
Propofol-induced Bronchodilation In Patients With Status Asthmaticus

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Citation

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Abstract

Asthma is an inflammatory disease of the airways which results in bronchospasm and respiratory failure. Despite administration of inhaled beta-adrenergic agonists and anti-cholinergics and systemic glucocorticoids, many patients remain bronchospastic and require ventilatory support. These patients usually require sedation to decrease agitation and allow for safer ventilation. A short acting sedative with intrinsic bronchodilating actions would be ideal for these patients. We present case histories on two patients with status asthmaticus and respiratory failure managed with propofol sedation. Clinical examination and airway resistance measurements indicated that propofol produced bronchodilation in these patients. These and other data suggest that propofol is an excellent sedative for use in patients with bronchospastic disease.

INTRODUCTION

Asthma is an inflammatory disease of the airways that affects more than 15 million people in the United States (1). Severe bronchospasm due to asthma is a common cause for admission to intensive care units. Despite use of inhaled beta-adrenergic agonists, anticholinergics, and glucocorticoids (inhaled or intravenous), persistence of bronchospasm may lead to respiratory muscle fatigue and respiratory failure (2). Such patients are admitted to the intensive care unit and supported with mechanical ventilation until such time as their respiratory function improves. Bronchospastic patients receiving mechanical ventilation frequently require sedation to decrease agitation and allow for safer ventilation of the patient (ie. to minimize the risk of ventilator associated lung injury).

The most commonly used sedatives in critical care units in the United States are benzodiazepines. These agents do not have any intrinsic bronchodilator properties although they may decrease peak airway pressures through sedation effects. Many patients require high doses of benzodiazepines administered via continuous infusion in order to achieve adequate sedation. Prolonged effects from continuous sedation with benzodiazepines have been associated with an increase in complications and prolonged ventilator, ICU, and hospital stay (3, 4). Thus, a short acting sedative with intrinsic bronchodilating properties would be ideal for the

management of ventilation in patients with severe bronchospasm.

We report two patients with severe bronchospasm requiring ventilator support who were managed with propofol sedation (Propofol, Astra-Zeneca, Wilmington, Delaware). Clinical examination and measurement of airway resistances indicate that this sedative produced bronchodilation. We also review previous published information supporting a bronchodilatory role for propofol in the management of severe bronchospasm.

CASE REPORTS

Case 1: A 50 year old black female presented to the hospital with crampy abdominal pain, nausea, vomiting, and watery diarrhea which had been getting progressively worse over the prior week. She denied fever, chills, sweats, difficulty breathing, or upper respiratory symptoms. Past history was significant for insulin requiring diabetes mellitus, asthma controlled with inhaled short-acting beta-adrenergic receptor agonists as needed, and a previous hysterectomy. The patient had never been intubated for asthma. Her medications were insulin and the inhaled beta-adrenergic agonists. Physical examination revealed an afebrile obese black female complaining of abdominal pain. Blood pressure was 117/72 mmHg, heart rate 100 beats per minute, and respiratory rate 20 per minute. Physical examination was significant for a tender periumbilical hernia in the area of her previous

hysterectomy scar. Respirations were unlabored, lungs were clear to auscultation, and heart exam was normal except for tachycardia. The patient was felt to have a ventral hernia with entrapped bowel. She was taken to the operating room and the abdominal hernia was surgically repaired. The patient had no wheezing or respiratory problems noted intraoperatively. Post-operatively the patient was extubated and sent to the surgical ward. Upon arrival on the ward, she was noted to be in respiratory distress with diffuse inspiratory and expiratory wheezes. Her respiratory rate was 40-50 per minute. Tachypnea was associated with poor air movement, diffuse wheezing, and retractions. The patient was given repeated doses of albuterol by nebulizer, methylprednisolone 100 mg intravenously, and transferred to the medical ICU. Symptoms persisted for over two hours. An arterial blood gas revealed pH 7.15, pCO₂ 78 mmHg, and pO₂ 158 mmHg on 100% oxygen via face mask. The patient was intubated and supported with assist control mechanical ventilation. Propofol was begun and the rate titrated to sedate the patient so that she opened her eyes to painful stimuli (30-40 mg/hr). Within 2 hours, wheezing disappeared. Airway resistance assessed using peak and plateau pressures decreased (Table 1) (3). The patient was maintained on steroids and propofol for the next 8 hours at which time the propofol was discontinued, the patient allowed to awaken, and extubated. The patient received no additional bronchodilators until just prior to extubation. The patient was placed on maintenance steroids and an inhaled short-acting beta-agonist and transferred back to the surgical ward. The remainder of her hospital course was uncomplicated.

