

Effect of moderate alcohol upon obstructive sleep apnoea

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ABSTRACT: Moderate-to-large quantities of alcohol are known to aggravate severe obstructive sleep apnoea (OSA), however, the reported effects of moderate alcohol consumption upon mild-to-moderate OSA are inconsistent. Given the reported benefits of moderate alcohol consumption on cardiovascular mortality, recommendations regarding the management of patients with OSA are difficult to formulate. The aim of this study was to evaluate the effects of moderate alcohol on sleep and breathing in subjects with mild-to-moderate OSA.

Twenty-one male volunteers, who snored habitually, underwent polysomnography with and without 0.5 g alcohol·kg body weight (BW)⁻¹ consumed 90 min prior to sleep time, in random order. The mean blood alcohol concentration (BAC) following alcohol at the time of lights out was 0.07 g·dL⁻¹.

The distribution amongst the various sleep stages was not significantly altered by alcohol. The mean apnoea/hypopnoea index rose from 7.1±1.9 to 9.7±2.1 events·h⁻¹ (mean±SEM, p=0.017); however, there was no significant change in the minimum arterial oxygen saturation measured by pulse oximetry Sp_{o2}, apnoea length or snoring intensity. Mean sleep cardiac frequency rose significantly from 53.9±1.4 to 59.9±1.9 beats·min⁻¹ (p<0.001) and overnight urinary noradrenalin increased from 14.9±2.3 to 18.8±2.3 nmol·mmol creatinine⁻¹ (p=0.061) on the alcohol night compared to the nonalcohol night.

To conclude, modest alcohol consumption, giving a mean blood alcohol concentration of 0.07 g·dL⁻¹, significantly increases both obstructive sleep apnoea frequency and mean sleep cardiac frequency.

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The treatment of obstructive sleep apnoea (OSA), a condition commonly associated with cardiovascular disease and autonomic disturbance, usually includes lifestyle modification such as avoidance or minimization of alcohol [1]. However, health practitioners frequently tell patients that alcohol, taken in moderate quantities, has beneficial effects upon cardiovascular mortality [2, 3]. In particular, published guidelines suggest a "safe upper level" of four standard (10 g alcohol) drinks of alcohol per day in males before the adverse effects of hypertension, heart and liver disease develop [4–7]. For an 80 kg male, this would equate to 0.5 g alcohol·kg body weight (BW)⁻¹.

Alcohol, consumed in large quantities (>1.0 g alcohol·kg BW⁻¹), sufficient to increase the blood alcohol concentrations (BAC) to >0.075 g·dL⁻¹, increases apnoea frequency, length and associated hypoxaemia in patients with OSA [8–11]. However, the effects of alcohol at lower doses (0.5–1.0 g alcohol·kg BW⁻¹) on OSA are less clear. When subjects were given 0.5 g alcohol·kg BW⁻¹ (with a corresponding mean BAC of 0.075 g·dL⁻¹), COLLOP *et al.* [12] observed a significant rise in the mean apnoea/hypopnoea index (AHI), from 10 to 20 events·h⁻¹. In contrast, BLOCK *et al.* [13] found no difference in the AHI (2.8 to 3.0 events·h⁻¹) when subjects, with milder OSA, were given 1 g alcohol·kg BW⁻¹ (BAC 0.075 g·dL⁻¹). Similarly, TESCHLER *et al.* [14] found no difference in the

AHI (44–51 events·h⁻¹) when males with severe OSA were given 0.5 g alcohol·kg BW⁻¹ (BAC 0.05 g·dL⁻¹).

In order to further understand the effects of alcohol on sleep-disordered breathing and associated autonomic disturbance, the authors undertook a randomized controlled study to determine the effects of moderate alcohol consumption on snoring severity, sleep quality, apnoea/hypopnoea frequency and on the markers of sympathetic activity in male subjects with habitual snoring and various levels of OSA.

