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Bedtime Ethanol Increases Resistance of Upper Airways and Produces Sleep Apneas in Asymptomatic Snorers

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Abstract

Nasal continuous positive airway pressure (nasal CPAP) and polysomnography were used to analyze the time course of the effect of bedtime ethanol on resistance of upper airways and on the number of respiratory pauses during sleep. On one night, six asymptomatic nonalcoholic male snorers drank 2 ml/kg of 100 proof vodka mixed in orange juice (ethanol dose, 0.79 gm/kg, giving a peak blood alcohol level of 71.8 ± 33.3 mg/dl). On a second night they received a placebo (1–2 drops of vodka floated on top of the orange juice). We measured (a) the minimum nasal CPAP required to eliminate snoring, (b) the number of hypopneas and apneas during each hour of sleep and (c) the arterial oxygen saturation (SaO_2) by ear oximetry. On the alcohol night there was a significant increase in the CPAP pressure required to eliminate snoring (placebo 4.8 ± 1.7 cm H_2O , alcohol 6.2 ± 1.5 cm H_2O). The number of respiratory events per hour of sleep (apnea index) was 7.5 ± 2.1 for ethanol nights versus 3.8 ± 2.7 for placebo nights ($p < 0.0125$). An apnea index of greater than 5 is generally considered abnormal. There was no significant difference in the number of desaturation events (declines of 4% or more in the SaO_2) or in the mean SaO_2 , but the minimum SaO_2 was significantly lower on the ethanol night (placebo $89.8\% \pm 1.6$, alcohol $86.8\% \pm 2.7$, $p < 0.05$). The effect of this dose of alcohol on airway resistance was most pronounced during the first 2 hr after ingestion.

Respiratory depression is a major cause of death in ethanol overdose.¹ Moderate doses of ethanol producing blood levels commonly seen in social drinkers have been shown to diminish the ventilatory responses to hypercarbia and hypoxia.^{2,3} Normal sleep also reduces ventilatory drive in a variety of mammals including humans⁴ and these sleep-related effects can be aggravated by ethanol.^{5–8}

Nasal continuous positive airway pressure (nasal CPAP) is a technique commonly used to treat obstructive sleep apnea.^{9,10} It has been shown that the critical nasal CPAP pressure necessary to abolish snoring can be used as an indirect measurement of the upper airway resistance.⁶ We used this method to evaluate the effect of ethanol on upper airway resistance in a group of men who reported heavy snoring but considered themselves otherwise normal. We correlate these measurements with polysomnographic data and with the number of respiratory pauses and arterial desaturation events during sleep. Our data extend available information on ethanol-related deficits in respiration during sleep by (a) describing the time course of changes and (b) showing that bedtime alcohol adversely affects respiration during sleep in the population of asymptomatic male snorers.

METHODS

Subjects

Candidates were recruited through a newspaper advertisement for male snorers who were willing to drink ethanol and sleep in our laboratory for a fee of \$50 per night. The history of snoring was confirmed by a self-made audio cassette recording during a night that was representative of the candidate's sleep. Prior to admission into the study, these cassettes were reviewed by two of the investigators (S. J. H. and M. S.) to be sure that clearly audible snoring was present and that there was no evidence of sleep apnea, such as respiratory pauses or resuscitative snoring. Prospective subjects were interviewed to exclude those with ethanol or other substance dependence or any medical or psychiatric disorder that would preclude sleeping in a laboratory setting and wearing a nasal CPAP device. The nasal CPAP mask is held tightly over the nose by straps behind the head and is connected to a blower delivering an adjustable, continuous positive pressure into the airway (Respironics, Sleep Easy™).

Our subjects were six men whose demographic data are summarized in Table 1. All of them engaged in occasional or moderate social drinking but none had an alcoholic parent.

