

Nocturnal oxygen saturation in advanced chronic obstructive pulmonary disease after a moderate dose of ethanol

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Nocturnal oxygen saturation in advanced chronic obstructive pulmonary disease after a moderate dose of ethanol. P.E. Brander, T. Kuitunen, T. Salmi, M. Partinen.

ABSTRACT: The effect of a moderate oral dose of ethanol (0.5 g·kg⁻¹ body weight) on nocturnal arterial oxygen saturation (Sao₂) was evaluated in nine male patients with advanced chronic obstructive pulmonary disease (COPD), (median forced expiratory volume in one second (FEV₁) 0.9 l, arterial oxygen tension (Pao₂) 9.3 kPa, arterial carbon dioxide tension (Paco₂) 5.3 kPa). During the four study nights (two after alcohol and two after placebo intake), the patients were monitored by whole-night computerized recordings of Sao₂ (Biox-oximeter), airflow (thermistors) and respiratory as well as body movements (static charge sensitive bed).

After alcohol intake, the mean blood ethanol concentration (SEM) in the evening was 42(2.3) mg·100 ml⁻¹. Alcohol intake was associated with a marginal deterioration of nocturnal oxygenation; the mean (SEM) nocturnal Sao₂ was 88.4(2.0) % after alcohol ingestion and 89.1(1.6) % after placebo ingestion, respectively. Only during the first 2 h in bed was there a statistically significant difference in Sao₂ in favour of placebo (p<0.05).

It is concluded that moderate alcohol intake in the evening, corresponding to "social" drinking, did not substantially aggravate nocturnal oxygenation in our patients with advanced COPD and mild to moderate daytime hypoxaemia. *Eur Respir J*, 1992, 5, 308-312.

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Nocturnal worsening of hypoxaemia is a common feature in patients with chronic obstructive pulmonary disease (COPD). The deepest oxygen desaturations occur in rapid eye movement (REM) sleep [1-3]. The nocturnal fall in oxygen saturation is suggested to result from a combination of hypoventilation and ventilation/perfusion imbalance [4-6]. The best predictor of the severity of nocturnal hypoxaemia is the level of oxygenation during wakefulness, patients with a reduced resting daytime arterial oxygen tension being the most hypoxaemic during sleep [7, 8]. Any factor increasing hypoventilation during sleep might induce clinically significant nocturnal oxygen desaturation even in such COPD patients, whose waking level of arterial oxygen tension is only slightly reduced.

Moderate doses of alcohol slightly depress the ventilatory responses to hypoxaemia and hypercapnia in normal subjects [9]. In patients with COPD, excessive alcohol ingestion before sleep is reported to decrease the total sleep time, alter the sleep stage distribution and decrease the nocturnal arterial oxygen saturation [10].

The aim of this study was to evaluate the effects of a moderate dose of alcohol on nocturnal arterial oxygen saturation in patients with advanced COPD.

Patients and methods

Patients

Nine male patients with advanced COPD participated in the study after informed consent. They all had irreversible airways obstruction with a forced expiratory volume in one second (FEV₁) <45% of the predicted value and mild to moderate hypoxaemia during wakefulness. None had had an exacerbation of COPD within the preceding 4 weeks. Patients with a history and/or signs of chronic alcohol misuse, abnormal serum γ -glutamyltransferase (γ -GT), or hepatic or gastrointestinal disease were excluded, as were patients with sleep disordered breathing due to some other cause, such as sleep apnoea or thoracic deformities. Four patients were current smokers and five were ex-smokers. All patients were treated for COPD with a wide variety of bronchodilator and corticosteroid therapies: inhaled β_2 -sympathomimetics (all patients); inhaled ipratropium bromide or oxitropium bromide (six patients); oral slow-release theophyllines 400-900 mg·day⁻¹ (eight patients); inhaled beclomethasone or budesonide 800-2000 μ g·day⁻¹ (five patients). None was on long-term oxygen therapy. In addition, four of the nine patients

were also treated for associated cardiovascular diseases. The medication applied was continued unaltered during the study.

Before the study, the patients were examined clinically and their FEV₁, diffusing capacity of carbon monoxide (DLCO) and supine resting arterial blood gases were recorded.

