

Lung function changes by ethanol inhalation

E. ŽUŠKIN*, A. BOUHUYS† and M. ŠARIĆ‡

**Andrija Štampar School of Public Health, Zagreb, Yugoslavia*, †*Yale University School of Medicine, New Haven, Connecticut, U.S.A.* and ‡*Institute for Medical Research and Occupational Health, Zagreb, Yugoslavia*

(Received 14 February 1980; resubmitted 23 July 1980; accepted for publication 23 September 1980)

Summary

The acute effect of ethanol inhalation on ventilatory capacity was studied in a group of six healthy volunteers and the results were compared to those obtained after the inhalation of a saline solution. There was a significant decrease in flow rates on partial expiratory flow-volume (PEFV) curves up to 90 min after ethanol inhalation. FEV₁ values did not change significantly, either after ethanol or saline aerosol. Pretreatment with atropine did not prevent the acute reductions in flow rates in comparison with the reductions without atropine. Pretreatment with disodium cromoglycate (DSCG) considerably diminished the acute reductions of flow rates caused by ethanol inhalation. These results suggest that ethanol in some persons may act, at least partly, through releasing mediators with bronchoconstrictive action.

Introduction

Alcoholics may have a high prevalence of chronic non-specific lung disease, not fully explained by their concomitant smoking habits (Banner, 1973; Emirgil *et al.*, 1974; Šarić, Lucić-Palaić & Horton, 1977). Inhibition of ciliary motion and of alveolar macrophage function, aspiration, and altered ventilation-perfusion relations are some factors thought to be responsible for this prevalence (Heinemann, 1977). Oral ingestion of alcoholic beverages but not of ethanol may provoke asthmatic reactions, prevented by disodium cromoglycate (DSCG), in patients with asthma (Breslin, Hendrick & Pepys, 1973). This suggests that the beverages caused airway constriction via release of chemical mediators in the human lung. Ethanol itself, in contrast, inhibits mediator release in sensitized lung tissue and bronchi of the guinea-pig (Mongar and Schild, 1957; Fleisch *et al.*, 1976). Lung function studies in healthy and asthmatic subjects have given conflicting results. Ethanol may increase the vital capacity of asthmatic patients (Herxheimer & Stresemann, 1963), and cause no change (Herxheimer & Stresemann, 1963) or a decrease of vital capacity in healthy persons

Correspondence: Dr. E. Žuškin, Andrija Štampar School of Public Health, Rokefellerova 4, 41000 Zagreb, Yugoslavia.

(Johnstone & Reier, 1973). In one non-asthmatic person controlled experiments with oral ethanol showed evidence of bronchoconstriction, partially inhibited by DSCG but not by atropine (Geppert & Boushey, 1978). All previous studies concern effects of ingested or intravenous ethanol or alcoholic beverages, which makes it difficult to distinguish between direct effects on the airways and secondary effects related to systemic effects of ethanol, or response to its metabolites.

This study is concerned with the effect of ethanol, administered in the form of aerosol, on airway calibre (as inferred from flow-volume curves) in healthy subjects, and the concomitant effect of disodium cromoglycate.

Subjects and method

Six healthy subjects, two atopic and four non-atopic, (4 women, 2 men: age range 28–45 yr; 5 non-smokers and 1 regular smoker) inhaled 25% aerosol ethanol in water, or saline as a placebo for 30 min. During the exposure, subjects were seated, breathing quietly through the mouth and with the nose closed. The aerosol was produced by a Bird micronebulizer (Bird Corp., Palm Spring, Ca.) which produces a mist of liquid particles 0.5–4.0 μm in size at an air pressure of 20 p.s.i. All experiments were performed at the same time of day. There was at least a 5-day interval between ethanol and saline exposures.

The ethanol inhalation was conducted again after pretreatment with 40 mg of disodium cromoglycate (DSCG) or a placebo (lactose), both administered by Spinhaler® 20 min before exposure.

