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Effect of Bedtime Ethanol on Total Inspiratory Resistance and Respiratory Drive in Normal Nonsnoring Men

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Abstract

We have previously reported that bedtime ethanol (2.0 ml/kg of 100 proof vodka) increases upper airway closing pressure in males who habitually snored but were otherwise healthy. We also observed that some of these snorers developed obstructive apneas. To explore this phenomenon in more detail, we measured the inspiratory resistance (R_I) and respiratory drive after bedtime ethanol in 10 nonobese men (ages 23 to 33) with no history of snoring. Subjects went to bed wearing a tightly fitting valved mask over the nose and mouth that allowed measurement of inspiratory and expiratory flow, pressure in the mask, and endtidal CO_2 . We measured R_I by calculating the pressure difference between the mouth and a balloon positioned in the midesophagus. Respiratory drive was quantified by the inspiratory occlusion pressure ($P_{0.1}$), the ventilatory response to hyperoxic hypercapnia ($\Delta\dot{V}_E/\Delta P_{ET}CO_2$), and the ventilatory response to isocapnic hypoxia ($\Delta\dot{V}_E/\Delta S_aO_2$). Measurements were made during waking and during stage 2 NREM sleep on two nights: (1) when the subjects drank 1.5 ml/kg of 100 proof vodka in orange juice over a 30-min period 15–45 min before lights out and (2) when the orange juice contained less than 0.1 ml of vodka floating on the top. Eight of the nine men in whom we had technically adequate measurements showed a rise in R_I during NREM sleep above the waking level on both control and ethanol nights and the sleeping R_I was greater on the ethanol than on the control night. There was a tendency for $P_{0.1}$ to be higher during sleep and greater on the ethanol night, suggesting that the neural output to the respiratory muscles was not depressed and may have been stimulated by the inspiratory “loading” secondary to the increased R_I . The hypercapnic response was significantly depressed during sleep. Whereas the response tended to be less on the ethanol than on the control night, the difference was not significant. The hypoxic response showed little change from waking to sleeping and no significant change with ethanol. We speculate that inspiratory loading due to increased upper airway resistance tends to stimulate respiratory drive and thereby partially offsets the depressant effect of ethanol on the central respiratory chemoreceptors.

Keywords

Ethanol; Respiratory Drive; Sleep; Upper Airway Resistance

The depressant effect of ethanol on respiratory drive has been recognized for many years.^{1–4} More recently, we and others have shown that moderate doses of ethanol taken at bedtime can have another deleterious effect on respiration by increasing the upper airway resistance. Ethanol increases snoring in men who snore and worsens the severity of apneic episodes in patients with obstructive sleep apnea.^{1,5–9} However, there are no data examining the effects of ethanol on inspiratory resistance in nonsnorers whose upper airway remains relatively patent during sleep. This study was done to characterize and analyze the magnitude of changes in

inspiratory resistance and respiratory drive after a group of normal young men who regularly drank ethanol were given a moderately intoxicating dose shortly before retiring. These data may help us to understand the effects of ethanol on breathing during sleep in older subjects and those with respiratory disease.

METHODS

Subjects

We recruited 10 nonobese men (see Table 1) who denied snoring and who were classified as light to moderate drinkers by the Alcohol Research Center Intake Interview that assesses the quantity, frequency, and variability of ethanol¹⁰ and drug use/abuse.¹¹ This interview is based on the Schedule for Affective Disorders and Schizophrenia,¹² but focuses on information most likely to be seen in alcoholic patients. The interview was done during a 1- to 2-hr subject screening visit with one of us (either P.L. or B.B.). We further screened candidates with the Sleep Disorders Center Questionnaire and an intake interview with a Scripps psychiatrist to exclude any psychiatric disturbance that would make them unable to meet the demands of our experiment.