Procedure

Testing was performed in the General Clinical Research Center at Scripps Clinic and Research Foundation on two nights separated by approximately 1 week. On the first night, subjects received ethanol in the form of 100 proof vodka mixed in orange juice at a dose of 2 ml/kg of body weight (0.79 gm/kg). On the second night, they were given a placebo (1–2 drops of vodka floated on top of the orange juice). They were instructed to drink their cocktail within 15 min. Blood Alcohol Levels (BAL) were determined by standard spectrofluorometric assay¹¹ from samples taken from an indwelling, heparinized venous catheter at 25, 60, and 180 min after they finished the cocktail. We did not inform the subjects on which night they received ethanol.

The polysomnographic technicians and the patients were not informed on which night they were given alcohol or placebo but we elected not to randomize the treatment order. We believed that ethanol on the first night would, to some extent, compensate for lack of familiarity of the laboratory environment and the discomfort of the CPAP device. If the alcohol had been given on the second night the subjects would probably have slept better than they had on the placebo night. By giving the alcohol on the first night when the subjects would tend to sleep less well we expected to favor the null hypothesis that alcohol does not exaggerate the effects of sleep on resistance of airways and apneic/hypopneic events.

Subjects underwent full polysomnography while on nasal CPAP for the entirety of both nights. Periodically, during artifact-free episodes representative of NREM sleep and REM sleep, CPAP pressures were manipulated and measurements were made of the CPAP pressure necessary to eliminate audible snoring as heard from by the technician approximately 3–5 meters from the subject's bed (critical CPAP pressure).

Data Analysis

The signal from an ear oximeter was fed through an analog-to-digital converter and stored every 2 sec on a microcomputer for later analysis.^{12, 13} A hypoxic event was defined as a decline in the SaO_2 of 4% from its previous peak value which was continuously updated from a "window" of the preceding 2 min. The hypoxic event was determined to end when the SaO_2 had risen by 4% from the nadir recorded during the event or when 3 min had elapsed from the onset of the event, whichever occurred first. The arbitrary termination of events at 3 min was done to prevent slow baseline drifts of the oximeter from being recorded as desaturation events. The EEG, electrooculogram, and electromyogram portions of the record

were scored by standard criteria into Wakefulness, Stages 1–4 of NREM sleep, and REM sleep.¹⁴ Polygraph tracings of respiratory airflow (recorded from a thermistor taped to the upper lip near the nostril) and respiratory effort (recorded from thoracic and abdominal respiratory inductance plethysmographs). Because of extensive artifact associated with the subject's movement throughout the night, the airflow thermistor and the inductance plethysmographs were not quantitatively calibrated beyond assurance that respiratory airflow and effort during quiet recumbency were clearly reflected on an ink-writing oscillograph. We employed standard sleep laboratory criteria for defining apneas and hypopneas.¹⁵ Apneas are defined as pauses in thermistor-monitored airflow of 10 sec or more. Hypopneas are defined as drops of 66% or more in thermistor-monitored airflow lasting 10 sec or more with simultaneous changes in effort tracings, increases in effort signifying obstructive events and decreases signifying central events. Data were analyzed by means of repeated measures, analyses of variance. Contrasts between each of the conditions were done with Dunnett *t* tests and, when it appeared that the data might not be normally distributed, with two-tailed Wilcoxon signed-rank tests.

RESULTS

Table 2 gives individual data and group means for blood alcohol levels (BAL) and selected respiratory and polysomnographic measurements. Five of six subjects recognized on which night they were taking a significant amount of ethanol. The mean peak BAL of 71.8 mg/dl was well below the level of legal intoxication (100 mg/dl). The subjects frequently were aroused by changes in the CPAP pressure and by blood sampling as well as by the unfamiliarity of the laboratory environment. However, the polysomnographic data indicated that routine sleep laboratory parameters were not significantly different on ethanol and placebo nights. For ethanol versus placebo nights, respectively, sleep latency was 13.4 ± 18 vs. 25.6 ± 33 min ($p = \text{ns}$), sleep duration was 242.8 ± 66 vs. 253.6 ± 27 min ($p = \text{ns}$), and sleep efficiency was 72.6 ± 16 vs. $76.9 \pm 11\%$ ($p = \text{ns}$).

