Pulmonary Blood Flow Heterogeneity During Hypoxia Measured with ASL-FAIRER in Subjects with Prior High Altitude Pulmonary Edema (HAPE)

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Background

High pulmonary vascular pressures are important in the development of High Altitude Pulmonary Edema (HAPE), a potentially fatal disease. In the presence of hypoxia, pulmonary arterioles constrict (hypoxic pulmonary vasoconstriction, HPV). In the healthy individual, this serves to shunt blood away from poorly ventilated regions of lung. At high altitudes, all regions of the lung are exposed to hypoxia, and pulmonary arterial pressure rises. Uneven HPV has been proposed as an inciting mechanism in the development of HAPE, exposing parts of the pulmonary capillary bed to high pressure/flow, and stress-related vascular injury. We therefore hypothesized that subjects with a history of HAPE would demonstrate increased heterogeneity of pulmonary blood flow during hypoxia compared to subjects without a history of HAPE.

Methods

17 healthy subjects in 3 groups: (1) HAPE-S (history of HAPE, n = 5); (2) CON (repeated high altitude exposure without illness, n = 6); and (3) NOR (no history of altitude exposure, n = 6), underwent magnetic resonance imaging with arterial spin labeling (ASL) using a Vision 1.5 T whole-body magnet (Siemens Medical Systems, Erlangen, Germany). The specific sequence used, ASL-FAIRER, characterizes pulmonary blood flow distribution (resolution ~ 2 x 3 x 15 mm) by creating a magnetically tagged bolus using specialized radiofrequency pulses. Pairs of images, with/without spin tagging were obtained and subtracted to yield perfusion weighted image maps where signal intensity is directly proportional to blood flow. Data were collected from a single, posterior, coronal slice in triplicate at each time point, during normoxia and after 5, 10, 20 and 30 minutes of normobaric hypoxia (FIO_2 = 0.125, ~ 4500m equivalent altitude). Relative dispersion (RD, = standard deviation/mean), an index of blood flow heterogeneity was determined for all time points.

Results

Average arterial oxygen saturation (SpO_2) during hypoxia was not different between groups. The normoxic RD was not different between groups (0.94±0.05 HAPE-S; 0.94±0.05 CON; 0.87±0.06 NOR, means ± SE), however RD was increased during hypoxia in HAPE-S (to 1.10±0.05 after 30 min, $p<0.0001$) but not in CON (0.91±0.05) or NOR (0.87±0.05). At 20 and 30 min. of hypoxia, the RD relative to SpO_2 was significantly elevated in HAPE-S.

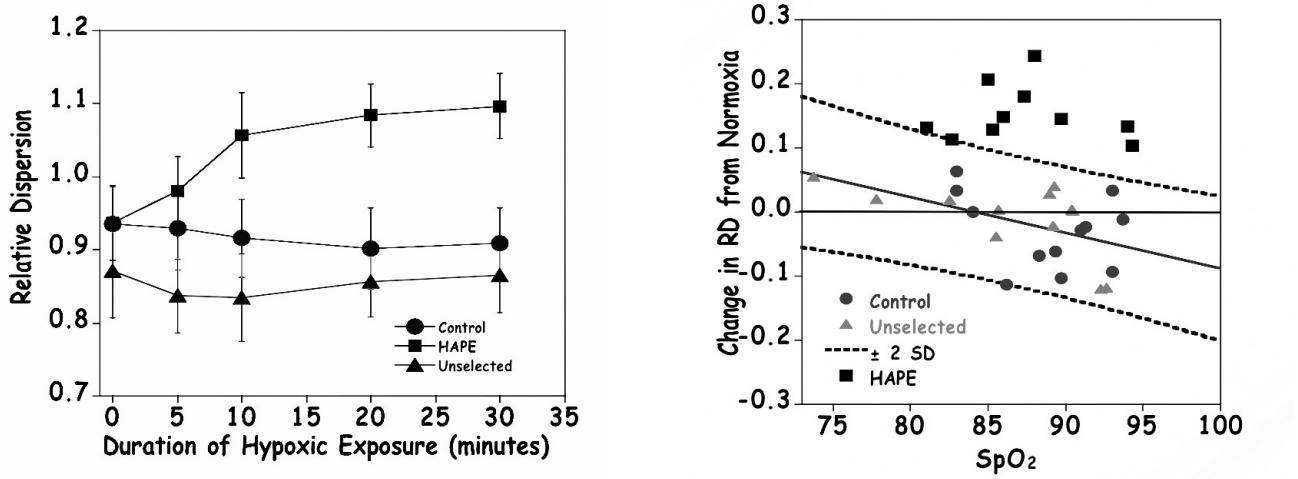

Figure 1. Pulmonary blood flow heterogeneity (RD) increases during hypoxia for subjects with past history of HAPE (HAPE-S) but not for control (CON) or unselected (NOR) subjects.

Figure 2. Change in RD from baseline as a function of SpO2 achieved. At all levels of hypoxia, HAPE-S subjects have a significant increase in RD (greater than 2 standard deviations above values for CON and NOR).

Conclusion

These results indicate that HAPE-S individuals have increased heterogeneity of pulmonary blood flow in response to hypoxia exposure compared to CON and NOR, likely resulting from uneven HPV. This supports the hypothesis that uneven HPV is an important mechanism in the development of HAPE.