The Perioperative Management of Asthma

Richard Applegate, Ryan Lauer*, John Lenart, Jason Gatling and Marisa Vadi
Department of Anesthesiology, Loma Linda University School of Medicine, USA

Abstract

Anesthesiologists encounter asthmatic patients routinely. This common disease frequently complicates the perioperative care of those patients who live with it and can occasionally lead to life-threatening complications. This review takes the anesthesiologist’s perspective to discuss asthma and how asthmatic patients can be safely guided through an anesthetic. We will discuss frequently used asthma medications, pre-operative disease optimization, management of intra-operative bronchospasm, and post-operative considerations for asthmatic patients. Anesthesiologists can make a positive difference in the outcomes of these patients with proper preoperative evaluation using a stepwise approach to disease management and by minimizing bronchoconstriction and effectively treating it when it develops.

Keywords: Asthma; Anesthesia; Perioperative

Introduction

Asthma is a chronic pulmonary disease characterized by airway inflammation and hyper-responsiveness resulting in episodic wheezing, coughing, breathlessness, chest tightness, and reversible airflow obstruction [1]. Contributing factors include genetics, atopy, and respiratory syncytial virus infection in infancy. Common environmental triggers are pollen, mold, animals, dust, tobacco smoke, and anxiety.

Asthma prevalence varies by region, with published reports ranging from 0.7% to 18.4%. It is estimated that up to 300 million people are affected worldwide [2]. The National Center for Health Statistics reported increased asthma prevalence in the United States between 2008–2012 [3]. Their findings indicated an overall asthma prevalence of 7.7% for adults and 9.5% for children, with a slightly higher prevalence in women (9.2%) than in men (7.0%). Others have reported similar data, with some experts calling the recent increase in asthma prevalence an “epidemic” [4,5]. Despite these concerns, the overall number of asthma-related hospitalizations and deaths has decreased, possibly due to improved prevention of attacks through inhaled steroid use and novel pharmaceutical agents introduced over the past decade [6].

Asthmatics carry an increased risk for perioperative complications and thus present unique challenges for the anesthesiologist [7,8]. In this article we will discuss frequently used asthma medications, preoperative disease optimization, management of intraoperative bronchospasm, and postoperative considerations for asthmatic patients.

Pharmacotherapy

A stepwise approach to managing asthma, such as the treatment regimen proposed by the Global Initiative for Asthma [1], is recommended to gain and maintain preoperative disease control in asthmatics scheduled to undergo general anesthesia [9]. Patients are evaluated and placed on a discrete treatment “step” based upon symptomatology and severity of disease. As the disease increases in severity, the number and types of medications used to treat the patient also increase. This model of increasing therapy based on symptom control is easily applied to preoperative preparation of asthmatics (Figure 1). Each class of therapy will be discussed below.

β-Agonists

Inhaled β-agonists provide short-term relief from bronchospasm. Long-acting inhaled β-agonists may also be used for chronic asthma management, but only in conjunction with inhaled corticosteroids. A distinct advantage to this class of medications is that it includes a broad therapeutic window. The mechanism of action originates from stimulation of the β-2 receptor, activating adenyl cyclase and thereby increasing cAMP production. Cyclic AMP at the cellular level causes smooth muscle relaxation and increased mucociliary clearance [10,11]. Although β-agonists may be administered through oral and intravenous routes, inhaled administration provides both targeted end-organ administration and faster peak bronchodilatation with fewer systemic side effects [12,13]. A transdermal preparation of the β-agonist, tulobuterol, has been available in Japan for several years. It has shown promise as a long-acting β-agonist (LABA) in the control of asthma symptoms in adults and children [14,15].

Corticosteroids

Inhaled corticosteroids are potent anti-inflammatory agents that constitute the mainstay of therapy for patients with persistent asthma. Corticosteroids have been shown to reduce airway reactivity and block reactions to provocative allergens [16]. At the cellular level, corticosteroids reduce the number of inflammatory cells (eosinophils, T-lymphocytes, mast cells, dendritic cells) in the airways by inhibiting inflammatory cell survival and suppressing the production of chemotactic mediators [17–19]. Asthmatic patients who are treated with corticosteroids preoperatively have been shown to have a low incidence of complications during surgery [20]. The side effects of sore throat, hoarseness, and oral thrush can be common and are related to the dose and frequency of use [21]. Systemic corticosteroids are reserved for individuals with severe and uncontrolled asthma.

Leukotriene pathway modifiers

Leukotrienes are produced by inflammatory cells such as basophils, eosinophils, and mast cells. These inflammatory mediators generate bronchial edema, stimulate airway secretions, and induce smooth muscle...
Asthma disease (COPD). Anticholinergics are a mainstay of treatment for symptoms often comingle with those of chronic obstructive pulmonary disease. This review focuses primarily on asthma management but asthma coexists with other treatment modalities in a multi-faceted approach [22,23].

