

Involvement Of Neuronal Pathways In A₁ Adenosine Receptor-mediated Airway Hyperresponsiveness In A Murine Model Of Allergic Asthma

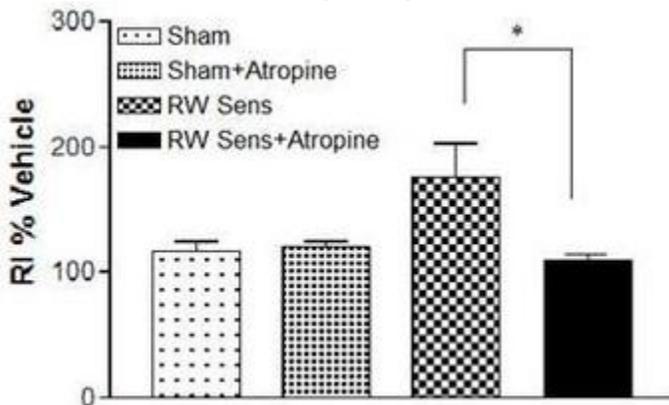
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Rationale: The ability of adenosine to induce airway hyperresponsiveness in asthmatic mice through its effect on four extra-cellular adenosine receptors is well documented. Specifically, the A₁ adenosine receptor has been shown to have a pro-inflammatory effect and to induce hyperresponsiveness in an allergic rabbit model of asthma (Nadeem, A, et al. 2006, Eur J Pharmacol, 551, 116-24). Recently, the A₁ adenosine receptor has been implicated in inducing airway hyperresponsiveness through neuronal pathways in naïve, non-allergic mice (Hua, X et al., 2007, Am J Physiol Lung Cell Mol Physiol., 293(1):L25-32). It remains unknown whether such a mechanism is involved in the allergic mouse model of asthma. **Methods:** In our study, C57 mice were sensitized to allergen by 200 ug injections of ragweed extract in alum on days 1 and 6 and challenged with 1% ragweed aerosol on days 11-13 of a two week allergen protocol (Fan, M, and Mustafa, SJ, 2002, Pulm Pharmacol Ther 15: 147-155.). On day 14, pulmonary resistance in response to aerosolized adenosine, 6 mg/ml was recorded with or without 20 µmol/kg atropine pretreatment. **Results:** Control animals received only alum injections and saline aerosol. Pretreatment with atropine significantly decreased ($p < 0.05$) the pulmonary response to adenosine in the sensitized and challenged mouse ($176 \pm 60\%$ of the response to vehicle in the untreated allergic mouse versus $110 \pm 10\%$ in the atropine treated allergic mouse, $n = 5-6$). **Conclusion:** These data indicate a cholinergic route for the activity of adenosine in allergic asthma, supporting a role for vagal neuronal pathways in this allergic mouse model of asthma.

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