Acute coronary syndrome secondary to paradoxical bronchospasm due to nebulized ipratropium bromide

Ramón Baeza-Trinidad and Jose-Daniel Mosquera-Lozano
Department of Internal Medicine, Hospital San Pedro (Logrono), Spain

Abstract
Ipratropium bromide is a muscarinic receptor antagonist used worldwide for management of chronic obstructive pulmonary disease (COPD) and acute asthma. It is considered a safe drug. Most common anticholinergic adverse effects are dry mouth, constipation and urinary retention. Cardiac and respiratory disorders are considered rare. We report a case of acute coronary syndrome secondary to its use.

Introduction
Ipratropium bromide is a short-acting nonselective muscarinic receptor antagonist used for bronchospasm and management of chronic obstructive pulmonary disease (COPD) and asthma [1,2]. The antagonistic action of ipratropium in the lungs leads to smooth muscle relaxation by inhibiting acetylcholine-induced reflexes facilitating entry of the air flow. It is poorly absorbed by the lung and gastrointestinal tract, so systemic adverse effects are rare [3]. Moreover, despite being acute myocardial infarction (AMI) more typical of beta agonist, ipratropium bromide can produce it by various mechanisms. We report a case of AMI secondary to paradoxical bronchospasm due to nebulized ipratropium bromide.

Case
Non-smoker 75 years old woman with hypertension, valvular heart disease with LVEF 45-55%, atrial fibrillation, obstructive sleep apnea-hypopnea syndrome (OSAHS), chronic bronchitis symptoms (the patient rejected spirometry) and morbid obesity (BMI 43) in treatment with domiciliary oxygen therapy to maintain an oxygen saturation of 88-90% (the patient did not tolerate non-invasive ventilation at home), carvedilol, digoxin, losartan, furosemide and acenocumarol was admitted to our hospital with dyspnea without chest pain in the context of heart failure (HF), chronic bronchitis and OHSAS decompensation. The clinical analysis showed a normal ultrasensitive T troponin (repeated 12 hours ago), pO2 of 76 mmHg with a pCO2 of 58 mmHg in blood gas analysis. Despite having no history of ischemic heart disease, an atrial fibrillation to 62 bpm with Q waves in leads DI and II of the electrocardiogram (ECC) was observed.

Discussion and conclusion
During the first administration of 2 ml of nebulized ipratropium bromide in relation to desaturation episode, the patient started with wheezings (that previously had not), tachypnea and subsequently central chest pain radiated to the neck and the right hemithorax and. The pain was relieved by stopping the nebulised ipratropium bromide and giving sublingual glyceryl trinitrate, being this last the possible cause of the improvement. The ECG showed a decrease of lateral ST (V4-V5) with atrial fibrillation and normal heart rate. The ultrasensitive T troponin concentration rose in 24 hours since the chest pain to 210 mg/l (normal <40 mg/l) being previously normal, so acute coronary syndrome was diagnosed. No catheterization was performed during admission. At hospital discharge, the values of cardiac damage markers were in normal range. Since then, the patient has remained at home without suffering similar episodes.

The reported patient illustrates an episode of AMI associated with ipratropium bromide in a patient with OSAHS ad chronic bronchitis in the presence of history of myocardial infarction (Q waves) and HF. This drug is used in episodes of decompensation in patients with OSAHS, COPD, and asthma, and given that our patient had clinical symptoms of chronic bronchitis (despite having no confirmatory spirometry of COPD) and OSAHS, we decided to use it in an episode of desaturation. Then, after starting nebulization as presented in the case, the patient developed worsening of general condition, tachypnea and generalized wheezing, symptoms of a possible bronchospasm.

The safety profiles of this drug comprise systemic anticholinergic events, including dry mouth, constipation and urinary retention, but cardiovascular events as cardiac disorders (supraventricular tachycardia and atrial fibrillation) and respiratory disorders (bronchospasms induced by the inhalation) are considered rare (1/10,000, <1/1000) [2,4]. Several factors may contribute to the increased of vascular risk associated with nebulized anticholinergics, such as the suppression of parasympathetic control of heart rate which is associated with an increased incidence of tachyarrhythmia [5], reduction in potassium concentrations [3] and a paradoxical bronchospasms induced by inhalation, as we expose in this case report, but the precise biological mechanism is uncertain [6]. According to the Naranjo Scale, we

Correspondence to: Ramón Baeza-Trinidad, Department of Internal Medicine, Hospital San Pedro (Logrono), Spain, Tel: 941 29 80 00; E-mail: rbaezat@riojasalud.es

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can establish the cause-effect association in the patient described as probable. There are publications that relate the use of beta adrenergics and AIM [7] but we did not found a case report which confirm this association with ipratropium bromide in literature. Therefore it would be interesting to carry out a deeper research since there are contradictory results among diverse publication [6,8].

This case shows us that, despite IAM considered an exceptional event, we must assess the risk-benefit of using ipratropium bromide in patients with cardiovascular risk.

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