Methods

Subjects

Male subjects, aged 30–60 yrs, who met the following criteria: habitual snoring, moderate alcohol consumption, absence of any significant medical conditions and free of regular medication, were recruited. Moderate alcohol consumption was defined as <1 g alcohol·kg BW⁻¹ for ≤5 days·week⁻¹. Subjects were recruited from advertisements placed around the hospital and from patients referred to the sleep clinic. The Ethics Committee of the Alfred Hospital approved the study and patients provided written informed consent.

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Sleep studies

Overnight sleep studies were performed in the usual manner with a computerized system (Somnostar®, SensorMedics Corp, CA, USA), two electroencephalogram (EEG) channels, left and right electrooculograms (EOGs) and submental electromyogram (EMG) for the determination of sleep stages. Sleep stages were manually scored according to standard criteria by an experienced scorer blinded to the patients' details as previously described [15]. Sleep efficiency was defined as total sleep time/time in bed and % sleep stage as the total time spent in a particular sleep stage/total sleep time. Electrocardiogram (ECG) and cardiac frequency were recorded continuously from precordial lead II; arterial oxygen saturation was measured by an ear pulse oximeter (S_{p,O_2}) (Fastrac, SensorMedics Corp, CA, USA). Chest and abdominal movements were monitored using respiratory effort bands calibrated for phase but not tidal volume (Resp-ez™, EPM Systems, VA, USA). Oronasal airflow was monitored by thermocouples (ProTech Services, WA, USA). Snoring was measured with an audiometer placed 1 m above the participants head (Rion NA-24, Rion Tokyo, Japan). Snoring intensity was calculated by: 1) the area under the curve of the sound intensity *versus* time graph, 2) the peak noise in rapid eye movement (REM) and non-REM (NREM) sleep, and 3) the % sleep time spent with noise >50 dB. Arousals were defined as episodes lasting ≥ 3 s in which there was a return of alpha activity associated with increased EMG activity [16].

An obstructive apnoea was defined as an absence of oronasal airflow for ≥ 10 s despite continued out-of-phase chest and abdominal movements. An obstructive hypopnoea was defined as a reduction in oronasal airflow for ≥ 10 s associated with a $\geq 2\%$ fall in S_{p,O_2} despite continued out-of-phase chest and abdominal movements, increased submental EMG activity, or snoring. Patients with central apnoea were excluded from the study. The AHI was defined as the total number of apnoeas and hypopnoeas divided by the total sleep time, and expressed as the number of events per hour.

Catecholamine measurements

Urinary noradrenalin (UNA) was measured from urine produced overnight during the period of the sleep study. Urine collection began after subjects had voided prior to retiring to bed (~22:00 h) and included all urine passed overnight, including the first morning void upon arising (~6:00 h). Urine was collected in acidified containers with 20 mL of 6 M HCL, and stored at 4°C prior to analysis. Noradrenalin was measured by high-performance liquid chromatography (HPLC) with fluorescence detection [17]. To take into account possible differences in renal function, UNA was adjusted for creatinine excretion and expressed as nmol·mmol creatinine⁻¹ as previously described [18].

Alcohol measurements

Blood alcohol levels were estimated from the alcohol concentration in the expired breath using an alcoholometer (Lion laboratories, South Wales, UK) [19].

Arterial blood gas measurements

An arterial blood gas sample was taken from the radial artery using a 25-gauge needle, and blood gases and pH levels were determined (ABL 500 Radiometer; Radiometer-Copenhagen, Denmark) immediately before the sleep studies.

Protocol

Eligible subjects underwent two sleep studies, a week apart, in random order with and without alcohol. Subjects were asked to refrain from alcohol during the day prior to sleep studies. Each subject was breathalysed upon arrival at the sleep centre to ensure no alcohol had been consumed prior to the study.

On the night of each sleep study, a standard hospital meal was provided at 19:30 h and thereafter sleep monitoring leads were attached between 20:00 and 21:00 h. Between 21:00 and 22:30 h, subjects consumed 0.5 g·kg BW alcohol⁻¹ (chilled white wine) or water depending upon randomization.

