Semi-Quantitative Assessment Of Localized Pulmonary Inflammation By Magnetic Resonance Imaging In Patients With Mild Allergic Asthma Following Segmental Allergen Challenge

J. Vogel-Claussen¹, F. Schaumann², J. Renne¹, J. Hinrichs¹, C. Schoenfeld¹, M. Guterlet¹, K. Hüper¹, C. Winkler², C. Faulenbach², N. Krug², F. Wacker¹, J.M. Hohlfeld¹,²

¹Fraunhofer Institute for Toxicology and Experimental Medicine, Hannover, Germany; ²Hannover Medical School, Hannover, Germany

Introduction

Segmental challenge with allergen or endotoxin is a powerful tool to study mechanisms of airway inflammation and to test for efficacy of anti-inflammatory compounds. The assessment of airway inflammation by bronchoalveolar lavage (BAL) requires a bronchoscopy. Moreover, repetitive procedures to study inflammation over time are not possible. Non-invasive assessment of airway inflammation by magnetic resonance imaging (MRI) might add to the diagnostic armamentarium and might allow for sequential assessment of inflammation.

Objective

The aim of this study was to investigate whether locally induced airway inflammation can be detected by magnetic resonance imaging and whether the MRI information corresponds to cellular inflammation in BAL.

Methods

11 Patients with mild intermittent allergic asthma with positive responses to inhaled allergen (either grass mix or house dust mite) underwent segmental allergen challenges. After a baseline (B) BAL, four segments were instilled with either saline (S: right upper lobe), a low dose of allergen (LA: medial segment of the right middle lobe), or a high dose of allergen in two segments of contralateral lungs (HA: lateral segment of the right middle lobe and a lingular segment). MRI at 1.5T (Avanto, Siemens, Germany) was acquired 6 hours and 24 hours after segmental challenge using different sequences (TrueFISP, VIBE, T2-HASTE, and T2-TIRM).

Furthermore, bronchoscopy with BAL was performed in all challenged segments to assess cellular response at 24 hours. Inflammatory changes were scored (0=normal, 1=peribronchial edema or small infiltrate, 2=peribronchial edema and small infiltrate, 3=peribronchial edema and moderate infiltrate ± effusion, 4=peribronchial edema and severe infiltrate and effusion). The eosinophilic cellular response was transferred into an inflammatory score (0–3) using quartiles and correlated to MRI scores.

Results

Segmental challenge with allergen but not saline induced a dose-dependent eosinophilic inflammation. The number of eosinophils /ml recovered volume [mean±SEM, 10⁴/ml] was low at baseline (B: 0.0±0.0) and after saline instillation (S: 0.1±0.0) but increased with low dose allergen (3.2±1.2) and high dose allergen (12.4±5.5 and 11.4±3.1, respectively) at 24h. With MRI inflammatory changes were best detected with T2-TIRM at 6 hours where scores (mean±SEM) were B=0±0; S=0.1±0.1; LA=1.5±0.2; HA=2.4±0.2/2.6±0.2 (two segments). T2-TIRM at 6 hours (r=0.53, p<0.0001) and 24 hours (r=0.52, p<0.0001) were best-correlated with eosinophilia.

Conclusion

Proton-based MRI can detect locally induced airway inflammation, which correlates to the respective cellular response. MRI might be applied to study the anti-inflammatory effect of new drugs after segmental challenge with allergen or endotoxin.

Acknowledgements

Supported by Deutsche Forschungsgemeinschaft SFB587 (B8).

Contact

Prof. Dr. Jens Hohlfeld, Fraunhofer ITEM
Nikolai-Fuchs-Str.1, 30625 Hannover, Germany
jens.hohlfeld@item.fraunhofer.de