Figure 1

Table 1: Case 1 Airway Pressures (Assist Control, FIO₂ 0.5, Rate 10/min, Peak flow 70 L/min, PEEP 0 cm H₂O)

	Tidal Volume (mls)	Peak Pressure (mmHg)	Plateau Pressure (mmHg)	Airway Resistance (mmHg)
No Propofol	700	50	20	30
Propofol	700	33	22	11

Case 2: A 50 year old black female was admitted to the ICU for treatment of status asthmaticus. Past history was significant for severe asthma (requiring multiple hospital visits but not intubation). The patient presented to the emergency room obtunded but without focal neurologic deficits, wheezing, and with labored breathing. The remainder of her physical examination was within normal limits. There was no history of upper respiratory symptoms, cough, fever, chills, or sweats. The patient was treated in the

emergency room with inhaled albuterol via nebulizer, subcutaneous epinephrine, intravenous magnesium, and intravenous steroids. An arterial blood gas revealed a pH of 7.125, pCO₂ 126 mmHg, pO₂ 243 mmHg (FIO₂=1) and the patient was intubated. The patient was transferred to the medical ICU. An infusion of Propofol (30-40 mg/hr) was started along with inhaled albuterol and ipratropium and intravenous methylprednisolone (60 mg every 6 hours). Repeat examination three hours following ICU admission revealed no wheezing. The patient was heavily sedated to a Glasgow Coma Score of 3 (Ramsey sedation level of VI). Although the chest X-ray remained normal, attempts to wean the patient from the ventilator over the next few days were unsuccessful because each time the propofol infusion was discontinued or the rate decreased by 50%, the patient developed wheezing, air movement diminished, expiration was prolonged, and peak airway pressures increased despite continuation of inhaled bronchodilators. These clinical findings reversed with resumption of the previous dose of propofol. The values in Table 2 were obtained during one episode in which the propofol was discontinued (all other medications were unchanged). Following one week of treatment with intravenous methylprednisolone, inhaled albuterol and ipratropium, and propofol, the patient was weaned from the ventilator and discharged from the intensive care unit.

Figure 2

TABLE 2: Case 2 Airway Pressures (Assist Control, FIO₂=0.3, Rate 12/min, Peak flow 70 L/min, PEEP 0 cm H₂O)

	Tidal Volume (mls)	Peak Pressure (mmHg)	Plateau Pressure (mmHg)	Airway Resistance (mmHg)
No Propofol	700	78	53	25
Propofol	700	57	50	7
No Propofol	600	67	46	21
Propofol	600	50	44	6
No Propofol	500	55	35	20
Propofol	500	44	34	10

DISCUSSION

The treatment of severe bronchospasm consists of pharmacologic agents aimed at reducing inflammation and reversing or preventing airway obstruction, intubation and mechanical ventilation for respiratory failure, and measures to minimize complications of ventilatory support including lung injury and infections. Standard pharmacologic agents used to treat bronchospasm are inhaled beta-adrenergic agonists, inhaled anticholinergics, theophylline, and corticosteroids (2). However, despite these pharmacological

agents, many patients require mechanical ventilatory support (2). Sedation is invariably required in awake patients.

Despite the frequent use of sedatives in the ICU setting, little data is available from which to draw conclusions regarding agents or combinations of agents which are best to use in bronchospastic patients. A report from the expert panel of the National Asthma Education and Prevention Program (6) does not address the use of sedatives in the treatment of bronchospasm. Sedation is usually avoided in non-intubated patients due to concern that they may decrease ventilatory drive and result in intubation. However, studies on the use of sedation in the treatment of asthma are lacking. An ideal sedative agent would have a short half-life, not aggravate bronchospasm, possess intrinsic bronchodilating properties, and decrease inflammation.