Statistical analysis

Data are expressed as mean \pm SEM. A p-value of <0.05 was regarded as significant. The Wilcoxon signed-rank test was used to compare the data.

Results

Twenty-one male subjects undertook the study. The mean age was 43.5 \pm 1.7 (range 34–59) yrs, body mass index (BMI) 27.8 \pm 0.8 (range 21–38) kg·m⁻² and average alcohol consumption was 13.1 \pm 1.4 standard drinks·week⁻¹.

The mean BAC was 0.07 \pm 0.01 g·dL⁻¹ following alcohol consumption just prior to lights out. On the alcohol night, compared with the control night, there was a significant reduction in NREM sleep latency (10 \pm 1 *versus* 19 \pm 3 min, $p < 0.01$) but no statistical difference in REM latency (125 \pm 10 *versus* 110 \pm 13 min, $p = 0.303$) (table 1). The distribution of sleep amongst the various sleep stages was unaffected by alcohol (table 1).

Table 1. – Sleep architecture and latency on control and alcohol nights

	Control	Alcohol
Time in bed min	464 \pm 6	452 \pm 4
Total sleep time min	400 \pm 11	399 \pm 8
Sleep period time min	447 \pm 7	441 \pm 5
Sleep efficiency	87 \pm 2	88 \pm 1
Wake % SPT	11 \pm 2	10 \pm 1
Stage 1&2 % SPT	58 \pm 2	60 \pm 2
Slow wave sleep % SPT	13 \pm 1	13 \pm 1
REM % SPT	19 \pm 1	18 \pm 1
NREM sleep latency min	19 \pm 3	10 \pm 1**
REM sleep latency min	110 \pm 13	125 \pm 10
Arousals events·h ⁻¹	17 \pm 2	19 \pm 3

Data are presented as mean \pm SEM. **: $p < 0.01$ *versus* control. % SPT: per cent sleep period time; REM: rapid eye movement; NREM: non-REM.

Table 2. – Effect of alcohol upon obstructive sleep apnoea, cardiac frequency and urinary noradrenalin

	Control	Alcohol
AHI events·h ⁻¹	7.1±1.9	9.7±2.1 [#]
Apnoea length (NREM)	16.0±0.7	17.2±1.2
Apnoea length (REM)	18.9±1.2	18.9±1.5
Snoring		
AUC AU	184±8	198±9
Peak intensity (NREM) dB	52.5±2.5	49.7±2.2
Peak intensity (REM) dB	47.7±2.4	46.4±1.8
% TST >50dB	40±18	39±18
Mean Sp,O ₂ %	95.9±0.4	95.3±0.4
Minimum Sp,O ₂ %	86.6±1.9	85.8±1.6
SPT with Sp,O ₂ <90% (%)	1.5±0.8	3.6±1.9
UNE nmol·mmol creatinine ⁻¹	14.9±2.3	18.8±2.3 ⁺
Urine volume mL	730±106	900±62
Cardiac frequency beats·min ⁻¹	53.9±1.4	59.9±1.9**

Data are presented as mean±SEM. AHI: apnoea/hypopnea index; REM: rapid eye movement; NREM: non-REM; AUC: area under the curve; AU: arbitrary units; TST: total sleep time; Sp,O₂: arterial oxygen saturation measured by pulse oximetry; SPT: sleep period time; UNA: urinary noradrenalin. [#]: p<0.025; ⁺: p=0.061; ^{**}: p<0.01.

On the alcohol night, compared with the control night, there was a significant increase in the total AHI (9.7±2.1 *versus* 7.1±1.9 h, p=0.017) (table 2 and fig. 1). There was no significant difference in the increase (alcohol-control) in the AHI for those subjects randomized to receive alcohol on the first night (n=10) compared to the control subjects (n=11), (change in AHI 2.4±2.9 *versus* 2.1±0.8 events·h⁻¹, respectively, p=0.561), suggesting that there was no order effect. There was also no significant correlation between the increase in AHI and baseline AHI (r=-0.225, p=0.465), body mass index (r=0.191, p=0.407) or age (r=0.052, p=0.853).

