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Bronchoconstriction in response to ipratropium bromide

Ipratropium bromide is a new anticholinergic compound that is used increasingly to treat patients with limited airflow obstruction. Paradoxically, however, it may cause bronchoconstriction in occasional patients with atopic asthma.¹ It has been suggested that this bronchoconstrictor response may result from increased viscosity of sputum in the airways¹ or perhaps from altered bronchial reactivity to anticholinergic drugs in these patients.² We report on a patient with extrinsic bronchial asthma who responded adversely to inhaled ipratropium bromide. We challenged the patient with two concentrations of ipratropium bromide and compared the effects with those of inhaled isotonic saline, atropine methonitrate, and sodium bromide solution to investigate the mechanism concerned.

Case report

While participating in a pharmacological study a 34 year old woman with atopic asthma and eczema developed pronounced and prolonged bronchoconstriction after inhalation of ipratropium bromide nebuliser solution (1 g/l isotonic saline) given through a Wright nebuliser. Her asthma was well controlled with sodium cromoglycate 20 mg four times a day, and she used salbutamol aerosol 200 µg as required for symptomatic relief. All her drugs had been stopped 12 hours previously.

She was asked to attend on five afternoons after having stopped her drugs for at least 12 hours. Forced expiratory volume in one second was recorded with a water sealed spirometer (Godart Pulmotest). After a stable baseline reading had been obtained she was made to inhale ipratropium bromide (0.25 g/l or 1 g/l), atropine methonitrate (10 g/l), sodium bromide (0.25 g/l), or isotonic saline through a Wright nebuliser at tidal breathing for five minutes. Ipratropium bromide, atropine, and sodium bromide were all dissolved in isotonic saline, and treatments were carried out in a single blind fashion. Forced expiratory volume in one second was recorded at one, three, four, seven, 10, 15, 20, 25, and 30 minutes after inhalations. She developed severe bronchoconstriction after inhaling ipratropium bromide (at both concentrations) and sodium bromide; isotonic saline did not cause any change from the baseline value of forced expiratory volume in one second

(figure). Bronchodilatation occurred after inhalation of atropine methonitrate, the maximal increase in forced expiratory volume in one second being 33% at 20 minutes; this increase was still present at 30 minutes.

Percentage change in forced expiratory volume in one second after inhalation of ipratropium bromide, atropine methonitrate, sodium bromide, and saline.

Comment

This patient developed bronchoconstriction within a minute after inhaling ipratropium bromide, with an appreciable fall in the forced expiratory volume in one second. A similar response was observed after challenge with sodium bromide solution. In contrast, she showed bronchodilatation after inhaling atropine methonitrate. The bronchoconstrictor response to ipratropium bromide was unlikely to have been due to changes in sputum viscosity or an altered bronchial reactivity to inhaled anticholinergic drugs as she did not show a similar response to atropine. Furthermore, the drugs were dissolved in isotonic saline to avoid airways responses induced by hypotonic and hypertonic solutions.³ The bronchoconstriction was most probably related to an adverse reaction to bromide. It is difficult, however, to postulate whether bromide acts directly on the bronchial smooth muscle or the vagal receptors or causes non-specific degranulation of mast cells.

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