One subject had a BAL of 49 mg/dl before the experimental drink was given indicating that he had had some alcohol before he came to the laboratory. We wondered whether Subject 1 could have received a larger dose of ethanol than intended on the placebo night but the progressive rise in the BAL from the baseline to 180 min suggests that the unexpectedly high values are due to “noise” in our analytic system.

On ethanol nights subjects showed significantly higher critical CPAP pressures, greater numbers of respiratory events (apneas plus hypopneas) and apneas per hour of sleep (p values < 0.05 , 0.02 , and 0.01 , respectively). Significant differences between ethanol and placebo nights were also obtained with Wilcoxon signed-rank tests (all p values < 0.025). On the ethanol nights four subjects showed an apnea index above the value of 5 per hour often used as the upper limit of normal¹⁶ while only Subject 3 showed an abnormal number on the placebo night. Subject 3 clearly had mild sleep apnea as indicated by an apnea index of 16.5 on the no-ethanol night. In addition, his oximetry tracing identified one REM-related period of repetitive desaturation typical of obstructive sleep apnea on the ethanol night.

The mean arterial oxygen saturation (SaO_2) and the number of desaturation events did not differ significantly on placebo and ethanol nights. However, five of the six subjects showed a greater number of desaturations on the ethanol night. The exception, Subject 3, had fewer desaturations on the ethanol night but those that occurred were more profound and his mean SaO_2 fell from 96.2% on the placebo night to 90.4% on the ethanol night. The minimum SaO_2 recorded during the ethanol night ($86.8\% \pm 2.7$) was significantly below that recorded on the placebo night ($89.8\% \pm 1.6$) ($p < 0.05$ by two-tailed Wilcoxon signed rank test).

Figure 1 presents blood alcohol levels (BAL) for the baseline (BL) and the three post-cocktail blood samples taken on the ethanol nights.

Figure 2 summarizes for each subject, the differences between the ethanol condition and the placebo condition in nasal CPAP pressures required to stop snoring. The data are displayed by hours after the time subjects were first asked to go to sleep (Lights Out) and are taken from representative CPAP measurements during NREM sleep. There was a significant Condition X Hours interaction ($p < 0.01$) with pressures during hours 1 and 2 elevated on ethanol nights.

For our sample, critical CPAP pressures during REM sleep appeared to be about equal to those during NREM sleep (4.9 ± 2.3 vs. 5.0 ± 1.8 cm H₂O; p ns). However, because of the frequent sleep disruptions and the REM sleep suppressing effect of ethanol during the first few hours of sleep, there were too few critical CPAP measurements during REM sleep to conduct a separate condition $\times$ hours ANOVA for REM sleep analogous to the NREM sleep ANOVA summarized in Fig. 2. The ethanol-related effects were seen mainly in the 2 h after sleep onset.

DISCUSSION

We attempted to exclude subjects with obstructive sleep apnea by means of an initial history and by monitoring a tape recording of their snoring for respiratory pauses and resuscitative snores. In spite of these precautions, one of our subjects clearly had mild sleep apnea. His results may have biased our data somewhat but the other five uniformly showed an increase in the apnea index and in the number of desaturation events on the night they received ethanol.

Scrima et al.⁸ studied six normal volunteers and found no increase in the number of apneas and hypoxic events when they received ethanol 0.8 gm/kg as compared with a no-alcohol night. However, they studied a younger (median age 26.5), thinner (median body mass index 22.6) group of subjects than we did. Their group included two women and they were not specifically recruited as snorers. In a group of six patients with obstructive sleep apnea (OSA) they found that the oxygen saturation decreased and the number of apnea events increased after ethanol. They gave their patients with obstructive sleep apnea 3 oz. of 80% proof spirits regardless of body weight and so their doses of ethanol were significantly less in the patients with OSA.