In all subjects the experiment with ethanol inhalation was also performed following pretreatment with atropine sulphate. On the first test day the subjects inhaled ethanol. On the second day subjects were given 1 mg of atropine s.c. 30 min before exposure. Each subject's pulse rate was recorded before and during the experiment.

Lung function

We measured lung function by recording partial and maximum expiratory flow-volume (PEFV and MEFV) curves with pneumotachograph-integrator device and a Brush 500 High Performance XY Recorder (Gould, Inc.) (Virgulto & Boyhuys, 1973). Measurements of lung function were performed before exposure, immediately after (0'), and repeatedly during the 4 hr after exposure. Three complete sets of curves were recorded on each occasion. From each set we measured one-second forced expiratory volume (FEV_1), maximum expiratory flow rates at 40% of the forced vital capacity (FVC) on PEFV curves, i.e. at total lung capacity (TLC) minus 60% of the FVC [MEF 40% (P)], and maximum expiratory flow rates at 50% of the FVC on MEFV curves (MEF50%). The mean value of the three curves were used as the result.

The significance of the differences in ventilatory measurements were determined by the *t*-test of paired observations.

Ethanol concentration

Ethanol concentrations in inspired and expired air were determined with a detector (Drage Tube Alcohol 100/a; measuring range 100–3000 p.p.m.) and a Drager gas detector pump. The inspired ethanol concentration was measured in the tube through which the subjects inhaled the aerosol. The ethanol concentration in the subject's expired air was measured twice: 5 min and 30 min after inhalation.

Results

Lung function

In all subjects, inhalation of ethanol aerosol caused cough at the beginning of inhalation; over the 30-min inhalation period most subjects experienced dryness of the throat. Three subjects reported chest tightness at the end of the period. No symptoms were reported after inhalation of saline aerosol. Also, none of the subjects noted symptoms usually associated with ethanol ingestion.

Figure 1 shows the mean data MEF40%(P) and FEV₁ in six subjects after inhalation of ethanol or of saline, expressed as a percentage of the control values.

Saline aerosol caused no significant changes in flow rates. In contrast, the ethanol aerosol decreased flow rates on the PEFV as well as MEFV curves over the entire 4-hr period after inhalation. For MEF50%, these decreases (range: -10% to -16%) were statistically significant, in comparison with the corresponding post-saline data points (range: +2% to +11%), from time 0 to 30 min. For the more sensitive MEF40%(P), the decrease following ethanol inhalation ranged from -8% to -37%, and the difference between post-ethanol and post-saline data points were statistically significant up to 90 min after inhalation ($P < 0.05$). FEV₁ values did not change significantly, either after ethanol or saline aerosol (Fig. 1).

The acute changes in MEF40%(P) after ethanol inhalation following placebo or DSCG administration are shown in Fig. 2 for two atopic subjects and in Fig. 3, the mean relative changes for four non-atopic subjects. Pretreatment with DSCG considerably diminished the acute reductions of MEF40%(P) after ethanol aerosol inhalation.

