P330

PDE inhibitors and the cough reflex

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Introduction: Phosphodiesterases (PDE) represent a group of 11 enzyme families with cAMP and cGMP hydrolyzing effect, leading to many pharmacological effects like bronchodilation, anti-inflammatory and immunomodulating action, etc. As both bronchoconstriction and inflammatory mediators can lead to stimulation of cough receptors, in this study, effects of non-selective PDE inhibitors (theophylline, theobromine) and selective inhibitors of PDE 1, 3, 4, 5 and 7 on the cough reflex were evaluated.

Methods: Inhalation of citric acid aerosol was used for cough provocation in healthy and ovalbumin-sensitized guinea pigs and number of cough efforts was registered after visual and acoustic control of skilled observer, with subsequent evaluation of airflow changes in double chamber whole body plethysmograph.

Results: Pre-treatment with theophylline and theobromine (10 mg/kg b.w. intraperitoneally) decreased number of cough efforts evoked by inhalation of citric acid aerosol (0.6 mol/l) in both healthy and ovalbumin-sensitized animals. Selective inhibitors (all 1 mg/kg b.w. intraperitoneally) of PDE1 (vinpocetin), PDE3 (cilostazol), and PDE4 (citalopram) showed antitussive effect in healthy guinea pigs. Contrary, the antitussive potential of PDE1 (vinpocetin), PDE4 (citalopram), and PDE5 (zaprinast) was observed in ovalbumin-sensitized animals.

Concluding this, administration of non-selective PDE inhibitors influenced the cough both in healthy and ovalbumin-sensitized animals, indicating the participation of bronchodilating action and suppression of airway hyperreactivity in cough suppression. From selective inhibitors, PDE4 inhibition seems to be the most effective in cough suppression, confirming its positive effects tested in chronic airway inflammatory diseases associated with bronchoconstriction and cough.

Supported by Grant VEGA No. 1/0030/11 and by project „Center of Experimental and Clinical Respirology II“, co-financed from EC sources.