Taasin and associates,¹⁷ by contrast, found a significant increase in the number of desaturations and hypopneic events in a group of asymptomatic men given ethanol 2 ml/kg. Their subjects were somewhat older (mean age 48.4) than ours but were less overweight (their mean weight/height was 0.44 kg/cm versus ours of 0.53).

Therefore the discrepancy between the results of Scrima et al. and those of Taasin et al. and of the present report could be explained by the differences in the populations studied. However, Block and associates, from the same laboratory as Taasin, have reported that nocturnal desaturation and hypopneic events are common, even in healthy young men.¹⁸ Possibly the computer-assisted method that we used to identify desaturation events is more sensitive to minor hypoxemic episodes than the method used by Scrima et al., which they did not describe in detail.

Nasal CPAP is thought to relieve obstructive sleep apnea by “splinting” the upper airway and decreasing the tendency of the soft palate and tongue to collapse against the posterior pharynx during inspiration.⁹ Therefore the critical nasal CPAP to abolish snoring can be considered a measurement, albeit quite indirect, of the resistance of the upper airways.⁶ The increased critical CPAP is evidence that alcohol increases the resistance of upper airways during sleep.

The increased apneas and hypopneas that we observed were very likely a manifestation of an ethanol-induced increase in resistance of upper airways. For example, the data of Bonora et al.

indicate that ethanol given to cats does, in a dose-dependent fashion, preferentially reduce activity of nerves that innervate upper airway musculature (hypoglossal and recurrent laryngeal nerves) over activity of the primary innervator of the diaphragm (phrenic nerve).⁷ The alcohol-induced increase in the number of apneas and hypopneas during sleep may also be explained by depression of central respiratory drive. During a period of obstructive apnea or hypopnea the alveolar carbon dioxide and consequently the inspiratory effort increase progressively with each inspiration that fails to deliver enough room air to lower the alveolar CO₂ to its set point. Eventually inspiratory drive rises enough to overcome any abnormal increase in the resistance of the upper airways. The duration of hypopnea could be increased either by an increase in upper airways resistance (which increases the inspiratory effort required to overcome it) or by depressed central respiratory drive (which decreases the rate of increase of inspiratory effort). Finally, if alcohol causes congestion of the nasal mucosa with consequent nasal obstruction, this could explain the increased number of apnea events. Wilhoit and Suratt recently reported that nasal occlusion consistently produces obstructive sleep apnea in normal non-obese young men.¹⁹

With the relatively low doses of ethanol used in this study it seems likely that the main effects were on the upper airways. It would have been necessary to evaluate central respiratory drive separately, for example by measuring the ventilatory response to hypercapnea or hypoxia, and to use a more direct and quantitative measurement of the upper airway resistance in order to evaluate the relative importance of these two potential mechanisms.

Our results confirm previous studies indicating that respiratory events during sleep are common in asymptomatic men and that they are significantly augmented by doses of ethanol regularly consumed by “moderate social drinkers.” Frank obstructive sleep apnea can be elicited in men in whom the condition has not been suspected after a careful history conducted by a physician trained in sleep disorders. It is not unreasonable to extrapolate our findings to the large number of overweight older men with occult or recognized cardiovascular and respiratory diseases who regularly drink greater doses of ethanol than those used in our study and in the others cited. These respiratory effects of alcohol during sleep may contribute to the increase in mortality that is known to occur during the night hours.^{20,21} We postulate the existence of a “sudden adult death syndrome” in these older men which could be as tragic in its psychological and economic impact on their families as the sudden infant death syndrome (SIDS). We suspect that a fraction of the money currently invested in research on SIDS would clarify our understanding of the pathology of this condition and lead to more effective treatment by identifying individuals especially at risk.

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Fig 1.