Study design

All patients had one acclimatizing whole-night recording. The results of this acclimatizing night were checked with the intention to exclude patients with an increased number of sleep apnoeas and were thereafter disregarded. Nocturnal recordings were then performed on two consecutive nights following intake of either alcohol or placebo. One week later, recordings after both alcohol and placebo were repeated on two additional consecutive nights. The order of the treatments (alcohol night followed by placebo night or vice versa) was randomized.

The alcoholic (0.5 g·kg⁻¹ body weight) drink consisted of 20% (w/v) alcohol in diluted fruit juice; the total volume of the solution ranged from 150–290 ml. The placebo drink was plain fruit juice.

The patients arrived at the hospital in the afternoon and had their supper three hours before the intake of alcoholic or placebo drinks. They started taking the drinks at 7.30 p.m. and finished them in 30 min. The absence of alcohol in expired breath was confirmed with an Alcolmeter® before the administration of the drinks. Blood was sampled for direct assay of blood ethanol concentration (BEC) at 10 p.m., just before the onset of night recording. The night recording was carried out in a patient ward in a quiet single room equipped with the computerized recording system.

After each two nights' experiment the patients were asked about their preference of nights.

Nocturnal recordings

We performed whole-night computerized recordings of the following parameters: transcutaneous arterial oxygen saturation (Sao₂) with an oximeter and a finger transducer (Biox 3700 Ohmeda); body and respiratory movements with a static charge sensitive bed (SCSB) movement sensor, and airflow with a three-channel thermistor in front of the nostrils and the mouth. The signals were sampled (32 samples·s⁻¹, Tecmar analogue-digital converter), rectified and integrated in epochs, stored onto the floppy disc of an IBM PC/XT computer and displayed on the computer screen during recording. The length of an epoch was 1.2 s for all of the signals. The compressed graphical output of the signals and the cumulative distribution of the nocturnal Sao₂ were printed in the morning [11]. The mean Sao₂ and the Sao₂ level below which the patient spent 10% of the

total recording time was noted (10th percentile Sao₂). The recording time was divided into one hour epochs and the mean Sao₂ was analysed for each epoch [12]. The supine waking Sao₂ at the beginning of the night recording and the proportion of time in bed spent below Sao₂ of 85% were separately calculated. The duration of periodic breathing suggestive of episodic apnoeas and/or hypopnoeas was noted [11].

The patients' mental condition was assessed using visual analogue scales (VAS) of 100 mm each before and after the sleep studies [13]. The extremes of the scales (0–100 mm) were: alert-drowsy; clumsy-well coordinated; proficient-incompetent. The subjective quality of the sleep after every recorded night was scored on a scale from 0 to 3 (0=very poor sleep, 3=good sleep).

Blood ethanol concentration

The blood ethanol concentration (BEC) was assayed both indirectly in expired breath using a digital Alcolmeter (Lion Alcolmeter SD-2®, Lion Laboratories Ltd, Barry, Wales, UK) and directly in blood samples by a gas chromatographic method (a modification of Perkin Elmer 8500®).

Statistical analysis

The differences between alcohol and placebo nights were tested using the paired t-test or the Wilcoxon signed rank test, depending on the distribution of the data. For each patient, the two alcohol values and the two placebo values were used for statistical analysis. The intra-individual standard deviations of the difference were calculated from the duplicate (two nights) recordings for each treatment. The agreement between the duplicate measurements was tested as suggested by BLAND and ALTMAN [14].

Results

The clinical characteristics of the patients are presented in table 1. Four patients were randomized to have the alcohol evening followed by the placebo evening and five patients were randomized to the opposite order of treatments. The mean (SEM) blood ethanol concentration (BEC) at 10 p.m. on the alcohol evenings was 42(2.3) mg·100 ml⁻¹.

In addition to the nine patients studied, one patient originally accepted failed to participate in the repeated experiment because of an exacerbation of bronchitis during the one week interval. His results are not considered further.

The mean(SEM) time spent in bed (from onset of recording to final awakening) was 478(19) min after alcohol (A) and 491(17) min after placebo (P) injection.

