Effects of temperature and humidity of inhaled air on the concentration of ethanol in a man's exhaled breath

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Summary

1. Ten healthy men each drank a moderate dose of ethanol in experiments to test if the temperature and moisture content of inhaled air could alter the concentration of ethanol in exhaled breath.

2. They breathed air at various temperatures and relative humidities (RH) for about 1 min before the concentration of ethanol and the temperature of end-expired breath were determined. Control breaths were analysed after the same men breathed ordinary room air (23°C, 55% RH). All tests were made during the postabsorptive phase of ethanol metabolism and the breath samples were analysed by gas–liquid chromatography.

3. When the men breathed cold dry air (5°C, 0% RH), the expired ethanol concentration decreased by 9.6 ± 0.69% (mean ± se) and breath temperature dropped by 1.40 ± 0.08°C. Cold moist air (5°C, 100% RH) decreased breath ethanol concentration by 6.4 ± 1.02% and breath temperature dropped by 1.1 ± 0.07°C. With hot dry air (80°C, 0% RH) as the breathing medium the concentration of ethanol was lowered by 4.3 ± 1.27% but expired breath temperatures were unchanged from the control tests. On breathing hot moist air (50°C, 100% RH), breath ethanol concentrations decreased by 10.3 ± 0.59%, even though breath temperatures rose by 1.8 ± 0.14°C above that of the controls.

4. Ethanol dissolves in the watery mucous membrane of the upper respiratory tract and can equilibrate with inhaled and exhaled air. It seems likely that during exchanges of heat and water vapour between respired air and the mucus, which largely depends on the temperature and humidity of inhaled air, the equilibrium of ethanol at the breath/mucus interface becomes disrupted. This leads to changes in the concentration of ethanol in expired air.

Key words: air, breath, ethanol, expiration, humidity, water vapour.

Introduction

Experiments in vitro have shown that the distribution of ethanol between air and blood, at equilibrium, is strongly temperature dependent [1–3]. As temperatures rise, the concentration of ethanol in the air phase increases and therefore the blood/air partition coefficient decreases. The average temperature coefficient of solubility for dilute solutions of ethanol in water and blood is 6.5% per 10°C for the temperature range of 20–40°C [4].

In the lungs, ethanol equilibrates between blood and alveolar air at about 37°C, but on exhalation the alveolar air is cooled and breath leaves the mouth at an average temperature of 34–5°C [5, 6]. Accordingly, the concentration of ethanol in expired breath is less than in alveolar air because re-equilibration occurs at a lower temperature [1]. Factors that warm or cool the breath from one subject to another or from time to time within the same subject are important to consider when blood ethanol concentrations are indirectly estimated by analysis of breath samples.

In this paper I report experiments to test the effect of temperature and humidity of inhaled air on the concentration of ethanol and the temperature of end-expired breath. The results are
relevant to breath ethanol determinations made under extreme ambient air conditions.

Methods

Subjects and conditions

Ten apparently healthy men, mean age 24 years (range 20–29) and mean body weight 69 kg (range 60–80), took part in the experiments. They were all used to moderate drinking and some regularly smoked cigarettes, although not during this study. They drank whisky in a volume which was sufficient to give a peak blood ethanol concentration of about 1.0 mg/ml (21.7 mmol/l). One hour after they finished drinking, breath samples were analysed to check on each subject’s phase of ethanol metabolism. When three successive breath tests, made at 15 min intervals, showed decreasing concentrations this was taken as indicating the postabsorptive phase of metabolism.

Breath analysis

Quantitative determinations of ethanol in breath samples were made with a Mk. II Gas Chromatograph Intoximeter (Intoximeters Inc., St Louis, U.S.A.). The volume of breath exhaled by each subject during a test was measured with a Wright respirometer [7] (British Oxygen Company Ltd, Harlow, U.K.) and was noted to the nearest 100 ml. The temperature profile of each exhalation was monitored with a thermistor device (Telemechanics Ltd, Camberley, U.K.). The thermistor bead was inserted through the flexible plastic breath tube (0.8 cm internal diameter) and mounted about 1 cm from the test subject’s lips. This type of thermistor bead has a negligible mass that requires pre-heating, and the response time constant in moving air is about 300 ms. This arrangement was heated to about 40°C between tests to avoid condensation of water on the thermistor bead. The temperature signals were calibrated with water baths at 32°C, 34°C and 37°C and were linear over this range. The temperature of breath rose steadily from start to end of a prolonged exhalation with a mean of 34.48 ± 0.402°C (mean ± sd) after a forced vital capacity manoeuvre. The experimental set-up and results of breath temperature and expired volume measurements are described in detail elsewhere [6].

