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Mechanisms of asthma and allergic inflammation

Characterization of the severe asthma phenotype by the National Heart, Lung, and Blood Institute's Severe Asthma Research Program

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Background

Severe asthma causes the majority of asthma morbidity. Understanding mechanisms that contribute to the development of severe disease is important.

Objective

The goal of the Severe Asthma Research Program is to identify and characterize subjects with severe asthma to understand pathophysiologic mechanisms in severe asthma.

Methods

We performed a comprehensive phenotypic characterization (questionnaires, atopy and pulmonary function testing, phlebotomy, exhaled nitric oxide) in subjectsÂ with severe and not severe asthma.

Results

A total of 438 subjects with asthma were studied (204 severe, 70 moderate, 164 mild). Severe subjects with asthma were older with longer disease duration ($P < .0001$), more daily symptoms, intense urgent health care utilization, sinusitis, and pneumonia (P â‰¤ .0001). Lung function was lower in severe asthma with marked bronchodilator reversibility ($P < .001$). The severe group had less atopy by skin tests ($P = .0007$), but blood eosinophils, IgE, and exhaled nitric oxide levels didÂ not differentiate disease severity. A reduced FEV_1, history of pneumonia, and fewer positive skin tests were risk factors for severe disease. Early disease onset (age < 12 years) in severe asthma was associated with longer disease duration ($P < .0001$) and more urgent health care, especially intensive care ($P = .002$). Later disease onset (age â‰¥ 12 years) was associated with lower lung function and sinopulmonary infections (P â‰¤ .02).

Conclusion

Severe asthma is characterized by abnormal lung function that is responsive to bronchodilators, a history of sinopulmonary infections, persistent symptoms, and increased health care utilization.

Clinical implications

Lung function abnormalities in severe asthma are reversible in most patients, and pneumonia is a risk factor for the development of severe disease.

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Key words

Severe asthma; definition; bronchodilator response; pathophysiology; phenotype; pneumonia

Abbreviations used

ATS, American Thoracic Society; ED, Emergency department; Fe_{NO}, Exhaled nitric oxide; FVC, Forced vital capacity; GERD, Gastroesophageal reflux disease; GINA, Global

Initiative for Asthma; HCU, Health care utilization; ICS, Inhaled corticosteroid; ICU, Intensive care unit; LABA, Long-acting Î²-agonist; NHLBI, National Heart, Lung, and Blood Institute; OCS, Oral corticosteroid; OR, Odds ratio; SABA, Short-acting Î²-agonist ; SARP, Severe Asthma Research Program

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