Does consumption of ethanol distort measurements of exhaled nitric oxide?

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\textbf{Summary}  
\textbf{Background:} Measuring FE\textsubscript{NO} is a novel and non-invasive way to monitor airway inflammation (e.g. asthma). This clinical study was designed to investigate whether drinking ethanol might distort FE\textsubscript{NO} measurements.

\textbf{Methods:} Twenty healthy subjects drank 0.40 g ethanol/kg body weight in 15 min. Measurement of FE\textsubscript{NO} started ~ 30 min before drinking and at various times afterwards for 4 h post-dosing. Ethanol concentrations were determined in venous blood by gas chromatography and in end-exhaled breath by infra-red spectrometry.

\textbf{Results:} The within subject standard deviation for determination of FE\textsubscript{NO} was 1.3 ppb, corresponding to a CV of 7.7%. The mean change in FE\textsubscript{NO} from pre-drinking levels during the 4 h testing was statistically significant (\(P<0.001\)) according to repeated measures ANOVA. In absolute units the mean change was small, \(-2.01\) and \(-1.94\) ppb at 3 and 4 h post-dosing, respectively (\(P<0.013\); \(P<0.005\)).

\textbf{Conclusions:} FE\textsubscript{NO} measurements were reproducible even in subjects with moderate concentrations of ethanol in blood and breath. The small decrease in FE\textsubscript{NO} observed at 3 and 4 h post-drinking was less than the intra-subject variations in FE\textsubscript{NO} measurements. The breath-alcohol concentrations in this study exceed all other endogenous volatiles, thus making it unlikely that other substances in human breath will bias the FE\textsubscript{NO} measurements.

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\textbf{Introduction}  
Non-invasive methods are highly desirable for use as diagnostic tools in clinical medicine.\textsuperscript{1,2} Asthma is a disease associated with inflammation of the airways and measuring exhaled nitric oxide (NO)
is a useful biochemical marker for this condition. The consumption of ethanol and the resulting blood- and breath-alcohol concentrations are exogenous factors that might skew the results of measuring nitric oxide in expired air.

The aim of this study was to test whether drinking a moderate dose of ethanol might distort the measurements of NO in exhaled breath determined by chemiluminescence.

Methods

Subjects

Twenty healthy subjects, 10 men with mean (SD) age 44 years (9.7), weight 79 kg (10.3) and height 178 cm (5.3) and 10 women mean age 35 years (8.5), weight 64 kg (12.2) and height 169 cm (4.4), participated in this study as paid subjects after approval by the university ethics committee and informed consent.

Conditions

In exactly 15 min each subject drank 0.40 g ethanol per kg body weight; prepared from 95% v/v ethanol and a non-alcoholic drink to give a final concentration of 20% v/v (~2 glasses of table wine (12% v/v)). The measurements of FE NO followed ATS guidelines starting at 30 min before drinking and then at 30 min, 1, 2, 3, and 4 h timed from start of drinking. Ethanol was determined in venous blood samples by headspace gas chromatography and in end-exhaled breath with a quantitative infrared analyser, the Intoxilyzer 5000 (CMI Inc., Owensbro, KY) developed for testing drunk drivers.

Alcohol consumption started 2–3 h after subjects had eaten lunch and no food nor drink or any strenuous physical activity was allowed 60 min before the start of testing. Triplicate determinations of FE NO were made at each time point and mean values were plotted to establish the concentration-time course and the effects of ethanol. The counter pressure (10–20 cm water) and flow rate (50 ml/s) parameters were measured and controlled by the NIOX NO Monitoring System (Aerocrine AB, Solna, Sweden).

Statistical analysis

Repeated measures ANOVA with and without gender as a covariate was used to evaluate the results. The precision of FE NO analysis with NIOX was found by one-way ANOVA using the triplicate measurements at each sampling time. The mean changes in FE NO from baseline values before drinking alcohol were evaluated by Student’s-paired t-test.