Table 1. - Patient characteristics (n=9)

	Median	Range
Age yrs	63	60-70
BMI kg·m ⁻²	23.3	18.4-29.7
FEV ₁ l BTPS	0.9	0.7-1.6
FEV ₁ /FVC %	40	31-71
VC l BTPS	2.7	1.6-4.4
DLco % pred	39	14-57
Pao ₂ kPa	9.3	5.9-10.0
Paco ₂ kPa	5.3	4.8-7.4

BMI: body mass index; FEV₁: forced expiratory volume in one second; FVC: forced vital capacity; VC: vital capacity; DLco: single breath diffusing capacity; Pao₂: supine waking partial pressure for arterial oxygen; Paco₂: supine waking partial pressure for arterial carbon dioxide. BTPS: body temperature, atmospheric pressure, saturated. Predicted values for DLco were calculated according to VILJANEN [15].

The mean nocturnal Sao₂ was slightly, though not significantly, lower after A than after P ingestion (88.4 (2.0) % vs 89.1 (1.6) %, p=0.114). The supine waking Sao₂ at 10 p.m. did not differ significantly between A and P evenings (91.1 (1.1) % after A and 91.7 (1.0) % after P, respectively) (table 2). In all patients, the degree and duration of marked nocturnal O₂ desaturation (Sao₂ <85%) were similar after A and P (table 2). During the first two hours in bed, however, Sao₂ was slightly and significantly lower after A than after P (figure 1). The cumulative time distribution curves of Sao₂ after A and P are presented in figure 2. The readings presented in the text, table 2 and figures 1 and 2 are calculated from the means of two alcohol and two placebo nights for each patient.

good except in patient No. 6 (fig. 3), who was the only one showing chronic respiratory failure (table 2) [14].

Periodic breathing suggestive of episodic apnoeas or hypopnoeas was observed in six patients in a total of 12 nights. The mean duration of periodic breathing was 31 min during seven nights after A and 23 min during five nights after P, with no significant difference between the treatments.

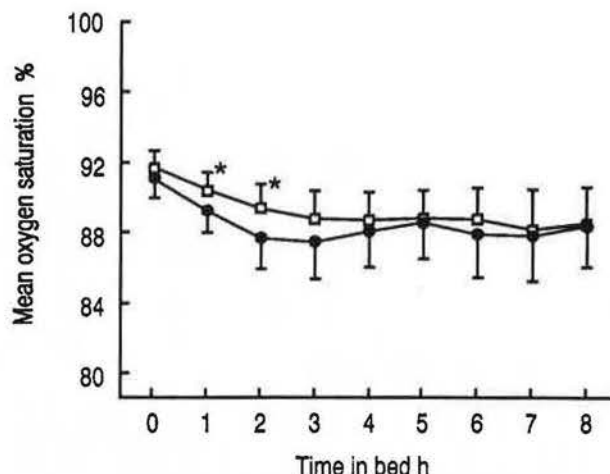


Fig. 1. - Nocturnal arterial oxygen saturation (Sao₂) after alcohol and placebo ingestion in nine patients with chronic obstructive pulmonary disease (COPD). Recording started at 10 p.m. Point 0 represents the mean supine waking Sao₂ at 10 p.m.; the other time points represent the average Sao₂ for one hour during two alcohol and two placebo nights. □: Sao₂ after placebo ingestion; ●: Sao₂ after alcohol ingestion. Bars denote SEM. *: during the first two hours of recording the difference was statistically significant (p<0.05, Wilcoxon signed rank test).

