

Successful Treatment of Severe Asthma Exacerbation with Sevoflurane Inhalation in the Intensive Care Unit

Case Report

Abstract

Inhaled anesthetics have known bronchodilator effects. Herein we report the case of a patient with a life threatening asthma exacerbation requiring prolonged intubation. His asthma was resistant to conventional measures, but eventually responded to sevoflurane inhalation. The mechanism of inhaled anesthetic bronchodilation and its potential role in therapy are discussed.

Keywords: Sevoflurane; Volatile anesthetics; Inhalation anesthetics; Status asthmaticus; Severe asthma exacerbation; Asthma; Intensive care unit

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Abbreviations: ABG: Arterial Blood Gas; WBC: White Blood Cell; ICU: Intensive Care Unit, ASM: Airway Smooth Muscle, ED: Emergency Department, SR: Sarcoplasmic Reticulum, VDCC: Voltage and Receptor Gated Channels, cAMP: Cyclic Adenosine Monophosphate, cGMP: Cyclic Guanine Monophosphate

Introduction

Bronchodilator properties of volatile anesthetics is well known in anesthesia practice and is utilized in the perioperative period in patients prone to bronchospasm [1]. Use of inhalation agents is uncommon in the intensive care unit. We describe a case of patient with severe asthma exacerbation requiring prolonged mechanical ventilation who was successfully treated with sevoflurane inhalation.

Case Presentation

A 32-year-old man with a history of moderate persistent asthma presented to emergency department with drowsiness, lethargy and marked dyspnea several hours after exposure to a known allergen-feline dander. Shortness of breath worsened rapidly over hours and was not relieved despite use of short and long acting beta agonists prior to arrival. He had a history of two prior episodes asthma exacerbations requiring intubation. On arrival, he was tachycardic, hypertensive (pulse 129/minute, blood pressure of 180/100 mm Hg.) and markedly tachypneic (respiratory rate of 40/minute). He was in respiratory distress using accessory muscles and was unable to speak in full sentence. He was noted to have diffuse wheezing with a prolonged expiratory time. His initial arterial blood gas analysis (ABG) showed pH of 6.9 with pCO₂ of 112 torr, pO₂ of 182 torr He had WBC count of 21.9 x 10³ per cubic milliliter and normal imaging studies including chest x ray. Volume control ventilator support was initiated after intubation and sedation with propofol. Empiric broad spectrum antibiotics were started. He was given methylprednisone in high dose. Inhaled albuterol was administered every hour and ipratropium every four hours.

On the second day, given lack of improvement in bronchospasm-Heliox with 70 % helium and 30 % oxygen gas were given with

each nebulization. On the third day, bronchial wash sample grew *Citrobacter*, *Koseri* and *Ceftazidime* was started due to sensitivity of the organisms. As there was no significant improvement, magnesium drip was started targeting a magnesium level between 2.5 mg/dL to 3.5 mg/dL. On the fourth day, an aminophyllin drip was added cautiously with monitoring for therapeutic levels and toxicity. Terbutaline injections were also started later on fourth day, because of persistent bronchospasm. He continued to be bronchospastic and failed spontaneous breathing trials.

On the fifth ICU day, as all the treatments were not effective, he was given a trial of sevoflurane inhalation. He was administered sevoflurane for two hours in the ICU. Anesthesia scavenging device was used along with regular suction equipment in ICU. His bronchospasm subsided and lung compliance improved markedly. He was extubated early in the recovery phase of anesthesia to prevent provocation of bronchospasm. Non-invasive positive pressure ventilation was administered for six hours subsequently. He had uneventful hospital course subsequently. Intensive asthma treatment was stopped after tapering. He was discharged after three days with tapering course of steroids and inhaler medications.

Discussion

Exacerbations of asthma are episodes of progressive increase in shortness of breath, cough, wheezing and/or chest tightness. For prehospital and emergency department (ED) treatment the Expert Panel (National Heart Lung and Blood Institute) recommends as initial treatments: oxygen for most patients, short acting beta 2 receptor agonist for all patients; adding multiple doses of ipratropium bromide for ED patients who have severe exacerbations (but ipratropium bromide is not recommended during hospitalization); and systemic corticosteroids for most patients [2]. The Expert Panel does not

recommend: methylxanthines, antibiotics (except as needed for comorbid conditions), aggressive hydration, chest physical therapy, mucolytics, or sedation.² The Expert Panel recommends that adjunct treatments such as magnesium sulfate or heliox may be considered to avoid intubation, but intubation should not be delayed once it is deemed necessary. Other adjunctive therapies to avoid intubation like intravenous beta2-agonists, intravenous leukotriene receptor antagonists and noninvasive ventilation have unproven role [2].