Of the 21 subjects, the AHI rose in 16, fell in four and was unchanged in one. There was no significant difference in BAC (0.07±0.03 *versus* 0.07±0.01 g·dL⁻¹, p=NS), age (44.2±2.0 *versus* 41.0±4.4, p=NS), BMI (27.6±1.1 *versus* 28.6±1.0, p=NS) or prior average weekly alcohol consumption (13.1±1.6 *versus* 14.3±3.8 drinks·week⁻¹, p=NS) between those subjects who showed an increase in the AHI

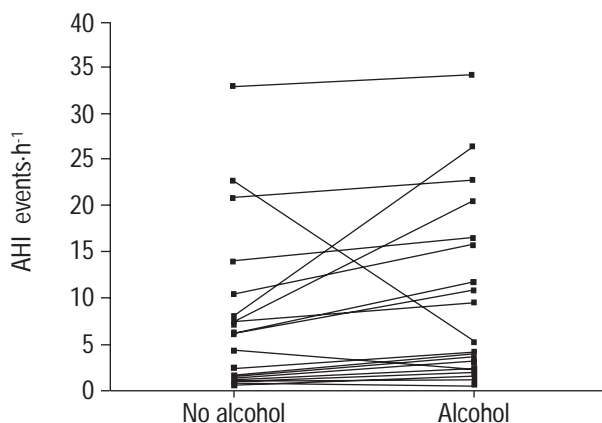


Fig. 1. – Individual apnoea/hypopnoea indices (AHI) of all subjects on control nights and alcohol nights. The mean AHI was significantly greater on alcohol (9.7±2.1 events·h⁻¹) than on control nights (7.1±1.9 events·h⁻¹, p=0.017).

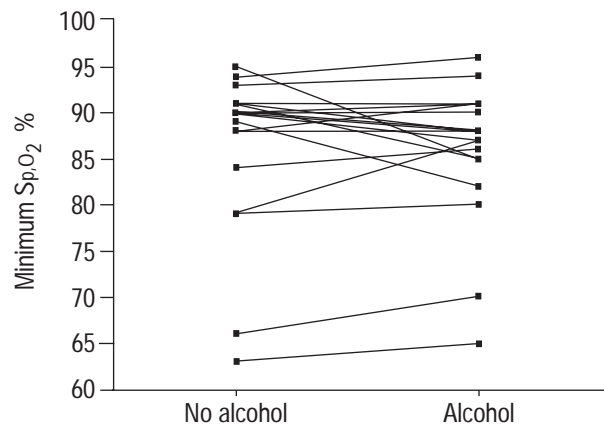


Fig. 2. – Individual minimum arterial oxygen saturation measured by pulse oximetry (Sp,O₂) values for all subjects on control and alcohol nights. There was no significant difference in minimum Sp,O₂ between alcohol (85.8±1.6%) and control nights (86.6±1.9%, p=NS).

with alcohol compared to those who showed a decrease. However, in all subjects with an AHI <5 events·h⁻¹ on the control night (n=11), the AHI remained <5 events·h⁻¹ on the alcohol night.

There was no significant change in the levels of apnoea-related hypoxaemia (fig. 2) or apnoea length during NREM or REM sleep with alcohol (table 2). Moreover, the sound intensity of snoring did not change significantly on the alcohol night compared with the control night (table 2).

There was a significant rise in the mean sleep cardiac frequency on the alcohol night compared with the control night (59.9±1.9 *versus* 53.9±1.4 beats·min⁻¹, p<0.01) (fig. 3), a rise that was associated with a trend towards an increase in UNA (18.8±2.3 *versus* 14.9±2.3 nmol·mmol creatinine⁻¹, p=0.061). Arterial blood gases, taken in a subgroup of six subjects, revealed a significant shift in pH towards acidemia (7.37±0.01 *versus* 7.41±0.01, p<0.05) and a trend towards hypocapnia (41.3±0.5 *versus* 44.3±0.6 kPa, p=0.061) without a change in oxygen tension in arterial blood (Pa,O₂) (88.3±2.6 *versus* 87.7±3.5 kPa p=NS) or Sa,O₂ (98.0±0.6 *versus* 97.7±0.5%, p=NS) with alcohol, compared with the control night, indicating a mild metabolic acidosis induced by alcohol.

