Integrated autonomic control of the bronchial circulation and 3rd generation airway dimensions during exercise in awake sheep

D. McLeod,[1] R. Gunther,[2] P. Seah,[1] A.W. Quail,[1] D.B.F. Cottee,[1] G. Parsons[2] and S.W. White,[1] [1]University of Newcastle, and Cardiovascular Research Program, Hunter Medical Research Institute, Callaghan, NSW 2308, Australia and [2]Pulmonary and Critical Care Medicine, UC Davis, Davis, CA 95616, USA.

Background. The onset of strenuous exercise induces increases in parasympathetic cholinergic bronchovascular constrictor activity, and causes bronchoconstriction of the left main bronchus in concert with sympathetic adrenergic constriction of systemic vascular beds (Quail *et al.*, 2007). The aim of this study was to define changes in bronchial blood flow (Q_{br}) and 3rd generation airway dimensions during moderate exercise, and to analyse the role of vagal and sympathetic nerves.

Methods. Eight ewes (35-50 kg) underwent left thoracotomy during general anaesthesia (*i.e.*, i.v. propofol 5 mg•kg^{-1}, followed by inhaled 2.5-3.5% isoflurane in oxygen) and were instrumented with pulsed-Doppler flow probes mounted on the bronchial artery, and transit time, plus single crystal sonomicrometer transducers mounted on the 3rd generation lingular lobe bronchus. These measured continuously Q_{br}, bronchial hemi-circumference ($CIRC_{br}$) and wall thickness (WALL TH_{br}). Aortic pressure (P_a) and central venous pressure (P_v) catheters placed in the superficial cervical artery and vein. Sheep were recovered for at least seven days prior to experimentation. In Protocol 1 (P1), eight sheep ran duplicate protocols on a horizontal treadmill at constant speed of 2.2 mph for 2 min, 10 min recovery, for analysis of the effects of moderate exercise on changes in Q_{br} and airway dimensions. In P2, five sheep underwent moderate exercise both before (autonomic-intact, INT) and after α_1- α_2-adrenoceptor blockade (α-BL) with i.v. phentolamine. In P3, eight sheep underwent moderate exercise before and after β-adrenoceptor blockade (β-BL) with i.v. propranolol, and in P4, before and after cholinoceptor blockade (chol-BL) with i.v. methscopolamine.

Results. In P1, during moderate exercise P_a and heart rate (HR) rose significantly. $CIRC_{br}$ fell immediately to 96% ($p < 0.001$) of resting levels with the onset of exercise, and remained at similar levels throughout exercise, before returning to resting levels at the cessation of exercise. With exercise onset, WALL TH_{br} rose to 102% ($p < 0.05$) of resting levels, remained at this level throughout exercise, before returning to resting levels during recovery. Q_{br} and blood flow conductance (C_{br}) fell immediately with exercise to 91% and 84% ($p < 0.05$) of resting control levels, respectively. Q_{br} and C_{br} returned slowly towards resting levels during exercise, and fell again briefly in recovery to 84% ($p < 0.05$) and 80% ($p < 0.01$) respectively, before returning to pre-exercise levels in recovery. In P2, moderate exercise caused a fall in $CIRC_{br}$ and rise in WALL TH_{br} in both the INT and α-BL states. The fall in Q_{br} with exercise was seen in both the INT and α-BL states, but the immediate fall in C_{br} with exercise onset in the INT state was not seen with exercise following α-BL. In P3, the response of airway dimensions following β-BL was similar to the INT response to exercise. Following β-BL, there was a significant fall in Q_{br} and C_{br} at the onset of exercise, and at 2 min into exercise, the latter fall not seen during INT exercise. In P4, following chol-BL, the fall in $CIRC_{br}$ (to 98% of resting levels, $p < 0.01$) with exercise onset, was smaller than that seen during INT exercise (95%, $p < 0.001$). Also, $CIRC_{br}$ in the chol-BL state returned towards control levels at 1 min into exercise, whereas it remained below resting levels for the duration of INT exercise. Following chol-BL, the changes in WALL TH_{br} with exercise were similar to those seen during INT exercise. The fall in Q_{br} and C_{br} with moderate exercise was seen in both the chol-BL and INT states, but the brief post-exercise fall in C_{br}, present in the INT state, was no longer present in the chol-BL state.

Conclusions. With the onset of moderate exercise, the reduction in airway hemi-circumference and increase in bronchial wall thickness indicate a fall in cross-sectional area, and thus an increase in airflow resistance at the level of the third generation bronchus. This exercise-induced bronchoconstriction occurs concurrently with vasoconstriction of the bronchovascular bed. The primary autonomic effect responsible for lower airway constriction during exercise is mediated through cholinergic pathways. The primary autonomic effects responsible for bronchial vascular constriction during moderate exercise are mediated by integrated α-adrenergic and cholinergic pathways. During moderate exercise, differential CNS resetting of autonomic activity simultaneously increases: i) sympathetic excitability to airway blood vessels to cause a mild fall in bronchial blood flow conductance; and ii) parasympathetic, vagal excitability to the bronchial wall to cause airway constriction, and bronchovascular constriction to complement sympathetic vasoconstrictor effects.

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