Microvascular blood flow in the airway mucosa modulates bronchoconstriction

Charles W. Emala, Sr.

Department of Anesthesiology, College of Physicians and Surgeons of Columbia University, New York, New York

IN THIS ISSUE of the Journal of Applied Physiology, Mazzone et al. (4) demonstrate the role of α-adrenergic control of airway vasculature tone, which in turn regulates the magnitude of airway smooth muscle response to bronchoconstrictive challenges. They demonstrate by intravital microscopy the α-adrenergic control of microvascular tone and subsequent effects on the magnitude of bronchoconstrictive challenges occurring by three routes: 1) direct topical application of ovalbumin, histamine, or capsaicin to the tracheal lumen; 2) intravenous neurokinin A. An elegant guinea pig model is employed where the distal trachea is cannulated to allow for ventilation of the animal and measurement of pulmonary inflation pressures while smooth muscle tone is measured in the proximal trachea while delivering bronchoconstrictive challenges to the tracheal mucosa. Whether these bronchoconstrictive challenges arise by inhalation, localized release, or delivery via the vasculature, vascular dilation reduces the magnitude of their effect presumably due to enhanced removal from the microenvironment of the airway smooth muscle. The authors did not attempt to determine if these α-adrenergic-mediated mechanisms were mediated by catecholamines originating from local nerves or from circulating sources, but the dense adrenergic innervation of these vessels demonstrated in the present study (4) suggest a local neuronal source.

Previous studies had suggested an important role of the vasculature in the magnitude and duration of bronchoconstriction. Bronchial blood flow was shown to effect the rate of recovery of bronchoconstriction induced by intravenous histamine in dogs (3) while pulmonary blood flow effected the rate of recovery of bronchoconstriction induced by inhaled or intravenous histamine but not intravenous acetylcholine or methacholine in dogs (2). Subsequent studies in sheep demonstrated that bronchial blood flow determined the rate of recovery of bronchoconstriction induced by intravenous methacholine (5) and manipulation of tracheal mucosal blood flow with vasopressin or nitroglycerin influenced the rate of recovery of bronchoconstriction induced by inhaled allergen (1). This latter study was important because it showed that either intratracheal (i.e., bronchial or pulmonary) blood flow or extratracheal tracheal submucosal blood flow could influence the duration of a bronchoconstrictive challenge. These earlier studies laid the foundation for the present investigation, which combined elegant in vivo/in situ measurements of airway smooth muscle contraction with intravital imaging of airway wall microvasculature and functional airway smooth muscle contraction studies in isolated guinea pig airway rings in organ baths.

A large volume of literature exists in the study of both in vitro and in vivo airway smooth muscle contraction with in vitro studies widely used as a model of in vivo effects. This study (4) identifies a precaution that must be taken with the interpretation of in vitro studies of airway smooth muscle constriction since vascular contributions to the delivery and clearance of bronchoconstrictive agents is lacking in isolated airway preparations studied in vitro, while as demonstrated, vascular tone is a key modulator of bronchoconstriction in vivo. The present study (4) was performed in guinea pigs so it is unknown if the findings can be extended to human bronchoconstriction. However, earlier studies demonstrating the influence of pulmonary and bronchial blood flow on the duration of bronchoconstriction in sheep and dogs (2, 3, 5) suggests that the understanding of the influence of vascular control on the delivery and clearance of bronchoconstrictive agents may be widely applied across species.

These findings demonstrate that the delivery and/or clearance of bronchoconstrictive agents by the airway microvasculature is a key determinant of the magnitude of bronchoconstriction. These findings require an expansion of the paradigm by which we consider bronchoconstrictive agents’ effects on airway smooth muscle.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

REFERENCES