Anticholinergics are rarely used in the chronic management of pediatric asthma patients. Ipratropium is used primarily in adult patients, and only rarely used in chronic management of pediatric asthma patients. Severe acute asthmatic attacks may benefit by combining ipratropium with other treatment modalities in a multi-faceted approach [22,23]. This review focuses primarily on asthma management but asthma symptoms often comingle with those of chronic obstructive pulmonary disease (COPD). Anticholinergics are a mainstay of treatment for COPD [24].

Cromones

Cromolyn sodium and Nedocromil sodium stabilize mast cells and interfere with chloride cell function. These medications are used, only rarely, as alternative treatment for asthma in adults and are currently not recommended for use in children [1,16]. It is important to remember that these medications are not to be used for emergency treatment; rather, when used, should be part of a long-term preventative strategy.

Anticholinergics

Ipratropium bromide inhibits mucous hyper-secretion and decreases reflex bronchoconstriction by targeting airway muscarinic receptors. It may be administered either by a metered dose inhaler (MDI) or by nebulizer. The application of anticholinergics by current modalities results in insignificant systemic absorption and low side effects. Ipratropium is used primarily in adult patients, and only rarely used in chronic management of pediatric asthma patients. Severe acute asthmatic attacks may benefit by combining ipratropium with other treatment modalities in a multi-faceted approach [22,23]. This review focuses primarily on asthma management but asthma symptoms often comingle with those of chronic obstructive pulmonary disease (COPD). Anticholinergics are a mainstay of treatment for COPD [24].

Methylxanthines

Theophylline is a mild bronchodilator and anti-inflammatory medication [25]. It is seldom used as a primary therapy due to its narrow therapeutic index and decreased efficacy when compared to treatment with low-dose inhaled daily corticosteroids. It has been used successfully in adults, in low-dose, as adjunct to standard therapy for its anti-inflammatory properties [1]. Theophylline is useful as an oral rescue medication in patients with status asthmaticus [26]. Side effects can be significant and include nausea, vomiting, arrhythmias, headache, and seizures. Serum monitoring is required for high-dose regimens due to the narrow therapeutic index but the low-dose, anti-inflammatory type dosing can administered with less monitoring. Aminophylline is the only available intravenous methylxanthine in clinical use today. Care should be taken when used with halothane as concurrent use may cause ventricular dysrhythmias.

Preoperative Management

A thorough history and physical examination provides the anesthesiologist with information that allows for appropriate identification of level of disease, degree of symptom control, and anesthetic risk stratification. Review of baseline exercise tolerance, hospital visits secondary to asthma (including whether endotracheal intubation or IV infusions were required), allergies, and previous surgical/anesthetic history is essential. The patient's medication regimen should be reviewed and provides important clues as to level of disease severity. For instance, a patient on a single agent such as inhaled albuterol is likely to have mild, controlled disease while another patient requiring several different classes of asthma medications likely has more severe disease. Patients should be queried as to new medications, recent...
changes in the frequency or dose of medications, and the level of disease control on their current medication regimens. This thorough review of an asthmatic's history and the appropriate preoperative preparations (often done with a multidisciplinary approach) can significantly reduce the risk of adverse outcomes (Figure 2) [27-29].

The risk of intraoperative bronchospasm, one of the most feared complications of asthma, can be increased by the presence of atopy, eczema, allergic rhinitis, and other conditions of chronic inflammation [12,30]. A family history of asthma and atopy should be sought and is also a marker of increased perioperative risk [31]. Smoking or exposure to second-hand smoke contributes to poor asthma control and is also an independent risk factor for adverse respiratory events under general anesthesia [32]. If time permits, the patient should be advised to stop smoking for 2 months prior to elective surgery [33].

While a thorough review of pediatric asthma considerations is outside the scope of this article, the risk of bronchospasm in children with asthma and upper respiratory infections is markedly elevated [31,34]. In such a case, it is prudent to postpone elective operations for 4-6 weeks after the resolution of the infection.

Physical examination should include vital signs and assessment of breath sounds, use of accessory muscles, and level of hydration. The presence of labored breathing, use of accessory muscles, and prolonged expiration time suggest poorly-controlled asthma. Wheezing on auscultation is concerning, particularly if the wheezing is noticed in phases of the respiratory cycle other than end-expiration.