Apparatus

The inspiratory and expiratory ports of a standard continuous positive airway pressure mask (Respironics, Inc., Monroeville, PA) were attached by about 2 m of corrugated tubing to pneumotachygraphs and heated on the expiratory side (Hans Rudolph model 3800, Kansas City, MO). We added extra one-way valves on each side to overcome the tendency for the valves in the mask to leak when they became wet. A pneumatically activated balloon occluder (Hans Rudolph model 9340) was placed about 4 cm from the inspiratory port. The mask pressure was monitored through a small port in the mask and a second port was connected to an infrared CO₂ analyzer (Datex, Puritan Bennett, Los Angeles, CA) to monitor the endtidal CO₂ (P_{ET}CO₂). The rise time of the CO₂ analyzer was 10-90% in 0.2 sec, which was more than adequate to track endexpiratory plateaus in our subjects. The esophageal pressure was measured with a thin-walled balloon in the midesophagus with the negative side of the transducer attached to the mask pressure port. Pneumotachygraph and other pressures were measured with differential transducers and conditioned with carrier amplifiers (models MP45 and CD18-19, Validyne Instruments, Northridge, CA). The arterial oxygen saturation (S_aO₂) was measured with a pulse oximeter, using an ear probe (model 3700, Ohmeda, Biox, Boulder, CO). The inspired and expired flow, mask and esophageal pressure, P_{ET}CO₂, and S_aO₂ signals were all fed to a Hewlett-Packard model 216 computer. The computer controlled the switch that opened the inspiratory occluder. The occluder was closed during expiration and opened 100 msec after the onset of inspiratory effort, defined as a drop of 0.1 cm H₂O in the mask pressure. This produced a barely detectable sensation of a "sticky valve" in an awake subject and usually caused no arousal during sleep. The occluder could be programmed to close randomly every fourth to seventh breath or, if the subject showed arousability, it could be activated manually. A schematic diagram of the set-up is shown in Fig. 1.

Subjects underwent standard polysomnography for sleep staging and evaluation of respiration during sleep.¹³ We recorded the electroencephalogram from the central and occipital regions (C3/A2, O1/A2) and the electrooculogram from the outer canthi of the left and right eyes (LOC/A2, ROC/A1). The submental electromyogram (chin EMG) was recorded from electrodes placed on or beneath the chin. We recorded the EKG from leads positioned on the clavicles. Snores were recorded by means of a microphone taped to the neck positioned along the trachea. Chest and abdominal movements were recorded by inductance plethysmography using elastic bands placed around the ribcage and abdomen (Respirtrace, Ardsley, NY). Oxygen saturation was measured with two pulse oximeters (Ohmeda 3700, Boulder, CO) with probes attached to

both a finger and an ear lobe. The output from the oximeters was processed using a PC-based data acquisition and graphic analysis program (PROFOX[®]).¹⁴ All signals were recorded on a polygraph (model 78D Grass Instruments, Quincy, MA). Sleep staging was done according to Rechtschaffen and Kales scoring criteria.¹⁵

Data Analysis

The minute ventilation ($\dot{V}_E$) was calculated breath by breath from the expired volume and the time from the beginning of inspiration from one breath to the next. The inspiratory occlusion pressure ($P_{0.1}$) is defined as the pressure at the mouth 100 msec after the onset of inspiratory effort against a closed mouthpiece.¹⁶ We made the measurement by digitizing at 50 Hz the analog output of the pressure transducer situated in the mask. The occluder was closed during expiration, and the onset of inspiration was identified as the time when the mask pressure decreased below -0.1 cm H₂O. The slope of the pressure drop was calculated over the 5 data points starting with the first point that dropped below 0.1 cm H₂O. The $P_{0.1}$ equaled the rate of pressure drop in cm H₂O per 100 msec.

The response to isocapnic hypoxia ($\Delta\dot{V}_E/\Delta S_aO_2$) was measured by having the subject breathe from a bag containing 12 to 14% oxygen in nitrogen, chosen to achieve a nadir of about 80% in the S_aO_2 while the $P_{ET}CO_2$ was maintained constant by adding CO₂ to the inspired tubing about 1.5 m from the mask. The breath-by-breath $P_{ET}CO_2$ recording was displayed on the computer monitor, and we were able to keep the fluctuations less than 4 mm Hg from the baseline during each run. It took 2 to 3 min for the S_aO_2 to reach a nadir, and the hypoxia was continued for ~ 1 min before the subject was switched back to room air. Both desaturation and resaturation breaths were used to calculate $\Delta\dot{V}_E/\Delta S_aO_2$ if the subject did not arouse. Otherwise only the breaths before arousal were used. The nadir of the S_aO_2 was 79.3 ± 5.7 on the control night and 79.7 ± 4.8 on the ethanol night. When breaths with a tidal volume less than 100 ml were excluded, the correlation coefficient for $\dot{V}_E$ vs. S_aO_2 ranged from 0.65 to 0.88.

