MODULATION OF THE NON-ADRENERGIC, NON-CHOLINERGIC INHIBITORY SYSTEM BY ADENOSINE A_1 AND A_3 RECEPTORS IN THE GUINEA-PIG ISOLATED TRACHEA

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Background. Adenosine is able to affect the tone and reactivity of airways by modulating several cellular functions. Currently it is not known weather adenosine is able to regulate the activity of intrinsic inhibitory innervation in the airways. **Aims.** This study was aimed at evaluating the potential modulation exerted by the adenosine system, via A_1 and A_3 receptors, on the NANC inhibitory responses in the guinea-pig trachea. **Materials and methods.** The trachea of male guinea-pigs was removed, cleaned, deprived of epithelium, cannulated at each extremity and horizontally mounted in an organ bath containing Tyrode solution, maintained at 37 °C. The lumen of the isolated trachea was filled with the same solution and the intraluminal pressure variations were measured by means of a pressure transducer. The nerve-mediated inhibitory NANC responses to electrical field stimulation (EFS) at 3 Hz frequency were evaluated in the presence of hyoscine, piperoxan and propranolol. In order to evaluate both the amplitude and the duration of EFS-induced relaxations, the area under the curve (AUC) was measured as Pa · s. Contractions were measured as peak pressure minus baseline. Statistical analysis, was performed by analysis of variance. **Results.** NANC relaxations were significantly reduced in a concentration-dependent fashion after treatment with the A_1 agonist CCPA at concentrations from 100 nM up to 10 μM. However, the A_1 antagonist DPCPX (10 nM) did not prevent the effect of CCPA. DPCPX alone did also reduce EFS-induced relaxations. In the absence of stimulation, CCPA concentration-dependently contracted the preparations. This effect was antagonized by DPCPX, but was resistant to TTX, indicating the involvenment of muscular A_1 receptors. NANC relaxations were also reduced, though to a lesser extent, by the A_3 agonist, Cl-IB-MECA, in particular at concentrations of 1 and 3 μM. Pre-treatment with the A_3 antagonist MRS 1220 did not prevent the effect of the agonist. MRS 1220 alone did not affect EFS-induced relaxations. Cl-IB-MECA did not directly affect the tracheal tone in unstimulated preparations. **Conclusions.** The present data suggest that the adenosine system can affect airway responsiveness in the guinea-pig by modulating the NANC inhibitory response via A_1 and A_3 receptors. Due to the ineffectiveness of the antagonists, the specificity of this effect has not been fully defined. Based on our findings, the reduction of NANC inhibitory responses caused by endogenous adenosine acting at A_1 and A_3 receptors may contribute to the development of airway hyperresponsiveness in inflammatory conditions.