Table 2. - Individual data on nocturnal oxygenation

Pt no.	Awake supine		Alcohol			Placebo		
	Pao ₂ kPa	Paco ₂ kPa	awSao ₂ %	Sao ₂ <85% min	10%Sao ₂ %	awSao ₂ %	Sao ₂ <85% min	10%Sao ₂ %
1	10.0	6.6	91.0	4	86.9	93.0	7	88.1
2	8.8	5.0	94.0	0	90.7	94.5	0	90.2
3	9.0	5.2	91.0	7	87.2	90.5	4	87.4
4	9.5	5.3	93.0	3	87.6	94.0	2	87.2
5	9.5	4.8	95.0	0	92.2	95.0	0	91.0
6	5.9	7.4	83.5	502	66.4	85.0	511	70.9
7	9.5	5.3	91.0	71	82.3	92.0	31	85.1
8	9.3	5.2	89.5	17	85.0	91.0	5	87.0
9	8.6	5.5	91.5	1	86.8	90.5	0	87.4
Mean	8.9	5.6	91.1	67	85.0	91.7	62	86.0
SEM	0.4	0.3	1.1	55	2.5	1.0	56	2.0

Pao₂: partial pressure for arterial oxygen; Paco₂: partial pressure for arterial carbon dioxide; awSao₂: supine arterial oxygen saturation when awake at 10 p.m.; Sao₂ <85%: time spent below Sao₂ of 85%; 10%Sao₂: Sao₂ value below which the patient spent 10% of total recording time.

The standard deviations of the within-patient differences in mean Sao₂ between the two A and P nights were 2.6% (A) and 2.4% (P). There was no significant difference between the first and the second night with regard to the mean Sao₂ (p=0.282 between A nights and p=0.422 between P nights). Agreement between the two measurements of the 10th percentile of Sao₂ was

There was no difference in sleep quality assessed by the patients between alcohol and placebo nights. The sleep was considered fair or good (mean score 2.4 after both A and P ingestion). In 14 of the experiments, including two consecutive nights each, the patients reported that they slept better on the second than on the first study night. In four experiments sleep

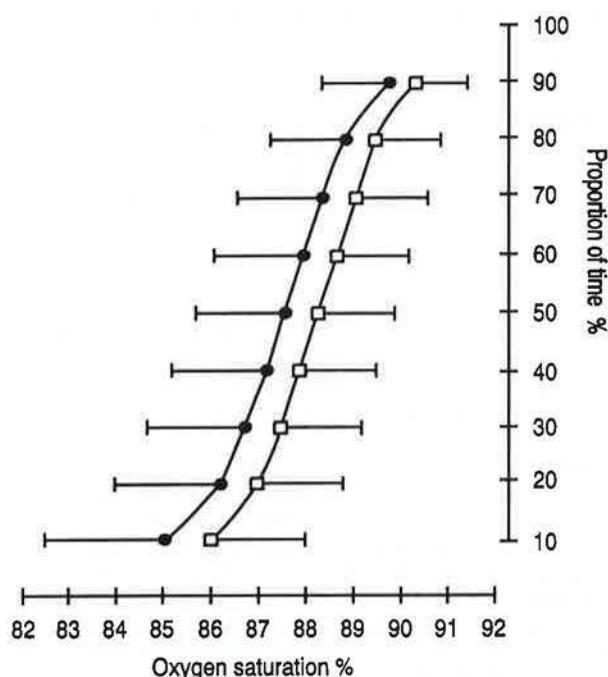


Fig. 2. - The cumulative time distribution curves of nocturnal arterial oxygen saturation (SaO_2) in nine patients after alcohol (●) and placebo (□) ingestion. On the vertical axis are the percentiles from 10 to 90 of the cumulative recording time (time in bed) and on the horizontal axis are the corresponding SaO_2 levels. Bars denote SEM. The curves denote the proportion of recording time spent below a given value of SaO_2 . At each time percentile, the SaO_2 level was slightly lower after intake of alcohol.