Mean ($\pm$ SEM) blood ethanol levels in mg/dl at baseline and 25, 60, and 180 min after ingestion of 100 proof vodka in orange juice at a dose of 2 cc per kg of body weight (ethanol: 0.79 gm/kg).

Fig. 2.

Nasal CPAP pressures required to stop snoring during NREM sleep as a function of time after either ethanol (0.79 gm/kg) in the form of 100 proof vodka mixed with orange juice or a “placebo” drink. Analysis of variance disclosed a significant condition $\times$ hours interaction ($p < 0.05$) with pressures during hours 1 and 2 elevated on ethanol nights.

Table 1
Demographic Data on the Six Male Snorers Who Served as Subjects

Subject	Age (years)	HT (cm)	WT (kg)	BMI [*]
1	38	195.6	93.2	24.4
2	45	171.0	94.5	32.3
3	44	182.9	122.0	36.5
4	35	180.3	70.9	21.8
5	33	177.8	112.9	35.7
6	70	172.7	82.8	27.8
Mean	44.2	180.1	96.1	29.7
SD	33.3	8.8	25.2	6.1
Median	41.0	179.1	93.9	30.1

* BMI, body mass index = weight in kg/square of height in m.

Blood Alcohol Levels (BAL), Nasal CPAP Pressures, Polysomnographic Parameters and SaO₂ Measures for Ethanol and Placebo Nights

Table 2

	Subject	BAL (mg/dl)			CPAP pressure (cm H ₂ O)	Respiratory events (apneas + hypopneas)	Sleep duration	Respiratory index (events/hr sleep)	Mean SaO ₂	Lowest SaO ₂	Number desaturations	% Time < 90%
		Baseline	25 min	60 min	180 min							
Ethanol nights	1	0.0	42.0	38.0	14.0	14	333.5	2.5	95.20	83.00	11.0	0.80
	2	0.0	88.0	85.0	55.0	19	183.0	6.2	90.40	84.00	11.00	32.40
	3	49.0	103.0	95.0	78.0	67	243.5	16.5	95.00	88.00	23.00	0.10
	4	0.0	61.0	43.0	32.0	39	264.2	8.9	96.00	90.00	8.00	0.00
	5	0.0	109.0	78.0	54.0	15	279.4	3.2	93.90	88.00	15.00	0.70
	6	0.0	28.0	50.0	16.0	19	153.4	7.4	95.20	88.00	9.00	0.00
Mean		8.2	71.8	64.8	41.5	28.8	242.8	7.5	94.3	86.8	12.8	5.7
SD		20.0	33.3	24.1	25.2	20.8	65.7	5.1	2.0	2.7	5.5	13.1
Placebo nights	1	0.0	5.0	3.0	16.0	2	258.3	0.5	95.10	88.00	5.00	0.10
	2	0.0	0.0	0.0	0.0	3	212.0	0.8	96.20	90.00	24.00	0.00
	3	0.0	0.0	0.0	0.0	71	251.0	17.0	96.60	92.00	6.00	0.00
	4	0.0	0.0	0.0	0.0	4	257.2	0.9	96.40	91.00	7.00	0.00
	5	0.0	0.0	0.0	0.0	1	295.5	0.2	94.90	88.00	8.00	0.00
	6	0.0	0.0	0.0	0.0	13	247.3	3.2	94.70	90.00	1.00	0.00
Mean		0.0	0.8	0.5	2.7	15.7	253.6	3.8	95.7	89.8	8.5	0.0
SD		0.0	2.0	1.2	6.5	27.4	26.7	6.6	0.8	1.6	8.0	0.0
Dunnett <i>t</i>		0.0	5.08	6.35	3.26	2.50	-0.48	3.14	1.46	3.12	1.07	1.06
<i>p</i> level			0.01	0.01	0.01	0.02	NS*	0.01	NS	0.01	NS	NS

* NS, not significant.