

Intraoperative care of severe bronchospasm

J. Du¹, J. D. Tobias²

¹The Ohio State University College of Medicine, Columbus, Ohio, USA

²Department of Anesthesiology & Pain Medicine, Nationwide Children's Hospital and the Department of Anesthesiology & Pain Medicine, The Ohio State University College of Medicine, Columbus, Ohio, USA

Corresponding author: J. D. Tobias, Department of Anesthesiology & Pain Medicine, Nationwide Children's Hospital and the Department of Anesthesiology & Pain Medicine, The Ohio State University College of Medicine, Columbus, Ohio, USA. E-mail: Joseph.Tobias@Nationwidechildrens.org

Keypoints

1. The incidence of asthma is increasing and is a risk factor for intraoperative bronchospasm, a life-threatening event. A comprehensive preoperative evaluation with focused perioperative interventions is key to mitigating the risks of intraoperative bronchospasm.
2. Preoperative interventions to decrease the incidence of intraoperative bronchospasm may include the avoidance of second-hand tobacco smoke, ensuring that there are no acute infectious concerns, preoperative administration of aerosolized medications (β -adrenergic agonists and anticholinergic agents), and preoperative administration of a short course of oral corticosteroids.
3. Intraoperative care for patients at risk for bronchospasm incorporates the careful selection of induction agent, neuromuscular blocking agent, airway device, and agents for the maintenance agents including volatile anesthetic agents.
4. The algorithm for treating acute intraoperative bronchospasm should include deepening the level of anesthesia, the administration of β -adrenergic agonists via the respiratory route, and for refractory cases, the administration of intravenous epinephrine may be required. Additional treatment options include magnesium and ketamine by bolus and infusion.

Abstract

The incidence of asthma, a chronic inflammatory disease of the airway that increases the risk of intraoperative bronchospasm, is increasing and thus a higher number of asthmatic patients are presenting for anesthetic care. As intraoperative bronchospasm can be an acute life-threatening event, recognizing and mitigating risk factors as well as having a specific treatment algorithm in place may be helpful to facilitate safe care. We present a 3-year-old child who developed intraoperative bronchospasm. The differential diagnosis of intraoperative

wheezing is presented, risk factors for intraoperative bronchospasm reviewed, and a treatment algorithm proposed.

Keywords

asthma, bronchospasm, anesthesia.

Introduction

Asthma is a chronic inflammatory disease of the airway, characterized by recurrent episodes of wheezing. It is characterized by the accumulation of excessive inflammatory mediators such as eosinophils and leukotrienes that result in inflammation and exaggerated smooth-

muscle reactivity and constriction.¹ Clinical manifestations classically include intermittent and reversible airway obstruction with cough, shortness of breath, wheezing, bronchospasm, and chest tightness. Treatment is generally categorized into immediate acting or long-term control using bronchodilators, anti-inflammatory medications including corticosteroids, leukotriene modifiers, and other biologic agents.¹

There are 300 million persons in the world with asthma and a 6.7% prevalence in the United States.² Asthma is the most common chronic disease in children, and asthma exacerbations are a leading cause of pediatric hospitalization.³ As the incidence is increasing, a greater number of children with asthma present for anesthetic care.¹ Cancellation or postponement of surgical procedures may be warranted for patients who present with worsening upper respiratory infections, fever, wheezing, stridor, rales, or purulent nasal discharge.² Regardless of the clinical scenario, intraoperative bronchospasm remains an acute life-threatening adverse event so having a specific treatment algorithm in place may be helpful to facilitate safe care. We present a 3-year-old child who developed intraoperative bronchospasm. The differential diagnosis of intraoperative wheezing is presented, risk factors for intraoperative bronchospasm reviewed, and a treatment algorithm proposed.

