

Case report

Development of increased airway responsiveness in two nurses performing methacholine and histamine challenge tests

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Two nurses who frequently examined patients with methacholine or histamine challenge tests developed increased airway responsiveness and symptoms of asthma. It is important to use a good system for evacuating the test aerosol during challenge tests.

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Bronchial hyperresponsiveness is a characteristic feature of bronchial asthma. Inhalation challenge test with methacholine or histamine is commonly used to test the degree of airway responsiveness both in the clinical diagnosis of asthma and in research. The challenge test is performed by inhalation of increasing doses of methacholine or histamine.

In our department, challenge tests with methacholine or histamine have been performed according to the method described by Cockcroft et al. (3) and Juniper et al. (6). The method consists of continuous generation of the test aerosols and inhalation by tidal breathing. The test aerosol is generated by a Wright nebulizer with an output of 0.13 ml/min. With the nose clipped, the aerosol is inhaled by tidal breathing for 2 min through a mask held loosely over the mouth. Methacholine or histamine is inhaled in doubling concentrations from 0.03 mg/ml to 16 mg/ml, although higher concentrations can be used especially for methacholine. The concentration of methacholine or histamine that causes a fall in the forced expiratory volume in 1 s (FEV₁) by 20%, is expressed as a PC₂₀ value. A PC₂₀ value < 8 mg/ml is considered to indicate an increased airway responsiveness (3). By this method there is a leakage of the test aerosol into the air surrounding the patient. The nurses performing the challenge tests are thus exposed to the test aerosol unless there is a very ef-

fective evacuation of the air surrounding the patient, or if a closed circuit system is used.

In the present report, the development of increased airway responsiveness in two nurses who frequently over a period of more than 2 years examined patients with methacholine or histamine challenge tests is reported. During the work they were exposed to small concentrations of methacholine and histamine.

Case reports

Patient 1. A 30-year old previously healthy nurse (non-smoker) performed methacholine challenge tests several times a week for more than 2 years. She never performed challenge tests with allergens. She had no history of atopy, asthma or respiratory diseases. In 1986 she underwent a fiberoptic bronchoscopy with bronchoalveolar lavage and bronchial mucosal biopsy as healthy volunteer without complication. She then had a vital capacity (VC) of 4.0 l (100% of predicted normal value) and a FEV₁ of 2.9 l (87% of predicted normal value). A skin prick test with 8 common allergens was normal and she had a PC₂₀ value > 16 mg methacholine/ml. During the autumn and winter 1988 she felt tightness of the chest, and during exercise in cold air she got dyspnoea and cough with expectoration, but she had no fever or other signs of infection. A new methacholine

line test in December 1988 showed a PC_{20} value of 3.5 mg/ml. Her VC was 85% and her FEV_1 was 72% of predicted normal value. The skin prick test was still normal. She stopped performing challenge tests and improved, but still needed treatment with inhaled terbutaline to remain free from symptoms.

Patient 2. A 34-year-old nurse (non-smoker) without previous symptoms of atopy, asthma or other respiratory disease, performed methacholine and histamine challenge tests almost daily for more than 2 years. She never performed challenge tests with allergens. In April 1986 she had a FEV_1 of 3.5 l (110% of predicted normal value) and a PC_{20} value of 28 mg histaminechloride/ml. For long periods in 1988 she performed up to 5 tests a day, and during that period she experienced irritation in the airways and tightness of the chest. In December 1988 she caught a common cold with fever, cough and dyspnoea and expiratory ronchi. She was treated with terbutaline inhalations and budesonide inhalations 200/ μ g twice daily, but she was still dyspnoic during exercise. In February 1989 she had a FEV_1 of 2.85 l (90% of predicted normal value) and a PC_{20} of 6.5 mg/ml. Her skin prick test was negative, as in 1986. She changed work but her symptoms persisted and she needed oral steroids for some weeks to improve.

Discussion

Both patients developed an increased bronchial responsiveness and symptoms of bronchial asthma after long-term exposure to small concentrations of methacholine and histamine. Patient 2 developed exaggerated symptoms after a common cold but she had experienced symptoms during work with methacholine and histamine challenge testings even before that time. The mechanisms underlying the development of asthma in our patients are not known but it is tempting to suggest that repeated exposure to methacholine and histamine might be involved.

To our knowledge there are, so far, no reports that bronchial asthma can be induced by histamine or methacholine challenge tests. We have reported that a single histamine chloride challenge test can induce an increase in inflammatory cells in bronchoalveolar lavage fluid 24 h after inhalation of histamine in normals (11). Asthma has been associated with an inflammation in the airways (1, 4, 5, 8). Increased airway responsiveness has been reported after

allergen-induced late asthmatic reactions (2) and also after toluene diisocyanate exposure (9). There are studies indicating that the allergen-induced late asthmatic reaction is associated with airway inflammation (10). Repeated exposure to small concentrations of histamine and/or methacholine may induce an inflammatory response in the airways and thereby increase airway responsiveness.

It is important to use a good system for evacuating the aerosol escaping from the face mask during challenge tests when using the method described. Delivery of the aerosol into an inspiratory/expiratory valve box connected to a mouthpiece, instead of delivery into a face mask allows evacuation of the expiratory air. This method does not alter the response and should be recommended (7).

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