



Case Report

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Aggravation of Seizure after Combined Nebulisation with Albuterol and Ipratropium Bromide



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Abstract

We present a case of a 65year old male patient who had been hospitalized for breathlessness (type II respiratory failure). He was treated with combined nebulisation of albuterol and ipratropium bromide. After 5 min of nebulisation he developed 2 episodes of generalized tonic clonic seizure (GTCS). It is suspected that there is a positive correlation between nebulisation with albuterol/ipratropium bromide combination and GTCS. Hence it is advisable that combination of albuterol and ipratropium should be avoided in patients of old age having medical history of seizures.

Keywords: Type II respiratory failure; GTCS, Albuterol; Ipratropium bromide

Abbreviations: (COPD): Chronic Obstructive Pulmonary Disease; (GTCS): Generalized Tonic Clonic Seizures; (RR): Respiratory Rate; (RICU): Respiratory Intensive Care Unit

Introduction

Chronic obstructive pulmonary disease (COPD) is a progressive airflow obstructive disorder which is mainly characterized by small airway disease (eg, obstructive bronchiolitis) and parenchymal destruction (emphysema) [1]. There are mainly two class of bronchodilators, i.e. β -2 adrenergic receptor agonists (eg, albuterol) and anticholinergic agents (eg, ipratropium) that are recommended as maintenance therapy for COPD. The inhalation of combined dosage form of ipratropium and albuterol has been shown to produce superior bronchodilation as compared to individual treatment of each class of drug [2]. Further, it is reported that combination of albuterol and ipratropium bromide nebulisation is used for quick relief of airflow obstruction and breathlessness [3]. This therapeutic regimen is most effective with fewer side effects. In our report, we present a case of generalized tonic clonic seizures (GTCS) due to combined nebulisation of albuterol and ipratropium bromide in a 65year old male patient who had been hospitalized for breathlessness issues.

Case Presentation

A 65year old male patient was having history of COPD with type II respiratory failure, seizure, stroke and breathlessness issues from last 6 years. He was hospitalized with severe

breathlessness which was aggravated in the last two days prior to reporting to the hospital emergency. He presented as conscious and oriented, having pulse rate 100/min, respiratory rate (RR) 22/min, blood pressure 130/80 mmHg, and normal blood oxygen saturation level (SpO₂) 95% at room temperature. He was nebulised with albuterol (2.5mg) and ipratropium bromide (125 μ g) for breathlessness (type II respiratory failure). However, after 5 min of nebulisation he developed 2 episodes of GTCS. In response to GTCS he was sifted to Respiratory Intensive Care Unit (RICU) and administered with loading dose of phenytoin 100mg TDS and intubated in emergency. Further, he was sedated with midazolam infusion 5mg/hr and put on volume control mode of ventilation. However, the patient had recurrent episode of seizure despite being on anti-seizure therapy.

During hospitalization period, following treatments were administered to the patient : tablet cefpodoxime-clavulanic acid 325mg BD, tablet losartan 50mg OD, tablet amlodipine 10mg OD, tablet phenytoin 100mg BD, tablet theophylline (controlled release) 400mg OD, tablet pantoprazole 40mg OD, tablet domperidone 10mg TDS, tablet prednisolone 15mg OD, nebulization with ipratropium 4 hourly, nebulization with budesonide 1mg BD, tablet moxonidine 0.2mg OD, capsule methylcobalamine OD, tablet citicoline BD, syrup potklor 3 t.s.f.

TDS. Also, after GTCS, patient was nebulised with budesonide 1mg BD and ipratropium bromide 125ug/4 hrs. During discharge from hospital, patient had following vitals: SpO₂ 95% at fraction of Inspired Oxygen 30%, pulse repetition frequency 140/min, RR 17/min, BP 139/93 mmHg. Patient was on respiratory tube feed. He was conscious but not oriented in time place or person. He was hemodynamically stable and pulmonary disease was also controlled. The patient was referred to neurological expert for abulia/aphasia management while his CECT showed no gross abnormality.

Discussion

COPD is a complex lung disease involving numerous pathophysiological mechanisms. Airflow limitation has long been identified as an important factor in this disease. Combination therapy is a common treatment strategy for managing the symptoms of patients with COPD. Combination of two bronchodilators with different mechanisms of action is more effective than either one alone [4]. Ipratropium and albuterol-combined in a single formulation, is widely used three to four times daily as maintenance therapy in COPD. This provides superior bronchodilation as compared to monotherapy with either drug [5]. This combination is considered to be safest therapy for COPD treatment and only some minor adverse effects have been reported till now. Recently, ZuWallack (2010), reported that with combined treatment of ipratropium bromide/albuterol inhalation, patients have common side effects such as headache, dizziness, nausea and hypertension that is related to albuterol [6]. Further, Lieberman (2004), reported the neurological adverse event related to anticholinergics are cerebral and include impaired concentration, confusion, attention deficit, and memory impairment [7].

However, in this report we have seen the aggravation of seizure after nebulisation of ipratropium and albuterol combination in patient having seizure history. This is the first report of such serious adverse effects in humans. However, there are a few preclinical studies (in vitro and in vivo) available to support our findings. Louis et al. (1982), suggested that deactivation of β_2 - receptors have anticonvulsant activity in PTZ-induced rat model of convulsion [8]. Further, Mueller et al. [9] suggested that β -receptor agonists are pro-convulsant and β -receptor activation may occasionally promote seizure activity. Lints et al. [10], suggested that propranolol attenuated all stages of seizure syndrome which indicates the involvement of β -receptors in induction of seizures [10]. Furthermore, Lupina et al. [11], suggested that concomitant treatment with β_2 -

adrenergic agonists together with aminophylline increase the risk of aminophylline-induced seizures.

Though there were no clinical data available to establish the involvement of albuterol in seizure induction but on the basis of available supporting preclinical studies we can suggest that albuterol may have a crucial role in aggravating seizure in patients of old age. No reports are available in literature which suggests the involvement of ipratropium in seizures. Hence, on the basis of our findings, we conclude caution should be exercised when administering combination of albuterol and ipratropium in old age patients with medical history of seizures.

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