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Defining the prostanoid component in mast cell-dependent constriction of isolated human small airways

Jesper Säfholm[1], Sven-Erik Dahlén[1], Mikael Adner[1]

[1] Experimentell astma- och allergiforskning, Karolinska Institutet

Introduction

Mast cell induced bronchoconstriction in asthma is triggered by allergens (IgE crosslinking). The relative role of prostaglandins (PGs) as mediators of the responses is debated and was therefore investigated in isolated human airways.

Methods

Human small airways (inner diameter of 0.5-2 mm) were isolated from macroscopically healthy human lung tissue specimens obtained from patients undergoing lobectomies (n=25). The segments were incubated overnight and mounted in tissue organ baths to measure smooth muscle contractions evoked by challenge with a monoclonal anti-human IgE antibody (anti-IgE) in presence or absence of pharmacologic inhibitors. The data are displayed as mean±SEM.

Results

In control segments, exposure to anti-IgE (5 µg/mL) caused a constriction (Emax:89±8%, n=11). Combined pre-treatment with the antagonists for H1 receptors (mepyramine; 1 µM) and CysLT1 receptors (montelukast; 1 µM) reduced the anti-IgE induced contraction by 52±6%, n=11. The residual component of the contraction was abolished by addition of the cyclooxygenase (COX)-1 enzyme inhibitor FR 122,047 (1 µM, n=6), but not by the COX-2 inhibitor etoricoxib (1 µM, n=10). The prostanoid-dependent contractile component was alternatively eliminated by either the thromboxane A synthase inhibitor ozagrel (10 µM, n=5) or the thromboxane TP receptor antagonist SQ-29,548 (1 µM, n=6).

Discussion

Mast cell dependent contractions of human bronchi are mediated by histamine, cysteinyl-leukotrienes and COX-1 generated contractile prostanoids acting on the TP receptor. In addition, the inhibitor data support that thromboxane A2 is the primary contractile prostanoid in human small airways.