The hypercapnic response ($\Delta\dot{V}_E/\Delta P_{ET}CO_2$) was measured by gradually increasing the flow of CO₂ into the inspired tubing to produce a rise of 8 to 10 mm Hg in the $P_{ET}CO_2$ over about 5 min. When the tidal volume was stable $\Delta\dot{V}_E/\Delta P_{ET}CO_2$ could be calculated from the breath-to-breath measurements. When it was variable there were marked fluctuations in $P_{ET}CO_2$ and so we measured the $\dot{V}_E$ over periods of 30 sec and took the greatest $P_{ET}CO_2$ during the interval as an estimate of the alveolar PCO₂. All breaths were used in calculating the $\dot{V}_E$. The maximum $P_{ET}CO_2$ was 53.7 ± 2.4 on the control night and 51.8 ± 4.6 on the ethanol night.

Inspiratory resistance (R_I) was calculated from simultaneous measurements of the pressure gradient from the midesophagus to the mouth (transpulmonary pressure) and inspiratory flow. In these normal subjects we would expect upper airway resistance to be large relative to lower airways resistance and that changes in lower airways resistance produced by ethanol would be negligible relative to the effects on the upper airway. We therefore assumed that measurement of the total inspiratory resistance would give us a reliable indication of upper airways resistance.

The transpulmonary pressure is the sum of the elastic recoil pressure of the lung and the pressure required to overcome the resistance to flow. During expiration the recoil pressure and the flow-generated pressure are opposite in sign, but during inspiration the “dynamic transpulmonary pressure” is the sum of the static recoil pressure and the pressure required to overcome inspiratory resistance. We can estimate the static recoil pressure by measuring its value at the expiratory and inspiratory points of zero flow and assuming a linear increase in recoil pressure as lung volume increases within the tidal range.

The esophageal and pneumotachograph pressure signals are phase matched by “delaying” the flow signal by 40 msec. The 40 msec delay was established by placing the esophageal balloon

connected to its catheter and pressure transducer within the pneumotachograph and exposing both to the same pressures, injecting and withdrawing air from a large-volume syringe through the inspired tubing. The computer stored the pressure and flow signals that were then “played back” and plotted in an X-Y mode on the computer screen with varying delays of the flow signal. A delay of 40 msec seemed to be the optimal phase adjustment.

The inspiratory resistance is the flow-dependent pressure divided by the flow at that instant. We determined resistance by recording the inspiratory flow and esophageal pressure for 30 sec. The phase-adjusted pressures and flows were played back on the computer screen and two cursors were used to select the beginning and end of the inspiratory flow plateau for a selected breath. We averaged the instantaneous resistances for each recorded point in the selected part of the inspiration. For each run, we averaged the resistance from 3 or 4 representative breaths.

Our primary statistical test was the analyses of variance (ANOVA). A level of $p < 0.05$ was considered significant.

Procedure

Subjects were studied two nights in the General Clinical Research Center of the Green Hospital of Scripps Clinic. On the first they received 1.5 ml/kg of 100% proof vodka in 480 ml of orange juice. On the second (from 1 to 3 weeks after the first) they were given orange juice with less than 0.1 ml of vodka floated on the surface. We chose not to randomize the order of the ethanol and placebo nights, reasoning that the sedative effect of the ethanol would partly offset any tendency to sleep less well on the first night when the apparatus was unfamiliar. Presenting the ethanol on the first night should, if anything, reduce the tendency of ethanol to depress respiratory drive and so order effects would tend to favor the null hypothesis. The polysomnographic apparatus was hooked up, and a small catheter was placed in an arm vein to sample blood for the ethanol level that was taken before the drink and at 25, 60, and 180 min after it was finished.

After the esophageal balloon was inserted the subject was asked to consume the drink over a 30-min interval. After he finished it he was allowed 15 to 30 min to prepare for bed. He then lay supine and we attached the rest of the monitoring equipment, including the mask. The lights were turned out and we began the awake measurements. If the subject fell asleep before the awake measurements were completed, we proceeded to collect the sleeping data once he had reached stage 2 sleep for a minute or two. We repeated the awake measurements later in the night at a time when the subject aroused and was unable to go back to sleep immediately. Neither awake nor asleep measurements were made later than 3 hr after the subject finished his drink when we made the final blood alcohol level measurement. All measurements were made with subjects in the supine position.