Figure 4 shows the mean relative changes in MEF40%(P) in six subjects after

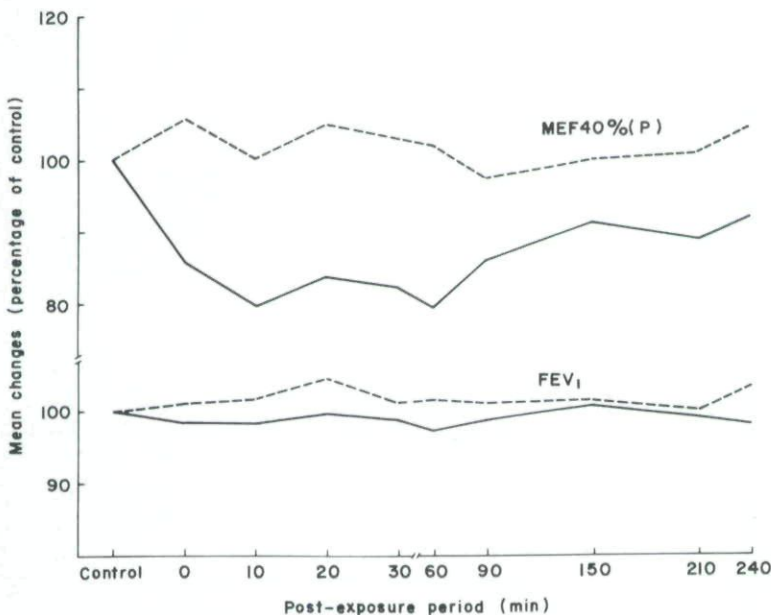


Fig. 1. The mean relative changes in MEF40%(P) and FEV₁ as percentage of controls in six subjects after 30-min inhalation of ethanol or normal saline. ---, saline; —, alcohol.

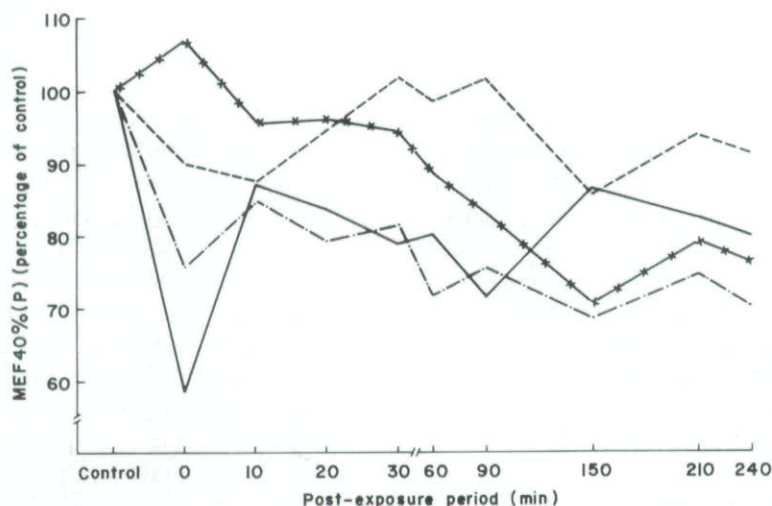


Fig. 2. The relative changes in MEF40%(P) as percentage of control in two atopic subjects after 30-min inhalation of ethanol following pretreatment with DSCG or a placebo for DSCG. Subject 1: —, placebo; ---, Intal. Subject 2: —, placebo; $\times$ — $\times$, Intal.

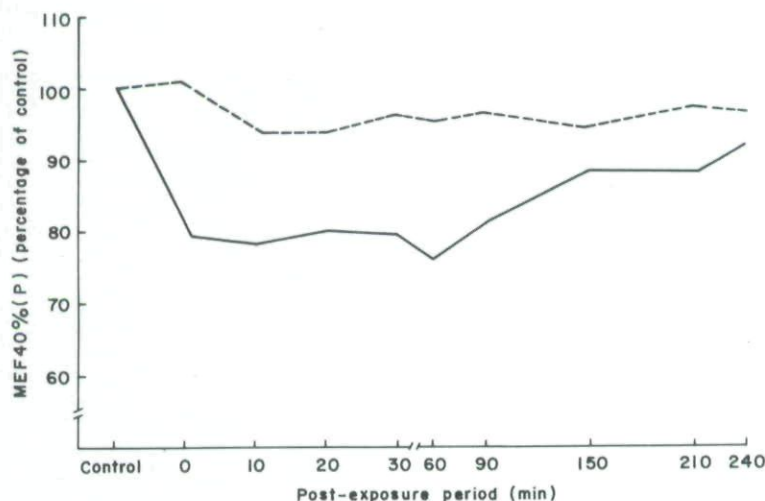


Fig. 3. The mean relative changes in MEF40%(P) as percentage of control in four non-atopic subjects after 30-min inhalation of ethanol following pretreatment with DSCG or a placebo. ---, Intal; —, placebo.

ethanol aerosol inhalation with and without pretreatment by atropine sulphate. There were no changes in acute reductions of flow rates when ethanol inhalation was administered to the subjects pretreated with atropine in comparison to that without atropine.