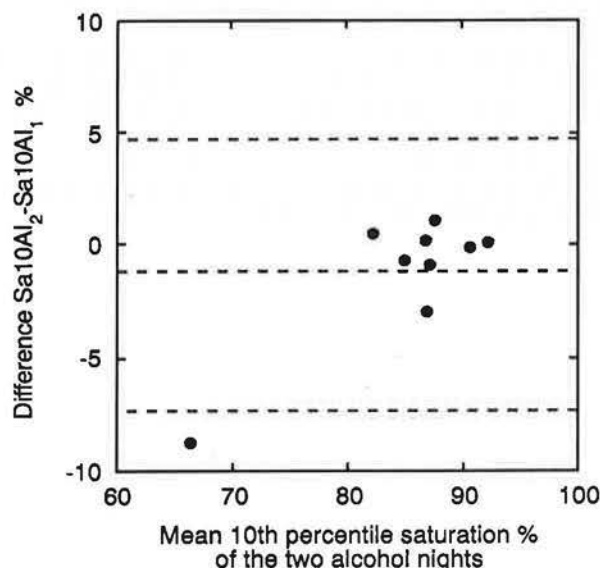


Fig. 3. - Intra-individual agreement between the duplicate measurements of the 10th percentile arterial oxygen saturation (SaO_2) (the SaO_2 value below which the patient spent 10% of the total recording time) after alcohol ingestion. $Sa10Al_1$: 10th percentile SaO_2 during the second alcohol night; $Sa10Al_2$: 10th percentile SaO_2 during the first alcohol night. Each point represents one patient ($n=9$). The difference between the two alcohol nights was plotted against the mean of the two alcohol nights. The middle dashed line shows the mean difference and the lower and upper lines show the two standard deviations of the mean. The 10th percentile SaO_2 was slightly lower during the first than during the second alcohol night, but the difference was statistically insignificant. The outlier in the left lower quadrant is patient No. 6 (table 2), who was the only one in chronic respiratory failure.

was considered similar in both nights. The patients' preferences were not related to the treatment (A or P).

The patients' subjective feelings of drowsiness, clumsiness and incompetence (VAS) were not significantly different after alcohol and placebo ingestion.

Discussion

Alcohol consumption, particularly in the evening, has been considered deleterious to patients with COPD [16]. In a group of five COPD patients, ethanol ingestion before sleep, resulting in a mean blood ethanol concentration of $130 \text{ mg} \cdot 100 \text{ ml}^{-1}$, was reported to cause a significant decrease of the mean nocturnal SaO_2 from 90.6% to 87.7%. The largest drop in oxygen saturation occurred during REM sleep (from 89.6% to 81.9%) [10].

In the present study we wanted to find out, whether alcohol intake mimicking a "social" drinking pattern, such as drinking a couple of beers or taking a night-cap, would worsen the nocturnal oxygenation in patients with COPD. We chose an alcohol dose of $0.5 \text{ g} \cdot \text{kg}^{-1}$ body weight, corresponding to about three glasses of wine in a 70 kg person [17]. The blood ethanol concentration before sleep ranged from 40–60 $\text{mg} \cdot 100 \text{ ml}^{-1}$.

The effects exerted by alcohol were trivial. We analysed separately several features of nocturnal oxygen saturation (the average values for nocturnal SaO_2 ; the SaO_2 at different time points during the time in bed; O_2 desaturation below 85%; the SaO_2 level for the 10th percentile of cumulative recording time; and the individual nocturnal SaO_2 data). There was no major change in any of these variables after alcohol ingestion. We observed a tendency to a slightly lower nocturnal SaO_2 after alcohol ingestion as compared with placebo. However, only during the early phase of night recording, from 10 p.m. to midnight, was the alcohol intake followed by a statistically significant, albeit trivial, lowering of SaO_2 . This finding is compatible with the predicted peaking of the blood ethanol concentrations during the early night [18].

Since we made duplicate experiments for each patient, the repeatability of the measurements could be evaluated. The nocturnal SaO_2 data were fairly well repeatable, which strengthens the reliability of our results. The level of nocturnal SaO_2 was more dependent on the level of oxygenation when awake than on the treatment itself. One patient only had severe daytime hypoxaemia with a Pao_2 of 5.9 kPa, combined with hypercapnia. He developed worsening of hypoxaemia during all four study nights to a similar degree regardless of treatment. His low waking Pao_2 placed him on the steep part of the oxyhaemoglobin dissociation curve, where even small changes in ventilation may cause large variations in SaO_2 . The moderate disagreement between the two measurements of the 10th percentile SaO_2 after alcohol intake

observed in this patient alone (fig. 3) may be due to the same mechanism.

In conclusion, we found that in our patients with advanced COPD and slight to moderate blood gas disturbances during wakefulness, the intake of moderate doses of alcohol in the evening did not substantially impair nocturnal oxygenation.

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