Sevoflurane leads to dilatation of distal airways and alveolar units, causing smaller amount of alveolar collapse and less distortion of the surrounding parenchyma resulting in a reduction in viscoelastic stress adaptation and inhomogeneity. These functional findings were supported by histological analysis [3]. Anesthetics cause bronchodilatation by reduction in intracellular calcium in airway smooth muscle (ASM) cells. Bronchoconstrictors, like acetylcholine and histamine causes calcium influx from sarcoplasmic reticulum (SR) stores and plasma membrane voltage and receptor gated channels (VDCC). Anesthetics are known to deplete SR stores by increasing Calcium "leakage" via calcium channels in smooth muscle-including ASM [4].

The effects of a variety of endogenous substances and bronchodilator drugs like B2 agonists are mediated via the cyclic adenosines like cyclic adenosine monophosphate (cAMP) and cyclic guanine monophosphate (cGMP). In ASM, Beta 2 agonists and nitric oxide donors inhibit the SR Ca²⁺ release response and Ca²⁺ influx via SOCE. Anesthetics and agents that elevate cyclic nucleotides act synergistically to almost completely inhibit SOCE, and this leads to a marked reduction of intracellular calcium. Sevoflurane synergize with cGMP and causes significantly greater SOCE inhibition. Although cGMP-elevating agents such as nitric oxide or nitrates are not commonly used clinically for bronchodilation, such interactions provide insight into potential alternative therapies in refractory airway hyper reactivity. cAMP and cGMP cross activate protein kinases A and G, resulting in common effects on smooth muscle [4].

Anesthetics are also known to inhibit muscarinic receptor activation. Inhalation agents also reduce airway smooth muscle tone by inhibition of acetylcholine release and by direct interference with intracellular contractile processes of ASM [5]. Hypoxia inhibits agonist-induced porcine tracheal smooth muscle contraction by a calcium independent mechanism mediated by protein kinase C and potentiates the inhibitory effect of volatile anesthetics on airway smooth muscle contraction. Treatment of asthmatic patients with excessive supplemental oxygen partially attenuates the inhibitory effect of volatile anesthetics on airway smooth muscle contractility [6].

The bronchodilator efficacy of various anesthetics after tracheal intubation in patients without asthma is greater for sevoflurane compared to halothane and isoflurane [7]. Sevoflurane has a relatively high rate of metabolic degradation and is also known to produce metabolites which are potentially nephrotoxic [5,6]. Nevertheless, its prolonged use is found to be safe in various case reports, including infants and pregnant women [8-12]. Sevoflurane has been shown to be quite useful in cases of difficult intubations like epiglottitis [13].

The main concerns with administering sevoflurane in the ICU are cost, monitoring and scavenging of the gas. With the use of various anesthesia conservative devices, most of the outgoing sevoflurane gas can be extracted by a filter and can be reused. Along with a closed anesthesia circuit, such devices markedly reduce the cost, the need of scavenging gas and the safety concerns for its use in the ICU [14]. Inhalation agents can be a very useful alternative to conventional sedative agents in mechanically ventilated bronchospastic patients [9]. Routine use of isoflurane with anesthesia conserving devices can be feasible and cost effective in ICU. Volatile agents may be potentially used as an ICU sedative in future in selected patients [15].

Our experience with use of Sevoflurane is unique because of its short duration. To our knowledge, this is the shortest duration of sevoflurane inhalation tried in the intensive care unit to relieve severe asthma exacerbation. With short duration of sevoflurane use, concerns of cost, scavenging and toxicity are minimal. Sevoflurane is potentially effective in breaking the vicious cycle of bronchospasm and bronchodilator inefficiency. Early use of sevoflurane in similar patients can reduce duration of mechanical ventilation, ICU stay and morbidity. Further research is warranted.

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