Case reports

Review of this case and presentation in this format is in accordance with the guidelines of the Institutional Review Board of Nationwide Children's Hospital (Columbus, Ohio). The patient was a 3-year-old male who presented for a punch biopsy of the left thigh and left forearm, bilateral ear tube insertion, auditory brainstem response monitoring, and repair of a recurrent inguinal hernia. His past medical history was significant for macrocephaly, global developmental delay, gross motor delay, dysplastic corpus callosum, hypertonia, atopic dermatitis, spasticity, cleft lip cleft palate, hearing loss, and pyloric stenosis. Despite the associated abnormalities, there was no unifying diagnosis or syndrome established. During a

previous anesthetic, there was a history of a difficult intubation. Chronic medications included cetirizine (5 mg PO once daily), hydroxyzine HCL (15 mg PO before bed as needed for itching), and an epinephrine injection (0.15 as needed for severe allergic reaction). Physical examination revealed macrocephaly with a cleft lip and cleft palate. Cardiovascular and pulmonary examinations were normal. There was no wheezing or cough noted. The patient was held *nil per os* for 6 hours. Premedication included midazolam (6 mg PO). The patient was transported to the operating room and routine American Society of Anesthesiologists' monitors were placed. Following the inhalation induction of anesthesia with sevoflurane in air and oxygen, a peripheral intravenous catheter was placed. Dexmedetomidine (4 µg) was administered and a laryngeal mask airway (LMA) placed. Following LMA placement, bronchospasm was noted with diffuse inspiratory and expiratory wheezing. The inspired concentration of sevoflurane was increased to 8% in 100% oxygen. Given the previous history of a difficulty intubation, endotracheal intubation with fiberoptic bronchoscopy (FOB) was attempted through the LMA. Due to limited mouth opening and decreased range of motion of the neck, it was impossible to advance the FOB through the vocal cords. A second attempt was not made due to additional bronchospasm. Fentanyl citrate (10 µg intravenously) and glycopyrrolate (0.1 mg intravenously) were administered. As the surgical procedure started, wheezing persisted despite deepening the level of anesthesia (8% sevoflurane) and the administration of albuterol using a metered dose inhaler through the LMA. Multiple intravenous doses of epinephrine (5-10 µg) were administered with limited response. Due to persistent bronchospasm, the decision was made to cancel the herniorrhaphy and complete only the skin biopsy and myringotomy tube placement. Although there was continued bronchospasm, ventilation and oxygenation were maintained (end-tidal carbon dioxide 50-60 mmHg) and oxygen saturation 97-99%. Dexamethasone (8 mg) was administered intravenously along with additional doses of

epinephrine (10-30 µg) given with minimal improvement noted. An epinephrine infusion was started at 0.01 µg/kg/min during emergence from anesthesia along with multiple additional boluses doses of epinephrine (10-30 µg). A chest radiograph was obtained which was unremarkable. As bronchospasm continued, a magnesium bolus dose (50 mg/kg) was administered followed by an infusion at 20 mg/kg/hour. There was some increased air exchanged noted. The LMA was removed, the patient was transported to the post-anesthesia care unit (PACU), and an aerosol treatment with ipratropium and albuterol was administered. He was subsequently transferred to the PICU for ongoing monitoring of his respiratory and hemodynamic status. He remained stable on room air. The epinephrine infusion was slowly decreased over the ensuing 3-4 hours and then discontinued. The magnesium sulfate infusion was stopped later than day. No additional treatment was required for bronchospasm. The respiratory viral panel was negative. The remainder of his postoperative course was unremarkable and he was discharged home on postoperative day 1.

Discussion

Intraoperative bronchospasm presents as audible wheezing, increased work of breathing, a prolonged expiratory phase or increased peak airway pressure during positive pressure ventilation. A significant reduction in or absence of air flow may result in no audible wheezing. Bronchospasm may occur in patients with pre-existing conditions including asthma, prematurity, acute respiratory infections, pulmonary edema, and acute lung injury or as an acute event related to sudden airway reactivity in a patient with no associated comorbid conditions.^{4,5} Bronchospasm may also be a component of other acute life-threatening conditions including aspiration or anaphylaxis. Additionally, wheezing may be heard with displacement or misplacement of the endotracheal tube (mainstem intubation), mucus plugging, or obstruction of any component of the breathing circuit.