The subjects slept poorly during the study, presumably because of the discomfort of wearing the apparatus and the arousing effect of the measurements. In addition, it is known that ethanol can disrupt sleep and we found that, in most subjects, there was little REM and slow wave sleep during the first 3 hr of the night. Therefore, we restricted our analysis to measurements taken during quiet breathing while awake and during well-established stage 2 NREM sleep. Data points for each subject represent an average of two to four measurements.

RESULTS

Table 1 summarizes the characteristics of our subjects and the highest blood ethanol level achieved during the study.

Our first two subjects were given a vodka dose of 2.0 ml/kg, but we reduced the amount after one (whose study could not be completed) experienced vomiting. We used the larger dose in a previous study without problems,¹ but the presence of the esophageal balloon may have increased the tendency to vomit. The lower dose was well tolerated and produced a peak blood alcohol level from 22 to 82 mg/dl.

Table 2 summarizes measurements of minute ventilation, mouth occlusion pressure, carbon dioxide response, and hypoxic response for all subjects according to sleep state and ethanol condition.

Mouth Occlusion Pressure

Waking $P_{0.1}$ differed little on control and ethanol nights, and there was no consistent effect of sleep on the control night. Seven subjects showed a rise in the $P_{0.1}$ above the waking level during sleep on the ethanol night, 2 were unchanged, and only 1 showed a decrease. The 3-way ANOVA showed a significant effect of state ($F = 16.3$, $p < 0.01$) but no significant effect of drink ($F = 1.68$, $p < 0.25$). Therefore there was no evidence of depression of respiratory neural output during sleep. In fact, it tended to increase on the ethanol night. There was no significant correlation between the $P_{0.1}$ and the change in R_I during sleep on either control or ethanol nights.

Hypercapnic Response

There was no consistent difference between the waking hypercapnic responses on control and ethanol nights. In eight subjects the sleeping response diminished on the control night, whereas one subject (subject 3) showed an increase. Likewise most subjects showed a decrease from waking to sleep on the ethanol night, with the exception of subject 3. Seven subjects showed a smaller sleeping hypercapnic response on the ethanol than on the control night. The three-factor ANOVA showed a significant effect of state on the hypercapnic response ($F = 6.47$, $p < 0.05$) but no significant effect of drink ($F = 1.30$).

Response to Isocapnic Hypoxia

The response to hypoxia was quite variable and there was no statistically significant effect of either state or drink. On the control night, 8 subjects showed a small decrease from waking to sleep, 1 showed no change, and subject 3 showed a slight increase. Note that we were unable to obtain complete data for subject 8. On the ethanol night the hypoxic response increased in 5 of 9 subjects. Subject 3 differed from the others in showing a very blunted hypoxic response (confirmed when we studied him ambulatory on another day). His minute ventilation was more than 50% greater on the ethanol than on the control night both waking and sleeping, and he showed the largest $P_{0.1}$ during sleep on the ethanol night. Subject 3 also differed from the rest of the group in showing little stimulation of ventilation by hypoxia while both sleep and ethanol appear to increase his respiratory drive.

The record from the microphone did not reveal snoring on the control night in any of our subjects and only occasional snores after ethanol. None of the subjects showed evidence of significant apneas or hypopneas, nor spontaneous desaturations of greater than 4%. Changes in minute ventilation were small and inconsistent in direction.

Inspiratory Resistance

Individual data are shown in Table 2. Figure 2 summarizes the major findings for total inspiratory resistance as a function of experimental condition and sleep state. The esophageal balloon catheter developed a leak in one subject and so results are reported only for the other nine.

In all subjects R_1 was greater during sleep than waking, both on the control and on the ethanol nights. In 8 of 9 sleeping R_1 was greater on the ethanol than on the control nights. The three-way ANOVA showed significant effects for both state ($F = 14.0$, $p < 0.01$) and drink ($F = 8.2$, $p < 0.05$). The one-factor ANOVA showed that the differences between waking and sleeping were statistically significant on ethanol ($t = 4.64$, $p < 0.01$) but not the control night ($t = 2.15$, $0.05 < p < 0.1$). The difference between sleeping values on control and ethanol nights was also significant ($t = 3.06$, $p < 0.05$).

