Ventilation and Heterogeneity in Mild-to-Moderate and Severe Asthmatics Using Hyperpolarized ^{3}He MRI

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Introduction

Asthma is a chronic pulmonary inflammatory disease characterized by the hyperresponsiveness and heterogeneous constriction of the respiratory airways, which leads to inhomogeneous ventilation distribution in the lungs. Clinical diagnostic methods such as spirometry and multi-breath nitrogen washout methods provide global and indirect assessments of the status of airway constriction, but they fail to provide details on the location and severity of the individual lung. To investigate how bronchoconstriction severity and distribution affects lung function in asthma, we performed hyperpolarized (HP) ^{3}He MRI to image the ventilation heterogeneity response of mild-to-moderate and severe asthmatics, compared to healthy subjects at baseline, after bronchial challenge, after deep inspirations (DI) following challenge, and after Albuterol administration.

Methods

The HIPAA-compliant research protocol in this study was approved by the local Institutional Review Board. Informed consent was obtained from all recruited subjects. Data were obtained from 9 asthmatic (5 severe, 4 mild-to-moderate) and 6 healthy subjects. HP ^{3}He static ventilation MRI scans were performed with a Fast Gradient Echo pulse sequence acquiring coronal multislice images with the following parameters: 46 cm FOV, 0.75 PhaseFOV, 128×256 matrix, 13 mm slice thickness, TE/TR 1.2 ms/5 ms, and interleaved data acquisition. For each scan, 1 liter of an approximately 33% HP ^{3}He- 67% N_2 mixture was administered for the subject to inhale. HP ^{3}He MRI was performed before Methacholine challenge (preMch), after Mch (postMch), after deep inspirations (postDI), and after Albuterol administration (postAlb). The acquired images were rigidly coregistered, then processed to yield local fractional volume occupied by HP ^{3}He and local ventilation heterogeneity. The local heterogeneity for each pixel of the lung images was computed by calculating the pixel intensity coefficient-of-variation for a region of interest around each pixel.

Results and Discussion

Representative preMch, postMch, postDI, and postAlb images and the corresponding heterogeneity and ventilation maps from each of the 3 subject groups are presented in Figure 1.

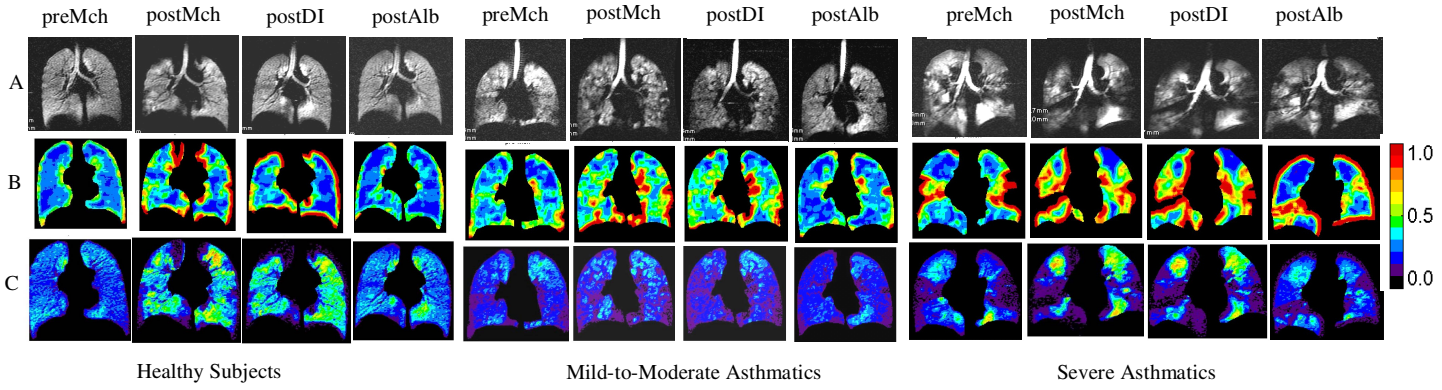

Figure 1. Row (A) Original HP ^{3}He images, row (B) corresponding heterogeneity maps, and row (C) corresponding ventilation maps, for preMch, postMch, postDI, and postAlb from a representative healthy subject, mild-to-moderate asthmatic, and severe asthmatic.

The quantitative ranges indicated by the color bars apply to both the heterogeneity and ventilation maps. At baseline, the HP ^{3}He MR ventilation images suggest fairly uniform homogeneous ventilation for healthy subjects. However, after the MCh challenge, the ventilation distributions clearly became more heterogeneous with some areas of very enhanced ventilation and some areas of ventilation deprivation. The heterogeneity maps also show widespread local variability in ventilation. After taking DI's, the healthy subjects are able to rehomogenize much of the ventilation. After Albuterol, the ventilation and heterogeneity recovers, and the images are visually very similar to those at baseline. For the asthmatic subjects, there are pre-existing elevations of ventilation heterogeneity as shown in the preMch images. After MCh challenge, similar to healthy subjects, ventilation distribution became more heterogeneous. Unlike the healthy subjects, DIs appeared to have little visual impact on ventilation distribution on the heterogeneity in the asthmatic lungs, however, they had a more of an effect on the mild-to-moderates than the severe asthmatics. Albuterol recovered the ventilation deprivation nearly to baseline. For each condition, we also calculated the heterogeneity score for the entire set of images. Mch challenge produced a ventilation heterogeneity score change from baseline that was largest in the healthy subjects, smaller in the mild-to-moderate asthmatics, and least in the severe asthmatics. The healthy subjects and mild-to-moderate asthmatics showed a recovery of the heterogeneity score following DIs, suggesting a bronchodilation effect, while the severe asthmatics had impaired bronchodilation. Albuterol was shown to reverse the induced heterogeneity from Mch in both healthy subjects and asthmatics. In separate experiments, when DIs were performed prior to Mch, in an effort to induce bronchoprotection by preventing the heterogeneity response to Mch, they were effective in healthy subjects, but less so in the asthmatics.

Conclusion

This study shows that HP ^{3}He MRI is effective for investigation of structure-function relationships between the lungs airways and alveolar regions, by depicting the ventilation distribution in both asthmatic and healthy subjects after induction of bronchoconstriction by Mch challenge and bronchodilation after a series of DIs or Albuterol. The response of the asthmatics to DIs suggests that airway remodeling may exist such that they are unable to bronchodilate in a manner similar to healthy subjects, to an extent that is dependent on the severity of the asthma.

Sponsors

NIH grants EB-001689 and HL62269