Pediatrics

The Effect of Chronic Hypoxia on Airway Remodeling in Murine Model of Asthma

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Background: Chronic hypoxia during growth and development results in adaptive responses to increase oxygen transport to tissues, such as increasing lung volume and lung diffusion. Asthma is characterized by airway hyper-reactivity, which can result from increased airway smooth muscle (ASM) and airway remodeling following airway inflammation. Chronic hypoxia may attenuate airway inflammation, airway reactivity and airway remodeling in patients with asthma. Measured by in vivo airway resistance in response to 50 mg/ml Ach, our preliminary data suggests that rats conceived and raised under chronic hypoxic conditions (15% O2) exhibit lower airway reactivity, compared to room air controls (20% O2) at baseline (0.397, 0.789 respectively) and following Ova sensitization/challenge (0.696, 1.159 respectively). We hypothesized lower airway reactivity was associated with less ASM in response to hypoxic conditions.
Methods: Sprague Dawley rats were conceived, raised and evaluated in 4 groups: hypoxia/PBS challenge (HA-PBS); hypoxia/Ova challenge (HA-Ova); normoxia/PBS challenge (RA-PBS); normoxia/Ova challenge (RA-Ova). The lung tissue (4 animals/group) was fixed, sectioned, and ASM was quantified by immunohistochemistry using imageJ software.
Results: Measured ASM (mm2) from each group was log transformed to normalize data acquired from various lumen sizes and the least square means of each group were calculated. Airways from HA-PBS animals (N= 59) tended to have the lowest ASM, and ASM progressively increased in RA-PBS (N=41), HA-Ova (N=58) and RA-Ova groups (N=38 airways) [-6.41, -6.3, -6.26, -6.17]. There was an excellent correlation between ASM and airway resistance; more ASM was associated with greater airway reactivity (Pearson correlation of 0.99).
Conclusions: Chronic hypoxia may suppress ASM development, as well as suppress the increase in ASM associated with atopic inflammation. Understanding the mechanisms that inhibit ASM growth under conditions of chronic hypoxia may provide insight into new therapies for asthma.