Effects of Inhaled Brevetoxins in Allergic Airways: Toxin-Allergen Interactions and Pharmacologic Intervention

William M. Abraham,[1] Andrea J. Bourdelais,[2] Ashfaq Ahmed,[1] Irakli Serebriakov,[1] and Daniel G. Baden[2]

[1]Division of Pulmonary and Critical Care Medicine, University of Miami at Mount Sinai Medical Center, Miami Beach, Florida, USA; [2]Center for Marine Science, University of North Carolina at Wilmington, Wilmington, North Carolina, USA

Abstract

During a Florida red tide, brevetoxins produced by the dinoflagellate *Karenia brevis* become aerosolized and cause airway symptoms in humans, especially in those with pre-existing airway disease (e.g., asthma) . To understand these toxin-induced airway effects, we used sheep with airway hypersensitivity to *Ascaris suum* antigen as a surrogate for asthmatic patients and studied changes in pulmonary airflow resistance (R_L) after inhalation challenge with lysed cultures of *K. brevis* (crude brevetoxins) . Studies were done without and with clinically available drugs to determine which might prevent/reverse these effects. Crude brevetoxins (20 breaths at 100 pg/mL ; $n = 5$) increased R_L 128 ± 6% (mean ± SE) over baseline. This bronchoconstriction was significantly reduced (% inhibition) after pretreatment with the glucocorticosteroid budesonide (49%) , the β_2 adrenergic agent albuterol (71%) , the anticholinergic agent atropine (58%) , and the histamine H_1-antagonist diphenhydramine (47%) . The protection afforded by atropine and diphenhydramine suggests that both cholinergic (vagal) and H_1-mediated pathways contribute to the bronchoconstriction. The response to cutaneous toxin injection was also histamine mediated. Thus, the airway and skin data support the hypothesis that toxin activates mast cells *in vivo*. Albuterol given immediately after toxin challenge rapidly reversed the bronchoconstriction. Toxin inhalation increased airway kinins, and the response to inhaled toxin was enhanced after allergen challenge. Both factors could contribute to the increased sensitivity of asthmatic patients to toxin exposure. We conclude that *K. brevis* aerosols are potent airway constrictors. Clinically available drugs may be used to prevent or provide therapeutic relief for affected individuals. *Environ Health Perspect* 113: 632-637 (2005).