The gas chromatograph response was calibrated by analysing head space ethanol-in-air vapour mixtures. The vapours were produced by equilibration of known strength solutions at 25°C. The precision and accuracy of this gas chromatographic method for breath ethanol analysis has been reported [8, 9]. From analysis of duplicate breaths (n = 100) the coefficient of variation of a single determination was 2.0% at a mean ethanol concentration in blood of 1.0 mg/ml (21.7 mmol/l).

Preparation of air-breathing mixtures

The test subjects inhaled cylinder compressed air after the air was conditioned in various ways: cold dry air (5°C, 0% RH), hot dry air (50°C, 0% RH), cold wet air (5°C, 100% RH) and hot wet air (50°C, 100% RH) were chosen as inhaling mixtures. The temperatures of air streams were measured just before subjects inhaled. Relative humidity of inhaled air was not measured but cylinder air is practically dry (0% RH) and a nebulizer was used to get 100% humidification [10]. Whether this method of humidification gives water vapour saturation or an aqueous aerosol or both was not demonstrated. Nevertheless, the water vapour content of nebulized air is vastly different from the ambient air inhaled in control tests.

To produce cold dry air, compressed air from a cylinder was passed through a coiled copper tube (3 m × 0.5 cm internal diameter), which was immersed in an ice–water mixture. Hot dry air was obtained by changing the iced water for boiling water. Air mixtures saturated with water vapour (100% humidified) were generated with the help of a nebulizer [10]. The inlet nozzle of the nebulizer was connected via a liquid feed tube to a water reservoir so that when compressed air (210 kPa) passed through the unit water rose in the plastic tube and became atomized to form a spray of droplets, as a mist, at the exit tube. The nebulizer was placed in iced water or boiling water to give cold or hot 100% humidified air respectively.

Breathing technique and breath sampling arrangement

Each subject attached a nose clip and breathed the conditioned air through a plastic mouthpiece tube (1.0 cm internal diameter), fitted to the nebulizer outlet or the copper tube, by taking deep inspirations and expirations on each breathing cycle. The subjects needed practice with the breathing procedure and air flow rates were adjusted as desired for most comfort. The temperature of each exhalation was measured and breathing cycles were continued until a steady high or low end-expired temperature was reached. This normally required eight to ten deep
inspirations and expirations of the conditioned air over about 1 min. At this stage subjects took a last deep inhalation, held the breath, and stepped forward to blow into the gas chromatograph device. The volume of breath expired and the temperature of the breath were recorded at the instant a breath sample was analysed.

Because the nose has a high efficiency to warm and moisten inhaled air, subjects were asked to breathe through their mouths to get maximum changes in expired temperature [11]. Only a few normal inspirations and expirations of room air were needed before ethanol concentrations and temperatures returned to control values.

**Evaluation of results**

Each subject served as his own control and the results were evaluated as intra-individual differences by Student's t-test. The control breath samples were taken when subjects breathed room air (23°C, 55% RH). Immediately after the control breath sample, subjects breathed one of the conditioned air samples and the concentration of ethanol and the temperature of breath were recorded. Ethanol metabolism occurring over the 3–5 min interval between analysis of the control and test samples was neglected. All breath samples were analysed after roughly the same volumes of breath were exhaled.

The difference in temperature between a test and control sample of breath was used to calculate an expected change in the concentration of ethanol. This expected change was calculated as 6.5% per 1°C, which is the temperature coefficient for ethanol solubility determined from experiments in vitro [4]. A similar method was used by Allott et al. [12] for adjusting partition coefficients of diethyl ether for changes in the equilibrium temperature. In the present work the maximum temperature change was about 2°C.

**Results**

Table 1 shows the breath temperatures and breath ethanol concentrations of subjects in control tests (breathing room air) and after they breathed conditioned air samples. The temperatures of control breaths were not significantly different (F = 1.16, d.f. = 3 and 71, P > 0.05). When subjects breathed cold dry air or cold air 100% humidified their breath temperatures were lowered by 1.4°C and 1.1°C respectively (P < 0.001). There were statistically significant decreases in the concentrations of ethanol when subjects breathed cold air (P < 0.001).
When subjects inhaled hot dry air, breath temperatures were not significantly different from those of the control tests \((P > 0.05)\), although breath ethanol concentrations were lowered by 4.3\% on average \((P < 0.01)\). When the breathing mixture was hot air saturated with moisture the average breath temperature increased by 1.8°C \((P < 0.001)\) whereas the concentrations of ethanol were significantly decreased \((P < 0.001)\). The percentage decreases in ethanol concentration were compared with the changes expected based on the differences in temperature. This gives an overall change in concentration \((\text{observed} - \text{expected})\). Table 1 shows that the decrease in ethanol concentration after cold air breathing could be attributed to the lower breath temperatures. The overall differences were not statistically significant \((P > 0.05)\).

