Inhalation of gaseous superoxide (GS) as adaptive oxidative training for asthma patients

N. Goldstein, G. Rothberg, T. Lewin, F.-R. Klefsch. Department of medical investigations, Goldberg & Lewin-Institute GmbH, Stahnsdorf, Germany, Rudolf Vorchom hospital, Humboldt University, Berlin, Germany

There is a direct correlation between the increased reactivity of the bronchial muscles and the endogenous oxidative stress (GS) suffered by the asthmatic. Two independent studies have been conducted into the influence of short-term intermitent GS inhalation on the reduction of OS and the improvement in the clinical picture of atopic asthmatics from different age groups. A total of 78 patients took part in the trials: 27 aged mean = 42 (Group A) and 51 aged mean = 12 (placebo-controlled double-blind trial in the case of Group B). In both groups there was a stable improvement in the spirometric parameters and clinical course in ca. 85% of cases. In Group A, a reduction of the initially high activity of superoxide dismutase and glutathione peroxidase (< 0.001) was observed, as well as an increase in activity of glutathione reductase in the erythrocytes (< 0.001) and an improvement in all major spirometric findings, including the results of the methacholine and salbutamol test. In Group B, a negative correlation between the initial values and the amount by which they changed was determined for PEF (r = 0.72; p < 0.0001), FEV1 (r = 0.52, p = 0.006), and PEF25% (r = 0.72, p = 0.001), as well as highly significant improvements in the scores with regard to subjective statements on frequency and severity of attacks, of coughing, and amount of sputum. The positive clinical findings arising out of this adjuvant therapy are being interpreted as the result of an adaptive course of training for asthma patients.

Epredione and its metabolites as antioxidants in the FeCl3-induced rats paw oedema

C. Mancini, M. Nicola, B. Lumachi. Research Center, Edmond Pharma, Milano, Italy

An in vivo test in rats based on the development of paw oedema due to the free radical inducer FeCl3 was set up to evaluate epredione and three metabolites (Met I, II and III) activity. Passoni et al. (1992) suggested that the test is a valuable tool to assay compounds with antioxidant activity, being glutathione (EEDO) 1100 mg/kg i.p., sodium selenite (0.5 mg/kg i.p.) and GSH-ethylater (610 mg/kg i.p.) well soluble. Its validity was also showed. The present study, set up like Passoni method in rats, proves that glutathione and sodium selenite give reproducible results (oedema inhibition 52% and 49.3%, respectively); moreover epredione at 600 mg/kg per os, and metabolites Met I, II, III (all at 600 mg/kg per os) significantly reduce the paw oedema development: 45.5% the former and between 19.7 and 50.7% the metabolites. These findings are related with those obtained by Pozzi in vitro assay (1990) to measure the inhibition of the NADPH-dependent lipid peroxidation in rat liver microsomes by the same metabolites and epredione. We conclude that epredione, inactive in vitro, shows its in vivo oedema test anti-oedematos effects through its metabolites. The weight of these findings concerns the epredione therapeutic indications in respiratory diseases in which free radicals are involved.

Effect of selective and non-selective phosphodiesterase inhibitors on allergen-induced contractions in passively sensitized human airways

S. C. M. Canning, M. Nicola, B. Lumachi. Research Center, Edmond Pharma, Milano, Italy

The non-selective phosphodiesterase (PDE) inhibitors theophylline (Theo) and 3-isobutyl-1-methylxanthine (BIMX) block allergen-induced constriction of human airways in vitro by a dual mechanism involving a direct relaxant effect on smooth muscle and inhibition of cysstein leukocinase release from airways [Morton, B.E. et al. Am J Respir Crit Care Med 1995; 151: A388]. To further determine the involvement of PDE isozymes we investigated the effect of the methylxanthine adenosine receptor antagonist 8-phenylxanthine (8-PX) and the selective PDE inhibitors moproton (Mop; type 3), Rp73401 (RP; type 4) and zardarvine (Zard; type 3/4) in addition to Theo and BIMX on allergen responses of human airways in vitro. Airways from 33 patients were sensitized overnight with IgE-rich serum (IgE levels > 600 U/ml) containing specific antibodies (FAST class > 3) against allergen (D. farinae). Contractile responses were assessed in the organ bath by standard techniques. Compared to sensitized controls, pretreatment with Theo, BIMX and Zard inhibited concentration-dependently the contractile responses to allergen, whereas 8-PX, Mop and RP had no significant inhibitory effect. The response to a submaximal allergen concentration (3 U/ml) was almost completely suppressed by concentrations of 1 mM Theo (94 ± 2% inhibition; n = 8), 100 μM BIMX (92 ± 8%; n = 5) and 3 μM Zard (99 ± 1%; n = 4); the concentration-effect curves were shifted to the right with a reduction of the maximal responses. We conclude that combined inhibitions of PDE3 and PDE4 is effective in suppressing allergen-induced contractions of sensitized human airways and that adenosine antagonism plays no role in the action of methylxanthines in inhibiting this response. Supported by SchlossWellcome, U.K. and Byeki Guldin, Germany.

