr>
<tr>
<td>Mean duration of apnea (sec)</td>
<td>15.25 ± 7.08</td>
<td>14.8 ± 7.96</td>
<td>.006</td>
</tr>
<tr>
<td>Mean duration of desaturation (sec)</td>
<td>18.49 ± 9.78</td>
<td>13.12 ± 9.2</td>
<td>NS</td>
</tr>
</tbody>
</table>
nights 1 and 2 has previously been reported as the first night effect.  

**DISCUSSION**

This study once again verifies the presence of episodes of sleep apnea and nocturnal oxygen desaturation in asymptomatic postmenopausal women.  

Thirteen of the 18 subjects had episodes of sleep apnea on the placebo night, and two subjects had more than 30 episodes of apnea per night. Five subjects reached low saturations of 85 percent or less. These findings contrast markedly with studies of premenopausal women in whom few apneic events occurred and in whom no episode of desaturation was found, but are similar to the findings in men.

We have previously reported that alcohol ingestion before bedtime caused more sleep apnea in men, but did not do so in premenopausal women. The current study shows that the effect of an identical amount of ingested alcohol by postmenopausal women was similar to the effect on the younger women, and little additional disordered breathing or oxygen desaturation occurred.

Multiple studies have shown that alcohol ingestion promotes sleep apnea in patients with disease, but little attention has been paid to the sex of the patients. Scrima et al studied the effect of 3 ounces of 80-proof alcohol on the frequency and severity of obstructive sleep apnea in six patients with the sleep apnea syndrome. In their study, five of the six patients were men, and in those five patients more hypoxic episodes at all levels of desaturation were present after alcohol ingestion. In the female patient, fewer overall episodes occurred after alcohol ingestion, although the small number of episodes of most severe desaturation were increased. Issa and Sullivan studied a total of seven patients who either had the sleep apnea syndrome or snored heavily; in all seven patients, alcohol ingestion exacerbated the sleep-induced breathing abnormalities. Although the text does not state that these patients were male, the conditions from which they suffered occur predominantly in male patients, and the text uses the male pronoun whenever an individual patient is mentioned. In another study, Issa and Sullivan measured airway closing pressures in five subjects who snored heavily and found that alcohol ingestion reduced upper airway stability and promoted sleep apnea. All five subjects were men. Finally, our research group reported that alcohol ingestion increased the numbers of episodes and the duration of apnea in 20 patients with chronic obstructive lung disease. Nineteen of these patients were men.

Thus, the reports of increased sleep apnea and nocturnal oxygen desaturation after ingestion of alcohol have largely resulted from studies of men. Similar effects do not occur in women, irrespective of their menopausal status.

Several recent studies have attempted to elucidate the mechanism whereby alcohol ingestion might cause more sleep apnea and more decreases in oxygenation. In 27 adult cats, intravenous alcohol was administered either by bolus or by constant intravenous infusion. Eighteen of the cats were decerebrate and nine were intact. Of the total of 27 cats, 24 were male. At blood alcohol levels between 75 and 153 mgdl⁻¹, respiratory activity of the posterior cricoarytenoid and genioglossal muscles were reduced, but contraction of the diaphragm was not affected. Such relaxation of the pharyngeal musculature would increase upper airway resistance and also allow the inspiratory negative pressure to cause suction collapse of the pharynx. Although the animals were awake during these stud-
ies, the results could easily be extrapolated to explain
the occurrence of obstructive apnea during sleep.  
In the studies of pharyngeal muscle tone in normal
human subjects,  ethanol alcohol, 1 ml·kg−1 body weight,
was ingested by mouth. Six men and six women were
studied and a mean blood alcohol level of 82 mg·dl−1
was produced, which is almost identical to the level
produced in our study. A selective depression of genio-
glossal muscle activity occurred after alcohol inges-
tion, and once again the contraction of the diaphragm
was not affected. Of considerable importance was the
finding that genioglossal depression by alcohol was
more prominent in the male subjects. A selective effect
of alcohol in men would be compatible with most of the
reports of sleep apnea after alcohol ingestion. The
current study and our study of premenopausal women
would strongly suggest that alcohol ingestion in women
of any age does not cause more sleep-related breathing
disorders.

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