DISCUSSION

In this study we have shown, as others have done before, that inspiratory resistance consistently increases from its waking level during NREM sleep and that this increase is augmented by ethanol. By contrast, the effect of ethanol on sleeping respiratory drive is variable and depends on the method used to assess respiratory drive.

Effects on Airway Resistance

It has been well demonstrated by others that during sleep the resistance of the upper airway increases, to a greater extent, in snorers than in nonsnorers.¹⁷⁻¹⁹ Ethanol has been shown to increase both waking and sleeping upper airway resistance. Robinson and associates²⁰ showed that the same dose of ethanol used in our study increased the upper airway resistance of healthy waking subjects by about 75% at 45 min after the drink and that the resistance was back to near the baseline level at 90 min. Bedtime ethanol studies by Issa and Sullivan⁹ and by our group¹ have demonstrated that in normal subjects who snore heavily a greater nasal continuous positive airway pressure mask pressure is required to abolish snoring. This implies that ethanol reduces the stability of the upper airway during sleep. Both of these studies included some over-weight subjects who showed apneic episodes during the study, even on the nights when they did not receive ethanol.

The primary mechanism for ethanol-related increases in upper airway resistance appears to be through a selective inhibition of upper airway motor activity. In cats, Bonora et al.²¹ found that ethanol selectively reduced the respiratory motor activity of the hypoglossal and laryngeal nerves in a dose-dependent fashion at blood levels of 83 and 134 mg/dl. Over these dose levels, the respiratory activity of the phrenic nerve was not appreciably affected. St. John et al.²² reported a similar differential depression of hypoglossal nerve activity versus phrenic nerve activity at blood levels ranging from 48 to 171 mg/dl. Krol et al.²³ made similar observations in normal humans, showing that after a dose of ethanol producing blood levels around 80 mg/dl there was reduction of the electromyographic activity in the genioglossus, but no change in minute ventilation or the ventilatory response to hypercapnia. They concluded that "the neural mechanisms underlying the respiratory activity of the genioglossus are more susceptible to depression by alcohol than those serving the muscles of the ventilatory pump."

Effect of Sleep on Respiratory Drive

In normal subjects respiratory drive, as assessed by the response to hyperoxic hypercapnia, is depressed from its waking level in NREM sleep, and to a greater extent in REM sleep.²⁴ This study confirms that the hypercapnic response diminished in stage 2 NREM sleep in most subjects. In our study there was a tendency for the hypoxic response to diminish from waking to sleep on the control night but the change was small and variable. Douglas et al.²⁵ reported a significant decline in the response to isocapnic hypoxia in all stages of sleep in 6 normal men but the change was small in stage 2 NREM. Their study was done in Denver, CO (altitude 1600 m), and it is possible that the results would have been different at sea level.

Others have also reported a variable ventilatory response to hypoxia during sleep, with some subjects showing an increased response.²⁶ The sleeping hypoxic response may be more susceptible than the hypercapnic response to genetic and endocrine factors. For example, the hypoxic ventilatory response has been shown to be maintained during NREM sleep in premenopausal women.²⁷

We recognize that the values we report for $\Delta\dot{V}_E/\Delta P_{ET}CO_2$, both waking and sleeping, are lower than most reported in the literature.²⁸ The explanation may be in part that these were not steady-state measurements. In addition, the level of hypercapnia we produced was necessarily mild because of the need to avoid arousing our subjects. The measurements needed to be completed within 3 hr after the drink was taken. Our mean $\Delta\dot{V}_E/\Delta P_{ET}CO_2$ during NREM sleep on the control night was similar to that reported recently by Badr and associates²⁹ who found that a steady-state increase in the $P_{ET}CO_2$ of 6 mm Hg increased $\dot{V}_E$ from 4.8 to 7.9 liters/min ($\Delta\dot{V}_E/\Delta P_{ET}CO_2 = 0.52$).

