

EVIDENCE FOR A ROLE OF ADENOSINE A₁ RECEPTOR IN BRONCHIAL HYPERREACTIVITY OF SENSITIZED WISTAR RATS

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Adenosine biological functions are mediated by four distinct G protein -coupled receptors, named A₁, A_{2A}, A_{2B} and A₃. In airways, each adenosine receptor subtype is involved in physiological processes and in the pathogenesis of inflammation [1]. There is much evidence that adenosine plays a provocative role in bronchial asthma; however, the receptor(s) subtype involved is still unknown [2]. In the present study we have investigated on the role of adenosine A₁ receptor on bronchial reactivity in sensitized Wistar rats. Animals (male Wistar rats, 200-250g) were sensitized with ovalbumin (100 mg/kg ip. and 100 mg/kg sc.); starting from the 21st day after sensitization, rats were challenged with an aerosol of ovalbumin (2 ml; 5 mg/ml) or saline. 24 hours thereafter, animals were anesthetized with urethane (sol. 10 % w/v; 10 ml / kg ip.), artificially ventilated and connected to a bronchospasm transducer to evaluate bronchial reactivity to ovalbumin (1 mg/kg iv.), adenosine (3 mg/kg iv.) and carbachol (10 µg/kg iv.). The effect of the pre-treatment with the A₁ receptor antagonist, 1,3-dipropyl-8-cyclopentylxanthine (DPCPX; 100 µg/kg iv.; - 5 min.), on the bronchial response to spasmogen agents was also evaluated. From different groups of sensitized animals, challenged with an aerosol of ovalbumin or saline, main bronchi were removed and localization of adenosine receptors was evaluated by immunohistochemical analysis. In sensitized ovalbumin challenged rats, both ovalbumin and adenosine caused a bronchoconstriction that was significantly increased compared to the bronchoconstriction observed in sensitized rats challenged with saline and in naïve rats (ovalbumin, 43.88 ± 4.91 % vs. 10.00 ± 1.52 %, p<0.01 and vs. 16.78 ± 3.20, p<0.001; adenosine, 32.95 ± 5.23 % vs. 5.29 ± 1.80 %, p<0.01 and vs. 12.53 ± 2.90 %, p<0.01. Bonferroni, n = 15 - 20). Pre-treatment with DPCPX significantly reduced the bronchial response to ovalbumin and adenosine in sensitized aerosolized rats. In bronchial tissue of sensitized rats challenged with ovalbumin there was a strong A₁ adenosine receptor immunoreactivity. Our data indicate that A₁ adenosine receptor is involved in airway hyperreactivity of sensitized Wistar rats.

[1] Spicuzza L., Di Maria G. and Polosa R. (2006) Eur. J. Pharmacol. 533: 77-88.

[2] Keir S., Boswell-Smith V., Spina D. and Page C. (2006) Br. J. Pharmacol. 147: 720-8.