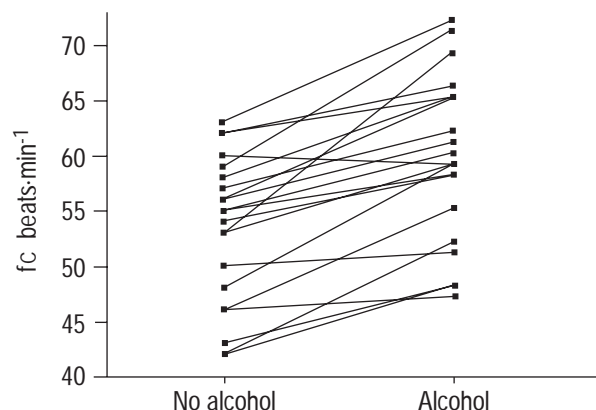


Fig. 3. – Individual mean sleep cardiac frequency (fc) data of all subjects on control and alcohol nights. The mean fc was significantly greater following alcohol (59.9±1.9 beats·min⁻¹) compared with control night (53.9±1.4 beats·min⁻¹, p<0.01).

On the control nights, the UNA correlated significantly with minimum S_{p,O_2} ($r=-0.600$, $p<0.001$) and mean S_{p,O_2} ($r=-0.435$, $p=0.045$), and showed a trend towards significance with total sleep time spent with $S_{p,O_2} <90\%$ ($r=0.417$, $p=0.075$) but not AHI ($r=0.382$, $p=0.106$) or the arousal index ($r=0.182$, $p=0.457$). Mean sleep cardiac frequency also correlated with the minimum S_{p,O_2} ($r=-0.455$, $p=0.039$), and showed significance with total sleep time spent with $S_{p,O_2} <90\%$ ($r=-0.403$, $p=0.070$), but did not correlate with the AHI ($r=-0.306$, $p=0.177$) or arousal index ($r=0.287$, $p=0.207$).

Discussion

The major finding of this study was that moderate alcohol intake (0.5 g alcohol·kg BW^{-1}), sufficient to increase the BAC to 0.07 g·dL $^{-1}$ resulted in a small but statistically significant rise in the frequency of obstructive apnoeas and hypopnoeas, without prolonging the apnoea length or worsening hypoxaemia. The effect of alcohol upon the AHI could not be explained by age or the body mass index. Moreover, mean sleep cardiac frequency increased significantly with alcohol. These results would suggest that the severity of obstructive sleep apnoea in subjects with habitual snoring may increase with moderate alcohol consumption prior to sleep time.

Alcohol minimization or abstinence is frequently recommended in the management of patients with obstructive sleep apnoea [1]. Proposed mechanisms for the adverse effects of alcohol upon OSA include selective reduction in genioglossus and hypoglossal motor nerve activity [20–23], increased nasal mucosa oedema and thereby increased resistance [21], a reduction in arousal response [8–10] and a reduced haemoglobin affinity for oxygen [23]. In addition, considerable evidence exists that alcohol fragments sleep, independent of apnoea status [24], which may further aggravate OSA [25]. Moreover, alcohol may have a direct toxic effect upon the myocardium [26].

Alcohol given in large quantities significantly worsens OSA [8, 9]. At doses of 0.9 – 3.0 g alcohol·kg BW^{-1} , AHI and apnoea length increased significantly resulting in greater hypoxaemia in seven males with severe OSA [8]. Similarly, TAASAN *et al.* [9] described an increase in OSA severity in subjects, asymptomatic of OSA, given 1 g alcohol·kg BW^{-1} . Moreover, BLOCK *et al.* [13] reported that apnoea was worsened by 1 g alcohol·kg BW^{-1} in males (but not in females) with mild sleep apnoea.