Care of the patient at risk for bronchospasm starts during the preoperative examination by identifying risk factors

and attempting to mitigate their impact on airway reactivity. Patients with a history of frequent prior asthma exacerbations especially those requiring ICU admission may be at higher risk for bronchospasm during intraoperative care. Specific anatomic abnormalities pose risks for intraoperative airway and respiratory complications including cleft lip or cleft palate.⁶ Preoperative interventions to consider include consideration of referral if needed to a pediatric pulmonary specialist, maximizing current chronic medication regimens including the use of inhaled corticosteroids, avoidance of second-hand tobacco smoke, ensuring that there are no acute infectious concerns, the preoperative administration of a short course of oral corticosteroids, and the administration of an inhaled β-adrenergic agonist and anticholinergic agent on the day of surgery (table 1).⁷⁻¹⁰

Parental and patient smoking cessation at least two months prior to anesthesia has been advised as tobacco smoke is a significant risk factor for perioperative bronchospasm, leading to increased respiratory complications and prolonged postoperative stays.⁸ Postoperative respiratory complications were reported in 8 of 96 patients with no exposure to second-hand smoke versus 44 of 156 patients exposed to second-hand smoke. Those exposed to second-hand smoke were 10-times more likely to develop laryngospasm after tracheal extubation. These effects were noted in patients exposed to as few as 10 cigarettes per day. Children exposed to second-hand smoke also have a higher incidence of bronchial reactivity, respiratory disorders, exacerbation of asthma symptoms, and respiratory complications after anesthesia.⁹ These effects are further exacerbated by active or recent upper respiratory tract infections. The presence of bronchitis, atopy, and viral upper respiratory tract infections have also been shown to significantly increase the risk of intraoperative bronchospasm.^{9,10}

Upper respiratory infections result in airway hyperreactivity that persists for several weeks following infections.¹¹ Children with active or recent URIs have been

shown to be 4-7 times more likely to have perioperative adverse respiratory events.¹²

Table 1. Perioperative care of the patient with asthma

1. **Preoperative interventions:**
 - a. Consultation with pediatric pulmonary or allergy specialist.
 - b. Maximize chronic medication regimens including inhaled corticosteroids.
 - c. Avoid second-hand tobacco smoke.
 - d. Ensure that there are no acute infectious concerns.
 - e. Short course of oral corticosteroids.
 - f. Inhaled β -adrenergic agonist (albuterol) and anticholinergic agent on the day of surgery (ipratropium).
2. **Intraoperative concerns:**
 - a. Intravenous induction may be superior to inhalation induction.
 - b. Intravenous induction agent: propofol or ketamine.
 - c. Choice of airway: laryngeal mask airway preferred over endotracheal tube.
 - d. Prevention of bronchospasm with the administration of glycopyrrolate, lidocaine, and dexamethasone after induction.
 - e. Maintenance anesthesia: sevoflurane preferred over desflurane.
 - f. Neuromuscular blocking agent: vecuronium or cis-atracurium may be preferred over rocuronium.
 - g. Avoid medications that cause histamine release such as morphine.
 - h. Theoretical concerns suggest avoidance of non-steroidal anti-inflammatory agents.
3. **Intraoperative treatment of bronchospasm**
 - i. Manual ventilation with 100% oxygen.
 - ii. Auscultation to ensure bilateral breath sounds.
 - iii. Cessation of surgical or airway stimulation.
 - iv. Chest radiograph if indicated.
 - v. Identification of potential anaphylactoid reactions.
 - vi. Inhaled albuterol delivered via metered-dose inhaler.
 - vii. Deepening the level of inhalational anesthesia.
 - viii. Intravenous epinephrine, bolus (1-2 μ g/kg) and infusion.
 - ix. Magnesium: bolus and infusion.
 - x. Ketamine: bolus and infusion.
 - xi. Corticosteroids (if not administered previously).
4. **Postoperative treatment of bronchospasm**
 - i. Consider assisted ventilation (BiPAP) for respiratory failure.
 - ii. Auscultation to ensure bilateral breath sounds.
 - iii. Chest radiograph if indicated.
 - iv. Inhaled albuterol delivered via high flow nebulization – consider continuous administration for severe bronchospasm.
 - v. Corticosteroids (if not administered previously).
 - vi. Magnesium: bolus and infusion.
 - vii. Ketamine: bolus and infusion.
 - viii. Intravenous β -adrenergic agonist (terbutaline).

