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


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 intermittent 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 (glucose-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 (p < 0.001) was observed, as well as an increase in activity of glutathione reductase in the erythrocytes (p < 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.

Surveys of selected occupational groups

2050 Health based selection for asthma, and not for chronic bronchitis, in pig farmers - A hypothesis

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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 most 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 < 0.0001), 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 dermatitis 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.

2061 Respiratory symptom and lung function changes occurring within 24 hours of re-exposure in British pig farm workers

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

Methods: FEV1 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 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 start of re-exposure (mean decreases 0.020, 0.043, 0.119 litres and 1.26, 7.86 and 17.70 litres/min respectively). The only statistically significant difference from pre-exposure values occurred 24 hours later for PEV1 (p = 0.0003) and PEFR (p = 0.02) representing 3.0% and 3.5% reductions respectively (paired t-test).

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 percentual 3.0-3.5% fall in expiratory flow rates at 24 hours was qualitatively significant and not due to diurnal variation. These changes may represent delayed airways inflammation from re-exposure to endotoxin and contribute to the pathogenesis of chronic airways limitation that has recently been shown in longitudinal studies of pig farm workers (Reynolds SJ et al, Am J Ind Med 1996; 29:33-40).

The non-selective phosphodiesterase (PDE) inhibitors theophylline (Theo) and 3-isobutyl-1-methylxanthine (IBMX) block allergen-induced contraction of human airways in vitro by a dual mechanism involving a direct relaxant effect on smooth muscle and inhibition of cysteiny1 leukotriene release from airways [Morton, B.E. et al. Am J Resp Crit Care Med 1995; 151: A388]. To further determine the involvement of PDE isoenzymes we investigated the effect of the methylxanthines 8-phenyltheophylline (8-PT) and the selective PDE inhibitors motapizone (Mota; type 3), RP73401 (RP; type 4) and zardaverinc (Zard; type 3/4). Experiments were conducted in human airways from 33 patients who were sensitized overnight (D.farinae).

Contractile responses were assessed in the presence of Theo, TB MX and Zard inhibited concentration-dependently the contractile responses to allergen, whereas 8-PT, Mota 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 ± 10% inhibition). The results (oedema inhibition 52.1% and 49.3%, respectively); moreover erdosteine and three metabolites (Met C, Mancini, M. Nicola, B. Lumachi.

The PDE isoenzymes involved in the anti-SOD effects of Theo and the metabolic pathways leading to novel agents with antioxidant activity, being glutathione (ED50 1100 μM), sodium selenite (50 μM), and GSH-ethylster (610 μM) were also studied. The present study, set up like that as described in rats, proved that gluthathione and sodium selenite give reproducible results (oedema inhibition 52.1% and 49.3%, respectively); moreover endostestine at 600 μg/mg per os) significantly reduced the allergen development: 45.5% the farmer and between 19.7 ± 5.7% the metabolites. These findings are related with those obtained by Pozzi in vivo assay (1990) to measure the inhibition of the NADPH-dependent lipid peroxidation in rat liver microsomes by the same metabolites and endostestine. We conclude that endostestine, inactive in vitro, shows the in vivo oedema test anti-oedema effects through its metabolites. The weight of these findings concerns the endostestine therapeutic indications in respiratory diseases in which free radicals are involved.

2049 Effect of selective and non-selective phosphodiesterase inhibitors on allergen-induced contractions in passively sensitized human airways


The selective non-phosphodiesterase (PDE) inhibitors theophylline (Theo) and 3-isobutyl-1-methylxanthine (IBMX) block allergen-induced contraction of human airways in vitro by a dual mechanism involving a direct relaxant effect on smooth muscle and inhibition of cysteiny1 leukotriene release from airways [Morton, B.E. et al. Am J Resp Crit Care Med 1995; 151: A388]. To further determine the involvement of PDE isoenzymes we investigated the effect of the methylxanthines 8-phenyltheophylline (8-PT) and the selective PDE inhibitors motapizone (Mota; type 3), RP73401 (RP; type 4) and zardaverinc (Zard; type 3/4) in addition to Theo and IBMX on allergen responses of human airways in vitro. Airways from 33 patients were sensitized overnight with IgE-rich sera (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, IBMX and Zard inhibited contraction-dependently the contractile responses to allergen, whereas 8-PT, Mota 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 IBMX (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 OskarWellcome, U.K., and Byk Guldén, Germany.