Bladder outflow obstruction induced by ipratropium bromide

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Summary: Three cases are described in which bladder outflow obstruction was produced by ipratropium bromide, a widely used anticholinergic bronchodilator which has been regarded as virtually free from systemic side effects. Many patients treated with ipratropium bromide are elderly males in whom prostatic hypertrophy is common and in these circumstances, large doses should be used with caution.

Introduction

Ipratropium bromide (Atrovent, Boehringer Ingelheim Ltd, Berkshire) is a quarternary isopropyl derivative of atropine which is widely used for its bronchodilator effect in patients with chronic airflow limitation. Systemic absorption following inhalation is limited¹ and it has been regarded as virtually free from side effects when administered by this route.² A review of the literature has revealed no published report of symptoms of urinary retention following treatment with ipratropium bromide. This report describes three such cases, one of whom developed symptoms as an outpatient.

Case reports

Case 1

A 70 year old man with a 10 year history of progressive breathlessness and wheeze was admitted to hospital for management of recently increasing dyspnoea. He had no history of urinary symptoms and had not previously been treated with ipratropium bromide. Initial assessment indicated an acute exacerbation of chronic airflow limitation. Both symptoms and lung function improved with nebulized ipratropium bromide 0.5 mg and salbutamol 5 mg five times daily, and oral prednisolone 30 mg daily. However, 10 days following admission he complained of poor urinary flow. Examination revealed a large palpable bladder and moderately enlarged prostate. A urinary catheter was inserted, and 1000 ml of urine drained. Treatment with ipratropium bromide was stopped and it was subsequently possible to remove the catheter. Nevertheless, he continued to have mild symptoms of

bladder outflow obstruction and transurethral prostatectomy was performed 4 weeks following admission. Histology demonstrated benign prostatic hypertrophy.

Case 2

A 71 year old man with chronic airflow limitation was admitted to hospital because of increasing dyspnoea for one week which had become significantly worse in the preceding 24 hours. He admitted to nocturia twice nightly for approximately 6 months but there was no history of poor stream, hesitancy, or retention of urine and he had not previously been treated with ipratropium bromide. Initial assessment suggested an infective exacerbation of his airflow limitation. His chest X-ray demonstrated a right sided pneumothorax which resolved following insertion of an intercostal tube with underwater drain seal. He was also treated with nebulized ipratropium bromide 0.5 mg and salbutamol 5 mg five times daily, intravenous hydrocortisone 200 mg four times daily, intravenous ampicillin 500 mg four times daily, and oral prednisolone initially 30 mg daily. Four days later he developed lower abdominal discomfort and was unable to pass urine. Examination revealed a large palpable bladder and moderately enlarged smooth prostate. A urinary catheter was inserted and 600 ml of urine drained. Treatment with ipratropium bromide was stopped and 3 days later the catheter was removed. He subsequently had no symptoms of bladder outflow obstruction.

Case 3

A 72 year old man with acromegaly and chronic airflow limitation was referred to the respiratory outpatient clinic for assessment of his dyspnoea and productive cough. He was receiving bromocriptine 30 mg and cyclopenthiiazide with potassium daily,

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verapamil 40 mg three times daily (for atrial and ventricular ectopic beats), dapsone 50 mg daily (for dermatitis herpetiformis), diazepam 2 mg three times daily, and carbocysteine capsules 375 mg three daily. In 1983 a tracheostomy had been performed for stridor secondary to laryngeal dysfunction thought to be due to his acromegaly. At the time of assessment he had frequency of micturition, nocturia, and slight difficulty in initiating micturition but a satisfactory stream. He was started on nebulized ipratropium bromide 0.5 mg three times daily as an outpatient. This produced some improvement in his dyspnoea but after approximately one week he developed marked hesitancy of micturition and a poor stream. He stopped the ipratropium bromide of his own initiative and his urinary symptoms improved to their pre-treatment state. Rectal examination revealed enlargement of his prostate.

Discussion

This report describes the development of urinary retention in three patients during treatment with ipratropium bromide administered by a nebulizer. It is unlikely that the development of urinary retention was coincidental with the administration of ipratropium bromide since in each patient bladder outflow obstruction occurred after starting treatment and symptoms improved on stopping it.

A dose of 40 µg three times daily for 3 days has been reported to have no effect on the flow and volume characteristics of micturition in middle aged and elderly patients with chronic bronchitis.³ However,

larger doses than this are increasingly used, and the data sheet for ipratropium bromide advises caution in patients with prostatic hypertrophy. Doses ranging from 40 µg four times daily from a metered dose inhaler to 250 µg four times daily of a nebulized solution were used in five patients reported to the Committee on Safety of Medicines following the development of urinary retention or increased symptoms of prostatism. Single dose-response studies in patients with chronic bronchitis and partially reversible airflow limitation indicate that increasing the dose of inhaled ipratropium bromide to greater than 125 µg (0.5 ml of Atrovent respirator solution) will not produce a substantial further improvement in maximal forced expiratory volume in one second although the duration of effect may be prolonged.^{4,5} Thus the dose of 0.5 mg five times daily which was used in the present cases and which is not infrequently used when the drug is administered by a nebulizer, may be unnecessarily large.

Ipratropium bromide is widely used for its bronchodilator effect in patients with chronic airflow limitation. Many of these patients are elderly males who may have prostatic hypertrophy even in the absence of urinary symptoms. In these circumstances, ipratropium bromide should be administered with caution, particularly in view of the trend to prescribe larger doses than previously.

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