Airway reactivity in response to provocative agents such as cold hair, histamine, or aerosolized citric acid is increased by associated URIs.¹¹ Pre-synaptic muscarinic receptors (M₂) on vagal nerve endings that release acetylcholine are hypothesized to be inhibited by viral neuraminidases in the infected individual, thereby decreasing the affinity of the M₂ receptors for acetylcholine. This results in a decrease in the normal negative feedback loop of these receptors which act to block ongoing acetylcholine release in the normal, uninfected state. This results in exaggerated acetylcholine release, facilitation of the cholinergic pathway, and increased airway responsiveness.¹¹ Despite these concerns, universal cancellation of elective surgeries due to URIs is not practical and thus the decision to postpone or cancel surgeries requires a balance of risk and benefit. Cancellation is dependent not only on the severity and course of the infection, but also

the duration and complexity of the surgical procedure. Children with severe symptoms including mucopurulent secretions, productive cough, fever >38 °C, lethargy, or signs of pulmonary involvement should have elective surgeries postponed. Procedures can generally proceed in afebrile and otherwise healthy appearing children presenting with an uncomplicated URI with clear secretions.¹¹

A short course of oral corticosteroids is a useful preoperative adjunct to decrease perioperative complications in patients with a history of asthma. While chronic therapy for patients with asthma frequently uses inhaled corticosteroids to limit the systemic effects of long-term use, there is limited evidence-based medicine comparing a short course of oral versus inhaled corticosteroids prior to a surgical procedure. Given that most regimens advocated a 5-7 day course, this should limit concerns regarding adverse effects of more prolonged administration.^{13,14} Various regimens have been shown to be effective in improving lung function and lowering the incidence of operation-induced asthma attacks and post-intubation bronchospasm in adult patients, including oral prednisolone or intravenous methylprednisolone.^{2,14,15} The latter can be administered the day of the surgery with a two dose regimen, one preoperatively and one postoperatively. Pediatric dosing regimens have included oral prednisone (1 mg/kg/day, maximum 60 mg) for 3-5 days before surgery, two day course of oral dexamethasone (0.6 mg/kg, maximum 16 mg) once a day, or a single dose of oral methylprednisolone (1 mg/kg) 48 hours before surgery.¹⁰ Systemic corticosteroids enhance the function of the β -adrenergic receptors and M₂ receptors and act synergistically in combination with inhaled β -adrenergic agonists and anticholinergic agents.¹⁶ Additionally, the preoperative administration of inhaled β -adrenergic agonists (albuterol) 1-2 hours before surgery has been shown to prevent perioperative bronchospasm including airway reactivity following endotracheal intubation.¹⁰ The addition of an inhaled anticholinergic agent preoperatively may add further benefit

through their effect on airway muscarinic cholinergic receptors.⁵ Combined nebulized ipratropium bromide and a nebulized β_2 -adrenergic agonist results in greater bronchodilation than a β_2 -adrenergic agonist alone and may be useful in treating bronchospasm or in treating those with a poor initial response to β_2 -adrenergic agonist alone.⁵ These agents may be particularly effective in patients with viral-induced airway reactivity as the mediation of these effects is through enhanced cholinergic transmission due to dysfunction of the M₂ receptor. In our practice, for patients who routinely use a β_2 -adrenergic agonist and/or anticholinergic agent, we ask parents to administer these the evening before and the day of surgery. Alternatively, these can be administered preoperatively prior to transport to the operating room.

Intraoperative care to consider with patients at risk for perioperative respiratory adverse events include the method of anesthetic induction (intravenous versus inhalational), choice of induction and maintenance agent(s), and the airway device used. In patients with at least two risk factors for perioperative respiratory adverse events (PRAEs), intravenous induction with propofol has been shown to limit the incidence of PRAES when compared to inhalational induction sevoflurane with nitrous oxide.¹⁷ Propofol suppresses the laryngeal reflex and blunts the reflex bronchoconstriction that occurs following mechanical stimulation of the airway. This effects appears to be greater with propofol than the inhalational anesthetic agents.