Benzodiazepines remain the most common drugs used to manage patients on the ventilator with status asthmaticus. However, these agents have no direct bronchodilating properties and may accumulate in patients when administered by continuous infusion (especially when given for many days). Benzodiazepines do not have analgesic properties and frequently require co-administration with an opioid for analgesia. Despite use with opioids, many patients require paralyzing agents for ventilator management. Morphine is a sedative with analgesic properties. However, many clinicians avoid morphine due to its potential for histamine release and bronchospasm (2). Opioid induced vomiting and decreased gut motility are also undesirable effects. Ketamine possesses bronchodilating and sedative properties (7,8,9). However, ketamine effects are short lived, require frequent administration and the agent is associated with delirium-type reactions (10). Ketamine is also associated with sympathomimetic effects (ie. tachycardia, hypertension, myocardial ischemia) and lowering of the seizure threshold. In addition, ketamine increases laryngeal secretions and does not block pharyngeal and laryngeal reflexes. Ketamine is metabolized by the liver to norketamine, which possesses anesthetic properties and has a half-life of approximately 120 minutes. Hence, accumulation and prolonged sedation can occur with continuous therapy. For these reasons, ketamine is rarely used as the primary means of sedation in bronchospastic patients. Halothane is an inhalational anesthetic agent with bronchodilating properties. Administration of this agent is difficult in the ICU setting and requires use of an anesthesia machine. The drug is associated with hypotension and cardiac dysrhythmias. In addition, halothane sensitizes the heart to the

arrhythmogenic actions of beta-adrenergic agonists.

Propofol is a short acting intravenous sedative which possesses analgesic properties at high doses. It is easily administered in the ICU setting. The short half-life (minutes) of the drug allows easy titration to the level of anesthesia required to avoid paralysis. Propofol has anti-seizure properties (frequently used to treat status epilepticus) and blocks pharyngeal and laryngeal reflexes. The drug does not accumulate in patients with renal or hepatic disease and does not impair gut motility (facilitating enteral nutrition). The primary side effects are vasodilation and hypotension, which can usually be corrected with intravenous fluid administration. Hyperlipidemia may also occur.

Previous studies support a bronchodilating action for propofol. Although airway resistance was not measured, clinical case reports of propofol administration to patients with status asthmaticus (11) support a bronchodilating action. It has been reported to improve postoperative bronchospasm in two patients with COPD undergoing aortic valve surgery (12). Gasparetto and Conti (13) administered propofol or intralipid (the carrier for propofol) to patients with COPD during anesthesia and reported decreases in peak pressures, airway resistances, intrinsic positive end expiratory pressure, and dynamic compliance in the propofol group. Pizov et al (14) evaluated the effect of propofol versus barbiturates on wheezing following intubation (ie. during induction). Wheezing occurred in 45% of patients using a thiobarbiturate, 26% using an oxybarbiturate, and 0% using propofol. Hirota et al (15) evaluated the effect of propofol on airway diameter in dogs. Propofol increased airway diameter, an effect blocked by atropine. The authors concluded that propofol's bronchodilating actions were mediated via anticholinergic effects. Pedersen et al (16) evaluated the effect of propofol and ketamine on isolated guinea-pig tracheal preparations. Both agents produced tracheal relaxation and inhibited contractions induced by carbachol, histamine, prostaglandin F₂-alpha, and potassium.

There are rare reports of bronchospasm occurring in patients receiving propofol. To our knowledge, most episodes occurred during discontinuation of propofol. In addition, there have been a number of recent reports of propofol-induced bronchospasm occurring in patients receiving the sulfite containing propofol preparation rather than the EDTA containing propofol preparation. The sulfites may have induced bronchospasm.

In conclusion, we present two cases which demonstrate that propofol decreases airway resistance in patients with bronchospasm who require mechanical ventilation. Our experience to date with this agent suggests that it may be useful in the management of patients with severe bronchospasm. We believe that a prospective randomized clinical trial comparing propofol with benzodiazepines in the management of bronchospastic disease requiring mechanical ventilation is warranted.

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