Effect and mechanism of Allergen Specific Immunotherapy (AIT) on small airway dysfunction in children with asthma

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Abstract

Background: Small airway dysfunction (SAD) is a common problem in childhood asthma patients despite of asthma control therapy. The effectiveness and mechanism of allergen specific immunotherapy(AIT) on small airway dysfunction in children with asthma remains unclear. The purpose of this study is to investigate the the effectiveness of AIT on SAD and mechanism underline with special focus on basophil. **Methods:** 65 mild to moderate asthma children under regular ICS treatment for more than one year, but their FEF $_{75}$ remained below the 65% of predicted and with positive results of serum Der p or der f were enrolled. Asthma children underwent house dust mite (HDM) subcutaneous immunotherapy (SCIT) treatment for 6 months. Asthma control and lung function were evaluated every three months during HDM SCIT treatment. Basophil activation test was carried out before and after HDM SCIT treatment. RNA-sequence were performed in isolated basophil from peripheral blood after 6 mionths of HDM SCIT treatment followed by GO term and KEGG pathway enrichment analysis between patients with or without HDM SCIT treatment. **Results:** The patients' childhood asthma control test(C-ACT) scores have risen above the baseline value after 3 and 6 months' treatment. The percentage of patients with complete asthma control was also increased from 52.4% to 75.8% (after 3 months of AIT treatment) and 73.7% (after 6 months of AIT treatment). Meanwhile, the percentage of uncontrolled asthmatic patients (C-ACT score¡20) dropped from 9.52% to 3 % and 0% after 3 and 6 months' treatment of AIT, respectively. AIT treatment also improved lung function parameters such as FEV $_1$/FVC, FEF $_{75}$, FEF $_{50}$ and MMEF after the first 3 months' therapy (p¡0.05). FEF $_{75}$ values showed a highly significant, gradual and persistent increase (from 49.55 $\pm$ 1.27% at baseline to 65.56 $\pm$ 2.89 % and 71.89 $\pm$ 2.64 % after 3 months' and 6months' therapy, respectively). 24 of 32 patients were out of SAD after 6 months' treatment. BAT results revealed that AIT treatment significantly reduced basophil activity to HDM in vitro challenge from baseline. GO term and KEGG pathway enrichment analysis of basophil revealed that downregulated genes mainly involved in immune cell activation, antigen presenting procedure and Th cell differentiation. **Conclusions:** Our current study demonstrated that HDM AIT not only improved asthma symptom and clinic parameters, but also increased lung fuction parameters, especially improved SAD measured by FEF $_{75}$, FEF $_{50}$ and MMEF. We also demonstrated that HDM AIT reduced basophil activity. RNA-sequence of basophil revealed the inhibiton of phagocytosis and phagosome pathway which is required for the APC function of basophils and therefore may affect the polarization of Th2 cell differentiation. However, further in vivo and animal study are required to confirm those results.

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