When choosing an intravenous induction agent, propofol has been shown to be superior to thiopental, thiamylal or methohexital.¹⁸ Likewise, respiratory resistance after tracheal intubation was reported to be lower following a single induction dose of intravenous propofol compared to thiopental or etomidate.¹⁹ Although recent clinical trials have demonstrated the potential efficacy of propofol, the time-honored agent for the induction of anesthesia in patients with asthma remains ketamine. Through the release of the endogenous catecholamines, epinephrine and norepinephrine, ketamine has been shown to effectively

prevent or treat bronchospasm.^{20,21} Both propofol and ketamine protect against airway bronchoconstriction in response to tracheal intubation, decrease the incidence of wheezing in asthmatic patients, and relieve bronchospasm in patients with hyperreactive airway disease.^{18,20} In animal models, propofol and ketamine also produce local bronchoprotective effects by diminishing vagally induced airway constriction.²⁰

All of the inhalational anesthetic agents act as bronchodilators by a variety of mechanisms including direct and indirect actions on airway smooth muscle. Volatile anesthetic agents relax airway smooth muscle through various mechanisms that reduce intracellular free calcium, including inhibition of protein kinase C, calcium release from sarcoplasmic reticulum, and voltage-dependent calcium channels.²²⁻²⁴ Although these direct effects are equally shared by all of the volatile anesthetic agents, the direct irritant effects of desflurane counteract its bronchodilatory properties, provoking airway and bronchial constriction.^{25,26}

Other decisions that may impact the incidence of intraoperative bronchospasm include the choice of device for airway management and whether or not a neuromuscular blocking agent (NMBA) is used to facilitate endotracheal intubation. A greater incidence of bronchospasm has been reported with the use of an endotracheal tube (ETT) versus a laryngeal mask airway (LMA) in patients with upper respiratory infections.²⁷ As clinically appropriate, an LMA should be used in lieu of an ETT. Direct laryngoscopy stimulates oropharyngeal reflexes and may provoke bronchospasm directly or following placement of an ETT. NMBAs may blunt these processes and decrease the incidence and severity of airway reflexes, wheezing, and bronchospasm during endotracheal intubation.^{28,29} In a study including 566 patients undergoing emergent endotracheal intubation in the ICU, the administration of NMBAs was associated with a lower prevalence of hypoxemia and procedure-related complications, and significantly improved intubating conditions.³⁰

The choice of NMBA may also impact the incidence of bronchospasm. Agents that release histamine such as atracurium, mivacurium, and d-tubocurarine should generally be avoided.³¹ Innervation of the trachea and airway includes cholinergic fibers with modulation of airway tone through the release of acetylcholine with effects on both pre-synaptic (M2) and post-synaptic (M3 receptors). M2 muscarinic receptors act as negative feedback receptors and decrease further release of acetylcholine while M3 receptors on the smooth muscle act to cause bronchoconstriction. Modulation of this cholinergic pathway with augmented release of acetylcholine through partial blockade of M2 receptors and augmentation of the effects of acetylcholine on M3 receptors was the mechanism identified which caused significant bronchospasm with rapacuronium.^{32,33} Rapacuronium has since been withdrawn from the market due to its significant risk for precipitating bronchospasm. Other NMBAs may also modulate the cholinergic pathways, leading to theoretical concerns regarding their use in patients with asthma and airway reactivity.³⁴ Rocuronium has both M2 and M3 muscarinic receptor blocking effects in clinically used concentrations. Its M3 blocking effects at a given concentration are weaker than at the M2 muscarinic receptor, therefore providing a mechanism for causing bronchoconstriction at a time of enhanced vagal stimulation, such as tracheal intubation. Furthermore, just like rapacuronium, rocuronium has positive allosteric effects at the M3 muscarinic receptor, which may further enhance any bronchoconstriction.