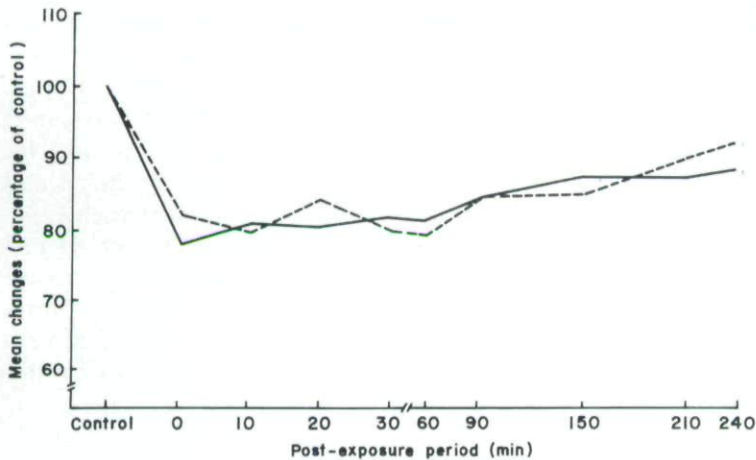


Fig. 4. The mean relative changes in MEF40%(P) as percentage of control in six subjects after 30-min inhalation of ethanol following pretreatment with atropine sulphate or with no medication. ---, atropine; —, alcohol.

Ethanol concentrations

The concentration of ethanol in inspired air varied between 0.18 and 0.20%. In expired air, ethanol concentrations at 5 min and at 30 min post-exposure in all subjects varied between 0.06 and 0.10%. Following pretreatment with DSCG, the concentrations of ethanol in the expired air were also from 0.6 to 0.10% after 5 min; however, after 30 min, the concentration was much smaller (less than 0.01%). Ethanol concentrations in expired air after pretreatment with placebo were similar to the ranges observed when no pretreatment had been given.

Discussion

Our results indicate that ethanol, administered locally to the airway mucosa by aerosol, consistently causes a decrease of airway calibre which is reflected in decreases of maximum expiratory flow rates on flow-volume curves, similar in magnitude to those observed after inhalation of other airway constrictor inhalants such as cigarette smoke (Žuškin, Mitchell & Bouhuys, 1974). This effect was inhibited but not completely prevented by prior inhalation of disodium cromoglycate. The effect of ethanol lasted about 90 min, after which maximum expiratory flows gradually returned towards control values. Since the inhalation of ethanol regularly induced cough in our subjects, a contribution of reflex bronchoconstriction (Simonsson, Jacobs & Nadel, 1967) to the initial decreases of flow rates cannot be excluded. However, no preventive effects obtained after administration of atropine sulphate indicates that cholinergic postganglionic pathway is probably not involved in airway narrowing caused by ethanol inhalation. In our previous study with hairspray (Žuškin & Bouhuys, 1974) 0.5 mg of atropine subcutaneously significantly prevented the acute reductions of flow rates after hairspray inhalation. The prolonged duration of the response and the effect of DSCG suggest that release of chemical mediators may play an additional role. Geppert & Boushey (1978) also favoured mediator release as the likely mechanism causing airway constriction after oral ethanol ingestion in a patient who regularly experienced asthma-like symptoms after ingestion of alcoholic bever-

ages but not under other circumstances. Recently Cohen *et al.* (1980) suggested that increased risk of airway obstruction in drinkers is probably the result of interaction with other factors associated with alcoholism rather than alcohol *per se*. In guinea-pig lung and bronchi, ethanol inhibits antigen-induced mediator release (Mongar & Schild, 1957; Fleisch *et al.*, 1976), but it remains possible that ethanol, like the histamine-releasing agent in textile dust (Nicholls, Nicholls & Boyhuys, 1966), releases mediators in human but not in guinea-pig lung tissue via a non-antigenic mechanism.