Surveys of selected occupational groups

Health based selection for asthma, and not for chronic bronchitis, in pig farmers - A hypothesis

P.E. Vogelvang 1, J.W.I. van der Gulden 1, C.P. van Schayck 1, H. Polgarberg 2, 1Department of General Practice and Social Medicine, Netherlands, 2Department of Pulmonology Dekkerswald, University of Nijmegen, Netherlands

To study the mechanisms of respiratory disease in swine confinement farming, a questionnaire survey was performed among 239 pig farmers and 311 non-exposed controls. Pig farmers are exposed to a number of factors promoting the development of both chronic obstructive pulmonary disease and asthma. Still, in prevalence studies, only an elevated prevalence of chronic bronchitis, and not one of asthma, is reported. The prevalence of chronic bronchitis (phlegm on most days for 3 months during the last 2 years) was significantly higher in pig farmers than in controls (15.5 vs 3.9%, p < 0001), whereas self-reported asthma was not (5.9 vs 5.5%, p = 0.84). However, childhood atopy, defined by questions on hay fever, asthma, atopic bronchitis or eczema in childhood, was significantly less prevalent in pig farmers, than in controls (9.9 vs 17.2%, p < 0.05). As expected, childhood atopy was significantly associated with self-reported asthma (prevalence odds ratio 10.5, 95% confidence interval 4.8-22.9, adjusted for age and pack years of smoking). Therefore, a lower prevalence of asthma among pig farmers would be expected. It is probable that people suffering from signs of asthma at an early age avoid a career in confinement farming. This leaves a selected group of farmers, less susceptible to a development of asthma than the population at large. The factors in confinement farming promoting development of asthma subsequently lead to a prevalence of asthma just as high as in controls. This selection mechanism probably does not apply for the gradually developing symptoms of cough and phlegm in chronic bronchitis.

In conclusion we hypothesize a health based selection of profession for asthma, and not for chronic bronchitis, in pig farmers, obscuring associations between occupation and asthma.

Respiratory symptom and lung function changes occurring within 24 hours of re-exposure in British pig farm workers

J.P. Hancock, H. Sandhar, J.R. Beach, I.A. Calvert, I.M. Harrington. Institute of Occupational Health, Birmingham University, Birmingham, UK


Aims: To test the hypothesis that delayed reductions in expiratory flow rates would occur in pig farm workers (also exposed to endotoxins).

Methods: PEV1 and PEFR were recorded by spirometer in 28 pig farm workers after a weekend off work just before and at approximately 5, 10 and 24 hours after start of re-exposure (the Monday shift -07.00 to 17.00). Each worker retrospectively scored reported respiratory symptoms on a scale (0-10) for the 24 hour period before and after re-exposure.

Results: There was a progressive decline in both FEV1 (Fig. 1) and PEFR from pre-exposure values occurred 24 hours later for FEV1 (p = 0.0003) and PEFR (p = 0.02) representing 3.0% and 3.5% reductions respectively (paired t-test).

Discussion: Overall these findings are not clinically significant. However the small reductions of 3.0% in PEFR after re-exposure for any respiratory symptom (Wilcoxon test).

In conclusion we hypothesize a health based selection of profession for asthma, and not for chronic bronchitis, in pig farmers, obscuring associations between occupation and asthma.

No significant differences were seen between symptom scores before and after re-exposure for any respiratory symptom (Wilcoxon test).

Discussion: Overall these findings are not clinically significant. However the small reduction of 3.0% in PEFR after re-exposure for any respiratory symptom (Wilcoxon test).