We found lower values for $\Delta\dot{V}_E/\Delta S_aO_2$ both waking and sleeping than Douglas and associates,²⁵ but the difference in altitude could be the explanation. Our results are similar to those reported for eucapnic hypoxia by Gothe and associates.³⁰

The $P_{0.1}$ is a valuable supplement to the classic measurements of chemosensitivity to assess respiratory drive during sleep. The measurement can be made even when the subject sleeps only intermittently or moves quickly from one sleep stage to another. Although it may be unreliable under conditions when the lung volume or thoracoabdominal mechanics vary,³¹ this should not be a problem in resting supine subjects. $P_{0.1}$ is thought to be a reliable indicator of central respiratory drive during wakefulness, showing a close correlation with the ventilatory response to hypercapnia.¹⁶ In anaesthetized cats it is closely related to phrenic nerve discharge.³² However, White³³ found no decrease in $P_{0.1}$ during NREM sleep in normal subjects. In fact, it was either maintained at or increased above its waking level and the increase tended to be greatest in snorers.³³ We did find in these nonsnoring subjects that there was a statistically significant increase in $P_{0.1}$ with sleep; that is, the two-way ANOVA showed a significant effect of state.

Effects of Ethanol on Respiratory Drive

Respiratory depression is a major cause of death in lethal ethanol overdose.³⁴ But, in doses sufficient to produce a blood alcohol level of 120 mg per dl, it does not consistently depress minute ventilation below its normal waking level.² On the other hand, ethanol did significantly depress the ventilatory response to hypercapnia when it was given intravenously, producing blood alcohol levels as low as 40 mg per dl.^{2,4} Sahn et al.⁴ demonstrated that ethanol depressed the response of healthy men to isocapnic hypoxia with a mean blood alcohol level of 112 mg/dl. Their work was done in Denver (altitude 1600 m), and the results might have been different at sea level.³⁵

We are not aware of any published data on the effects of ethanol on respiratory drive during sleep. In this study we found that the effect of ethanol during NREM sleep was variable, and it differed depending on what method was used to assess respiratory drive. Most subjects showed a diminished sleeping hypercapnic response on the ethanol night but in four subjects the response to hypoxia was greater on the ethanol than on the control night. In four subjects, in addition to the outlier subject 3, the $P_{0.1}$ was greater on the ethanol night and three of these subjects also showed a greater hypoxic response on the ethanol night. Therefore, we speculate that, in some subjects, ethanol actually augments respiratory drive during sleep.

An increased inspiratory load has been shown to increase inspiratory effort in awake humans. During NREM sleep, following an initial fall in tidal volume, $P_{0.1}$ has been shown to increase

when an inspiratory resistance from 4 to 10 cm H₂O/liter/sec is added to a valved face mask in normal sleeping men.³⁶ Although we found no significant correlation between the increase in P_{0.1} and the increase in R_I, the changes we observed in R_I were of the same order of magnitude.

The net effect of ethanol on respiratory drive probably depends on the interaction between several factors. The inspiratory loading due to increased upper airway resistance would tend to stimulate respiratory drive. The ventilatory response to hyperoxic hypercapnia, which is mediated mainly through central chemoreceptors, was in most subjects depressed by ethanol during NREM sleep. The response to isocapnic hypoxia is mediated through peripheral chemoreceptors, and it appears to be relatively resistant to the depressant effect of the low dose of ethanol that we administered. We speculate that, in some subjects, if there were any depressant effects of ethanol on the peripheral chemoreceptor response, the effect may have been offset by the stimulant effect of increased inspiratory resistance. The one subject with a deficient hypoxic response may have developed a compensatory increase in his response to both mechanical loading and hypercapnia. This would explain the unexpected increase in his hypercapnic response during sleep on both control and ethanol nights.

CONCLUSIONS

Our data confirm and extend findings on the ability of ethanol to increase upper airway resistance during sleep in healthy young men. However, it must be stressed that we studied only young, healthy, nonobese men. Obesity, advanced age, and snoring greatly increase the risk of developing sleep-related breathing abnormalities.^{37,38} These higher risk individuals may well show more deleterious effects from bedtime ethanol than did our subjects. The clinical and public health importance of ethanol-mediated increases in upper airways resistance during sleep should not be underestimated. Ethanol can cause apnea in snorers and increases sleep-related breathing abnormalities in patients with obstructive sleep apnea. Apart from any direct pressor effect it might have, ethanol, by promoting sleep apnea, clearly plays an important role in hypertension. Several epidemiological studies have demonstrated an increased incidence of hypertension and ischemic heart disease in snorers.³⁹⁻⁴² Ethanol is one of the most commonly used depressants and is most often taken during the evening hours rarely more than a few hours before nocturnal sleep.^{34,43} Over 18% of people with self-declared sleep problems use ethanol.⁴³ Better understanding of the effects of ethanol on respiration may shed some light on sleep-related increases in human mortality.⁴⁴⁻⁴⁶

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Fig. 1.
Schematic diagram of set-up.