In our experiments, the airway constrictor responses were associated with ethanol concentrations in expired air (0.06–0.10%). Thus, the effect we observed may occur frequently even in social drinkers, although it may pass subjective notice. It seems possible but difficult to prove that this acute airway constrictor effect of alcohol contributes to the development of the often suspected high prevalence of chronic obstructive lung disease in alcoholics.

Acknowledgements

The authors would like to thank Mrs. Louise Hayes for assistance.

References

- BANNER, A.S. (1973) Pulmonary function in chronic alcoholism. *American Review of Respiratory Disease*, **108**, 851.
- BRESLIN, A.B.X., HENDRICK, D.J. & PEPYS, J. (1973) Effect of disodium cromoglycate on asthmatic reactions to alcoholic beverages. *Clinical Allergy*, **3**, 71.
- COHEN, B.H., CELENTANO, D.D., CHASE, G.A., DIAMOND, E.L., GRAVES, C.G., LEVY, D.A., MENKES, H.A., MEYER, M.B., PERMUTT, S. & TOCKMAN, M.S. (1980) Alcohol consumption and airway obstruction. *American Review of Respiratory Disease*, **121**, 205.
- EMIRGIL, C., SOBOL, B.J., HEYMANN, B. & SHIBUTANI, K. (1974) Pulmonary function in alcoholics. *American Journal of Medicine*, **57**, 69.
- FLEISCH, J.H., CALKINS, P.J., TROXELL, T.C. & HOOKER, C.S. (1976) Inhibition of antigen-induced mediator release from guinea-pig lung by alcohols. *American Review of Respiratory Disease*, **114**, 1107.
- GEPPERT, E.F. & BOUSHEY, H.A. (1978) An investigation of the mechanism of ethanol-induced bronchoconstriction. *American Review of Respiratory Disease*, **88**, 135.
- HEINEMANN, H.O. (1977) Alcohol and the lung: a brief review. *American Journal of Medicine*, **63**, 81.
- HERXHEIMER, H. & STRESEMANN, E. (1963) Ethanol and lung function in bronchial asthma. *Archives Internationales de Pharmacodynamie et de Therapie*, **144**, 310.
- JOHNSTONE, R.E. & REIER, C.E. (1973) Acute respiratory effects of ethanol in man. *Clinical Pharmacology and Therapeutics*, **14**, 501.
- MONGAR, J.L. & SCHILD, H.O. (1975) Inhibition of the anaphylactic reaction. *Journal of Physiology (London)*, **135**, 301.
- NICHOLLS, P.J., NICHOLLS, G.R. & BOYHUYS, A. (1966) Histamine release by compound 48/80 and textile dusts from lung tissue *in vitro*. In: *Inhaled Particles and Vapours II*, (ed C.N. Davies), pp. 69–74. Pergamon Press, London.
- ŠARIĆ, M., LUCIC-PALAIĆ, S. & HORTON, R.J.M. (1977) Chronic non-specific lung disease and alcohol consumption. *Environmental Research*, **14**, 14.
- SIMONSSON, B.G., JACOB, F.M. & NADEL, J.A. (1967) Role of autonomic nervous system and the cough reflex in the increased responsiveness of airways in patients with obstructive airway disease. *Journal of Clinical Investigation*, **46**, 1812.
- VIRGULTO, J. & BOUHUYS, A. (1973) Electronic circuits for recording of maximum expiratory flow-volume (MEFV) curves. *Journal of Applied Physiology*, **35**, 145.
- ŽUŠKIN, E., MITCHELL, C.A. & BOUHUYS, A. (1974) Interaction between effects of beta blockade and cigarette smoke on airways. *Journal of Applied Physiology*, **36**, 449.
- ŽUŠKIN, E. & BOUHUYS, A. (1974) Acute airway responses to hairspray preparations. *New England Journal of Medicine*, **290**, 660.

This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.