Results

The within subject standard deviation for determination of FE NO was 1.3 ppb (coefficient of variation 7.7%). A statistically significant time-to-time varia-

Figure 1 Individual concentration-time profiles of exhaled nitric oxide (NO) before and after 20 subjects drank a small dose (0.4 g/kg) of ethanol (upper plot), the mean time-course of exhaled NO (middle plot) and the mean blood-and breath-alcohol concentrations (lower plot).
tion in $F_{ENO}$ was established by ANOVA ($F=6.8$, d.f.5 and 95, $P<0.001$). However, the mean decreases in $F_{ENO}$ were small, they reached statistical significance at 3 h ($-2.01 \pm 3.26$ ppb) and 4 h ($-1.94 \pm 2.65$ ppb) post-dosing ($P<0.013$ and $P<0.005$, respectively). After intake of alcohol the mean overall drop in $F_{ENO}$ was $-1.03 \pm 2.98$ ppb (median $-0.88$ ppb) and this was statistically significant ($P<0.001$).

Figure 1 (upper part) shows $F_{ENO}$ concentrations for individual subjects based on six successive measurements over 4 h. There were wide inter-individual variations in $F_{ENO}$ spanning from 5 to 30 ppb on an average. Figure 1 (middle part) shows the average time course of $F_{ENO}$ and the lower trace shows the corresponding blood- and breath-alcohol profiles.

The concentration of ethanol in breath and blood peaked at $\sim 30–60$ min after the end of drinking and except for tests made at 15 min all BrAC measurements (mg/2 l) were less than the coexisting venous BAC (mg/g). The mean $F_{ENO}$ showed small fluctuations during the first 90 min post-dosing slightly as the time after drinking increased (Fig. 1, middle part). For both men and women, the overall effect of ethanol on $F_{ENO}$ was miniscule.

Discussion

Because alcohol is so widely used in modern society and sometimes excessively, this study was designed to evaluate whether ingestion of alcohol might distort the analysis of $F_{ENO}$ owing to interference from ethanol in the breath. This could have a negative impact on reliability of $F_{ENO}$ measurements in clinical practice. However, the results from this clinical study showed that the changes in $F_{ENO}$ from baseline were small or negligible. We found a small decrease in $F_{ENO}$ at 3–4 h post-dosing compared with baseline values. This decrease occurred gradually and was most pronounced at 3 h post-dosing. It is important to note that the magnitude of the change was smaller than the accepted analytical variations with the NIOX® NO Monitoring System, being $\pm 2.5$ ppb for 95% range.

Ethanol is a major component of human expired air after drinking alcoholic beverages and the concentrations present exceed by several orders of magnitude all other endogenous or exogenous volatiles.1,2 Meijer et al.9 found that after breathing equipment was disinfected with ethanol the exhaled NO measured by chemiluminescence tended to decrease. However, the ethanol concentration was 5 vol% (50,000 ppm), being far in excess of that found in human breath after drinking alcohol. The effect of drinking alcohol on $F_{ENO}$ was not investigated.

Yates et al.10 published an article on the interaction between ethanol and $F_{ENO}$ after subjects drank 40 g ethanol (Vodka). They found that $F_{ENO}$ decreased slightly in asthmatic subjects ($N=9$) but not in healthy controls ($N=12$). However, the $F_{ENO}$ analysis was done at only one time point (15 min post-dosing) and the breath-alcohol concentration was reported as 136.4 units, which makes it impossible to compare with the dose of ethanol administered.

Our study increases knowledge about the lack of a confounding influence of ethanol on $F_{ENO}$ in human subjects when measurements were made repeatedly for up to 4-h post-dosing. Moreover, the NIOX is a dedicated instrument widely used in thoracic medicine as a test for inflammation in the airways.

Conclusion

This human study demonstrates that elevated concentrations of ethanol in breath might cause a slight drop in $F_{ENO}$ at 3 and 4 h post-dosing. This decrease was trivial and within the precision specification for the NIOX® NO Monitoring System. We conclude therefore that NIOX® is suitable for monitoring inflammation in the airways even if patients might have consumed a moderate amount of alcohol before the tests are made.

References