THE INFLUENCE OF CRAC ION CHANNELS BLOCKER ON INFLAMMATION AND CILIARY BEAT FREQUENCY IN CONDITION OF EXPERIMENTALLY-INDUCED ALLERGIC ASTHMA.

M. Sutovska, M. Kocmalova, M. Joskova, I. Kazimierova, V. Sadlonova, M. Adamkov[1] and S. Franova

Department of Pharmacology, Jessenius Faculty of Medicine, Comenius University, Sklabinska street 26, 03601, Martin, Slovakia, sutovska@jfmed.uniba.sk; kocmalova@jfmed.uniba.sk

[1]Institute of Histology and Embryology, Jessenius Faculty of Medicine, Comenius University, Mala Hora 4, 03601, Martin, Slovakia

Introduction: Ca^{2+}release-activated Ca^{2+} channels (CRAC) identified in immune and airway smooth muscle (ASM) cells, mediate Ca^{2+} influx essentially important for almost cellular functions. Emerging evidence pointed to their involvement in allergic diseases. Furthermore, therapeutic potency of CRAC blocker was evidenced previously using experimental animal asthma model and was expressed as significant decrease of ASM hyperreactivity, antitussive and anti-inflammatory effects. Presented work analyzed anti-inflammatory effect, including impact on ciliary beat frequency (CBF), on long-term administration of CRAC blocker.

Material and methods: Allergic airways inflammation induced by repetitive exposure of guinea pigs to ovalbumine (during 21 days) was followed by long-term (14 days lasted) therapy by CRAC blocker (3-fluoropyridine-4-carboxylic acid, FPCA). The influence of long-term therapy on cytokine levels (IL-4, IL-5 and IL-13) both in plasma and in BALF, immunohistochemical staining (c-fos positivity) and CBF *in vitro* were used for analysis.

Results and conclusion: Decrease of cytokine levels and c-fos positivity confirmed anti-inflammatory effect of long-term administered FPCA. Cytokine levels in BALF and distribution of c-fos positivity suggested that FPCA was less effective to inflammatory cells but more potent inhibitor of respiratory epithelium secretory functions than budesonide. Tested and control drugs only insignificantly reduced CBF. All these findings supported therapeutic potency of CRAC blocker in treatment of respiratory diseases associated with airways allergic inflammation, e.g. asthma.

Acknowledgements: Presented work was supported by the project "Centre of Experimental and Clinical Respirology II" co-financed from EC sources, grants VEGA No. 1/0020/11, 1/0127/13, MZ No. 2012/35-UKMA-12 and APVV No. 0305-12.