The concentration of ethanol in breath after subjects breathed hot dry air decreased \((P < 0.001)\) even though breath temperatures were unchanged \((P > 0.05)\). The maximum change in breath ethanol concentration was seen in experiments with hot air saturated with water vapor. Under these conditions expired ethanol was lowered by 10-3\%, despite a rise in breath temperature of 1.8°C. An overall increase in ethanol concentration of 11-7\% was expected from the rise in temperature.

**Discussion**

The upper respiratory tract is covered with a mucous membrane composed of 2-3\% mucus and 1-2\% salts, the rest being water [13]. One of the main functions of the upper respiratory tract is to condition inspired air so that, by the time air reaches the alveoli, it is warmed to body temperature and saturated with water vapor. This air conditioning involves an interaction between inspired air and the mucous blanket of the upper respiratory tract. The basic principles of heat and water exchange in the respiratory tract have been discussed in detail by Walker & Wells [14].

Ethanol is distributed throughout the body and enters into the water fraction of fluids and tissue so that the equilibrium concentrations reached depend on body water. Because the mucus of the upper respiratory tract is mostly water it gains ethanol by diffusion from the blood and also by absorption from the expired breath. The concentration of ethanol in the mucus during normal breathing will depend on the ventilation cycle. This is because inhaled air is normally ethanol-free and ethanol therefore evaporates from the warm mucous membranes. At the alveolar capillary interface ethanol equilibrates between blood and breath at body temperature. Because ethanol's concentration in alveolar air is now above the equilibrium level in the upper respiratory tract some will be extracted by the mucus when alveolar air is on its way out of the lungs. This loss from expired air compensates for the ethanol extracted by inhaled air. This model assumes that ethanol has not had time to reach the mucus by diffusion from the blood stream. Replacement directly from the blood seems unlikely within the short change-over time from inspiration to expiration because the mucus is separated from the blood by a relatively thick layer of cells [15]. Furthermore, the mucus/blood distribution ratio of ethanol at equilibrium will be about 1:1, whereas the breath/mucus ratio will be about 1:2300 [4]. These conditions favour a rapid re-equilibration of ethanol between the expired breath and the mucous membranes.

The demands placed on the mucus as a heat and water exchanger vary depending on the temperature and humidity of inhaled air. When subjects breathed cold air, the expired breath concentrations of ethanol fell below the control values. The differences between cold air saturated with moisture and cold dry air were insignificant. This is because the absolute water content of saturated air is low at temperatures near to the freezing point of water. The lower concentrations of ethanol with cold air breathing are accounted for by the lower temperature of exhaled breath as expected from changes in air/liquid partition ratios of ethanol as temperatures drop.

After subjects had breathed hot dry air their expired ethanol concentration was lowered by 4.3\% \((P < 0.01)\), despite there being no changes in expired temperature. Under these conditions \(\text{(low humidity)}\), evaporation of water and ethanol will occur during inspiration and the mucosa becomes cooled despite the high temperature of inspired air [14]. Evaporative cooling is an efficient process and outweighs the warming effect of hot dry air. The cooled mucosa recovers water and ethanol from the expired air and its temperature should fall below the control values. But it does not and so the fall in expired ethanol on breathing hot dry air cannot be attributed to a simple temperature effect. These findings are difficult to interpret because there may be several underlying mechanisms involved that call for specifically designed experiments beyond the scope of the present work.

Hot wet air presents a unique environment and the mucous membranes of the upper respiratory tract can gain heat. This means that expired air is no longer cooled on passage through the upper
Airway and can be expired saturated with water vapour at 37°C. The end-expired temperature rose to 36.1°C on average, almost 2°C above control tests, when subjects breathed hot wet air. Yet the concentration of ethanol in end-expired breath dropped by about 10%. A possible explanation for this finding is that small water droplets, present as an aqueous aerosol in hot wet air, are deposited in the first part of the airway and act as an absorption sink for expired ethanol. Based on the rise in expired temperature, expired ethanol should have increased by 11.7%.

The mucous membrane of the upper respiratory tract is a primary defence mechanism of the lungs and irritant gases with high solubility in water, such as SO₂ or NH₃, are barely detected in the delicate alveolar regions of the lungs [16]. The hazard posed by these water-soluble agents is met by the mucous film of the upper respiratory tract, which rids itself of the gases during exhalation. The role played by the mucus in liquid/gas exchanges of ethanol in the tract was first proposed by Wright et al. [17] and has now been accepted by others [18, 19]. Factors that influence equilibrium, such as the temperature and humidity of ambient air, must be considered when breath analysis is used to obtain quantitative estimates of ethanol in blood.

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References