Various other pharmacologic agents may provide protection against reflex bronchoconstriction following endotracheal intubation including anticholinergic agents or lidocaine. Given its lack of central nervous system effects, glycopyrrolate is frequently chosen for intraoperative administration. When administered prior to endotracheal intubation, it may provide protection against cholinergic-mediated bronchoconstriction.³⁵

The administration of aerosolized or intravenous lidocaine may also minimize reflex bronchoconstriction.

Postulated mechanisms include neural blockade of vagal reflex pathways and direct effects on airway smooth musculature.^{36,37} Finally, a single intraoperative dose of the corticosteroid, dexamethasone, may provide protection against postoperative bronchospasm through its anti-inflammatory effects.³⁸

Of primary importance during intraoperative care of patients with asthma is to have a specific algorithm for recognizing and treating acute bronchospasm (table 1). Treatment is directed at maintaining adequate oxygenation and ventilation while providing effective pharmacologic management to treat and reverse bronchospasm. Initial management includes the administration of 100% oxygen, manual ventilation, and cessation of any interventions including surgical stimulation that may be precipitating bronchospasm. Auscultation is suggested to ensure appropriate positioning of the endotracheal tube, identification of causes of upper airway obstruction including secretions, and identification of bronchial intubation or pneumothorax. There should be identification of anaphylactoid or anaphylactic reactions which may have precipitated bronchospasm. As indicated, a chest radiograph should be obtained. The depth of anesthesia should be deepened with an intravenous anesthetic agent (propofol) and the administration of increased concentration of the volatile anesthetic agent, sevoflurane. Close monitoring of hemodynamic function is mandatory as the depth of anesthesia is increased and ventilator support augmented as hypotension may ensue.

Additional therapy should include the administration of a β -adrenergic agonist (albuterol) via a metered dose inhaler, deepening the depth of anesthesia, and other therapies listed above. If bronchospasm is severe, limiting gas exchange, and preventing the effective delivery of aerosolized albuterol, intravenous epinephrine (1-2 $\mu\text{g}/\text{kg}$) should be considered. Persistent bronchospasm may require the administration of a bolus and/or continuous intravenous infusion of magnesium, ketamine, or even epinephrine.^{39,40} Magnesium has seen significant clinical use in the treatment of status asthmaticus in the ICU

setting. It results in bronchial smooth relaxation independently of the β_2 -receptor, by decreasing the transmembrane movement of calcium, blocking acetylcholine release thereby resulting in bronchodilatation. Dosing includes a bolus dose (25-50 mg/kg) followed by an infusion at 10-20 mg/kg/hour. Adverse effects include both hypotension from vasodilatation of the vascular smooth musculature as well as skeletal muscle weakness from the effects of magnesium at the neuromuscular junction. Hypotension can frequently be prevented by the slow administration of the bolus dose or the administration of an isotonic fluid bolus. During continuous infusions of magnesium, serum levels are monitored every 4-6 hours and the infusion adjusted accordingly. An additional therapy for the treatment of bronchospasm is the administration of a ketamine bolus (1 mg/kg) followed by a continuous infusion. Ketamine stimulates the release of endogenous catecholamines and decreases vagally induced airway constriction resulting thereby preventing bronchospasm.^{20,21,40}

In summary, we present a patient who developed significant intraoperative bronchospasm during an elective surgical procedure. Preoperative interventions, including maximizing chronic medication regimens (inhaled corticosteroids, anticholinergic agents, and β -adrenergic agonists), ensuring freedom from acute upper respiratory infections, avoidance of second hand-tobacco smoke, and a short course of oral corticosteroids may decrease the incidence of intraoperative bronchospasm. Various modifications in intraoperative care as listed in table 1 may also decrease the incidence of bronchospasm. A suggested algorithm for the intraoperative treatment of bronchospasm includes deepening the level of inhalational anesthesia, the administration of inhaled albuterol, and cessation of airway stimulation. Intravenous epinephrine, magnesium, or ketamine may be considered if escalation of care is indicated. Similar therapies should also be considered postoperatively as needed.

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