However, when alcohol is given in moderate doses (0.5 – 1.0 g·kg BW^{-1}), the effects upon apnoea severity are less clear. Some authors report an increase [9, 12, 27] and others no effect [13, 14] upon severity of OSA. BERRY *et al.* [10] reported 0.5 g alcohol·kg BW^{-1} did not alter respiration during sleep. TESCHLER *et al.* [14] suggested similar doses did not alter pressure requirements to maintain ventilation during sleep in patients with severe OSA.

Conversely, COLLOP [12] and SCRIMA *et al.* [27] have shown that doses of 0.5 g alcohol·kg BW^{-1} increased the AHI from 9 to 20 events·h $^{-1}$ [12] and the 2% dips in S_{p,O_2} from 134 to 210 per night [27]. The findings of the present study support the findings of COLLOP [12] and SCRIMA *et al.* [17] that alcohol does increase the frequency

of respiratory events even in the mild group of subjects and in the absence of increased snoring severity.

Findings of interest in this study were that moderate alcohol consumption had no significant effect on the mean apnoea length or arousal frequency. This observation could be explained by a greater depressant effect of alcohol upon upper airway muscle activity than on arousability. This would be consistent with previous data presented by BERRY *et al.* [10] who reported an increase in upper airway resistance without a significant change in apnoea length in subjects given alcohol.

Snoring intensity did not significantly change with alcohol consumption in the subjects studied. Although snoring is a hallmark symptom of OSA, it is rarely measured objectively, and there is no standard method to do so. In this study, snoring intensity was objectively measured with an audiometer placed 1 m from the mouth, a technique similar to that used by previous groups [28, 29]. Analysis was performed using the maximum for NREM and REM stages of sleep, with the area under the curve and the $\%$ sleep time >50 dB; therefore, the recordings are believed to be accurate.

Another interesting finding in this study was that there was a substantial rise in mean sleep cardiac frequency with alcohol, from ~ 54 to ~ 60 bpm, for which several possibilities exist. Firstly, it is possible that the rise was due to the elevation in AHI. However, OSA is usually associated with bradycardia during the apnoea and tachycardia at the terminating arousal. The net gain is usually no significant change in mean cardiac frequency. Moreover, the rise in cardiac frequency was observed in 20 of the 21 subjects studied, and even occurred in those five subjects who did not display a rise in AHI with alcohol. Therefore, the authors believe that the rise in cardiac frequency cannot simply be explained by an increase in OSA severity. Alternatively, the relative tachycardia may have been a response to peripheral systemic vasodilation, an acute effect which occurs with alcohol in subjects with intact baroreceptor function [30, 31]. This may also have contributed to a rise in the overnight urinary excretion of noradrenalin, as observed in this study. Alternatively, alcohol may have a direct sympathetic nervous system excitatory effect. Increased skeletal muscle sympathetic nerve activity, blood pressure and cardiac frequency were observed in awake normal subjects given 1 g alcohol·kg BW^{-1} suggesting that alcohol has a direct sympathoneural stimulatory function [30]. The arterial blood gas measurements that were observed suggested an alcohol-induced trend towards metabolic acidosis and hypocapnia, in the absence of hypoxaemia, which may reflect a manifestation of sympathetic stimulation.

To conclude, the effects of 0.5 g alcohol·kg body weight $^{-1}$, a level regarded as the safe upper limit by health authorities, on sleep apnoea in otherwise healthy habitual snorers with mild-to-moderate obstructive sleep apnoea were studied. A small but statistically significant rise in sleep apnoea severity, cardiac frequency and a trend towards an increase in overnight urinary noradrenalin was observed. Given the enormity of public health issues related to obstructive sleep apnoea, public health authorities, who provide statements regarding the safe levels of alcohol consumption, should also be reminded of the potential adverse effects of alcohol upon apnoea severity.

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