Fig. 2.
Total inspiratory resistance.

Table 1

Subject Characteristics

Subject no.	Age	Weight (kg)	Height (cm)	Body mass index (kg/m ²)	Maximum blood alcohol level (mg/dl)
1	31	84	183	25.1	61
2	24	71	177	22.9	82
3	25	70	183	21.1	42
4	27	82	183	24.6	25
5	24	78	180	23.9	62
6	31	76	185	22.2	44
7	30	73	183	21.8	57
8	31	103	187	29.6	63
9	33	84	177	26.9	22
10	27	75	172	25.1	56

Table 2

Individual Subject Data

Subject	$\dot{V}_E$ (liters/min)				$P_{0.1}^*$ (cm H ₂ O)				CO_2 response [†] (liters/min/mm Hg)				Hypoxia (liters/min/mm Hg)				$R_{I,\dot{V}_E}$ (cm H ₂ O/liter/sec)			
	Cw	Ew	Cs	Es	Cw	Ew	Cs	Es	Cw	Ew	Cs	Es	Cw	Ew	Cs	Es	Cw	Ew	Cs	Es
1	8.7	8.2	7.5	7.7	1.2	1.2	1.2	1.4	0.93	0.78	0.73	0.69	-0.36	-0.20	-0.31	-0.22	7.5	7.7	12.0	10.8
2	6.1	6.2	6.9	6.4	1.6	2.1	1.9	2.1	0.91	0.87	0.36	0.66	-0.19	-0.23	-0.13	-0.41	8.0	11.4	13.4	21.0
3	6.7	10.1	7.2	11.3	2.1	2.1	1.8	2.8	0.66	0.70	0.92	1.01	-0.01	-0.04	0.02	-0.02	11.8	9.9	25.0	30.3
4	6.1	5.0	5.7	5.9	1.4	1.1	1.4	1.3	0.81	0.64	0.67	0.66	-0.32	-0.04	-0.26	-0.45	NA	NA	NA	NA
5	5.2	4.7	4.2	4.4	0.5	1.5	0.5	1.6	0.70	0.75	0.35	0.22	-0.28	-0.37	-0.13	-0.18	9.6	11.7	13.0	24.7
6	7.8	6.6	7.2	6.2	1.6	0.9	1.5	1.3	0.79	0.34	0.58	0.23	-0.25	-0.16	-0.19	-0.19	10.5	17.2	16.4	17.5
7	6.2	5.1	5.7	5.3	1.2	1.0	1.2	1.2	0.84	0.80	0.47	0.35	-0.21	-0.24	-0.19	-0.14	8.2	5.3	10.0	12.6
8	6.9	7.2	6.2	6.5	1.4	1.7	2.0	1.7	0.49	NA	0.49	0.15	-0.29	NA	-0.23	-0.22	12.8	13.3	26.7	56.7
9	7.2	7.0	6.9	6.6	1.0	1.4	1.1	1.2	0.55	0.86	0.46	0.50	-0.09	-0.31	-0.07	-0.23	11.8	21.3	23.0	44.4
10	5.1	5.3	5.5	4.9	0.9	1.3	1.4	1.4	0.88	0.67	0.84	0.40	-0.16	-0.07	-0.16	-0.09	5.5	4.1	6.8	14.9
Mean	6.6	6.5	6.3	6.5	1.3	1.4	1.4	1.6	0.76	0.71	0.59	0.49	-0.22	-0.18	-0.17	-0.21	9.5	11.3	16.3	25.9
SD	1.1	1.7	1.0	1.9	0.4	0.4	0.5	0.5	0.15	0.16	0.20	0.27	0.11	0.12	0.09	0.13	2.4	5.5	7.0	15.5

Summary of minute ventilation, mouth occlusion pressure, carbon dioxide response, and hypoxic response for all subjects according to sleep state and ethanol condition. Cw = control condition, wake state; Ew = ethanol condition, wake state; Cs = control condition, NREM sleep; Es = ethanol condition, NREM sleep; NA = not available.

* Significant effect of state, sleep vs. wake ($p < 0.01$).

† Significant effect of state ($p < 0.05$).

Significant effect of state ($p < 0.01$), drink ($p < 0.05$), and state-drink interaction ($p < 0.05$).