Laboratory tests are not routinely required. However, in more severe disease a room air arterial blood gas may be useful in determining baseline oxygenation, carbon dioxide retention, and acid-base status. Pre-operative clinics nearly universally have pulse-oximetry available, which can serve as a reasonable surrogate for arterial blood gas in determining baseline oxygenation. A chest x-ray may be obtained to assess for lung hyperinflation and air-trapping. Peak flow measurements are recommended by the American Lung Association for disease self-monitoring and are easily performed at bedside. The suggested “zones” (green=80% or greater than usual, yellow=50-80% of usual, red <50% of usual) alert patients to their current respiratory status [35]. Spirometric tests can be ordered to assess the forced expiratory volume (FEV1), which reflects the degree of airway obstruction. The forced oscillometric technique is an emerging tool for assessing bronchial obstruction and reactivity. It seems particularly useful in children or other patients who may not be able to actively participate in spirometry [36]. Recently, the fraction of expired nitric oxide (FeNO) has been evaluated as measure of asthma control [37,38]. Further study is necessary determine how FeNO should be used along with clinical and spirometric evaluation for managing asthma [39]. Objective testing, physical exam, and a careful history need to be synthesized into an overall picture of the patient's current level of disease severity and control so that they can be effectively managed perioperatively.

Treatment options prior to surgery are based upon the level of the severity of the disease. Frequently, all that is needed is a short-term "step-up" in the treatment regimen. Controlled asthmatics may only need a short-acting β2 agonist just prior to surgery. Moderately controlled patients should add inhaled corticosteroids to their β2 agonists one week prior to surgery. Poorly controlled asthmatics may need to add oral corticosteroids to their regimen [29,40]. Preoperative use of oral corticosteroids has been shown to suppress production of inflammatory cytokines [19] and studies confirm the safety of perioperative systemic corticosteroids [41,42].

Patients should continue all medications through the day of surgery. Additional short acting β-agonists are indicated regardless of disease level, as benefits counteracting the bronchial constrictive response to
tracheal intubation have been demonstrated [29,43-47]. Preoperative anxiolytics such as midazolam assist in mitigating anxiety-induced bronchospasm [48]. The use of systemic steroids within the last six months is an indication for an IV stress dose of methylprednisolone or hydrocortisone [1,16].

Care should also be taken to evaluate the type of surgical procedure. The operative site has been shown to be a risk factor for perioperative pulmonary complications in asthma patients [49]. For example, upper airway surgery or any type of surgery involving the diaphragm may result in increased perioperative pulmonary morbidity.

**Intraoperative Management**

The overriding goal in anesthetizing an asthmatic patient is to avoid bronchospasm and reduce the response to tracheal intubation. Severe bronchospasm may cause fatal or near-fatal events such as irreversible brain damage due to inability to ventilate [9]. It is extremely important that the patient be at a deep level of anesthesia prior to instrumenting the airway, as tracheal intubation during light levels of anesthesia can precipitate bronchospasm. Regional anesthetic techniques should be considered when appropriate, to avoid airway instrumentation. The risk of pulmonary complications is lower when the surgical anesthetic was performed under epidural or spinal anesthesia [50].

Intravenous lidocaine has been successfully used to decrease airway irritability [47,51,52]. Some reports advocate direct lidocaine administration to the vocal cords for reduction of laryngospasm risk, but others report this practice may actually trigger airway hyperactivity; intravenous lidocaine administration may be preferable [53]. Antimuscarinics such as glycopyrrolate and atropine may decrease secretions and provide additional bronchodilatation if given in sufficient time prior to induction.

Propofol is the induction agent of choice in the hemodynamically stable patient due to its ability to attenuate the bronchospastic response to intubation both in asthmatics and non-asthmatics [54-56]. Care should be taken in patients with depressed cardiac function, as propofol decreases cardiac contractility and chronicity. Thiopental or etomidate may also be used as induction agents but lack the bronchodilating properties of propofol and in the case of thiopental, may lead to detrimental histamine release [54-56]. Ketamine is an ideal induction agent for hemodynamically unstable asthmatics due to its ability to produce direct smooth muscle relaxation and bronchodilatation without decreasing arterial pressure or systemic vascular resistance. However, ketamine-induced bronchodilatation is not as pronounced as with propofol [57,58].

Volatile anesthetics are excellent choices for general anesthesia, as they depress airway reflexes and produce direct bronchial smooth muscle relaxation [59]. Sevoflurane has emerged as the volatile agent of choice, as studies indicate it has the most pronounced bronchodilatory effect of all volatile anesthetics [60]. Desflurane increases airway resistance [61-63] and should be avoided in asthmatics, specifically at lighter levels of general anesthesia.

It is prudent to avoid instrumentation of the airway whenever possible for prevention of bronchospasm. Increases in airway resistance after endotracheal intubation have been shown to rapidly decrease after administration of isoflurane, implicating tracheal intubation as the cause of the increased resistance. Similar increases in airway resistance were not observed after insertion of laryngeal mask airways [64]. Thus, the use of a laryngeal mask airway or even mask ventilation, may be preferable to tracheal intubation in asthmatics. The benefits of a laryngeal mask airway must be balanced against the risks of an unsecured airway and in patients with severe gastroesophageal reflux disease, obesity, diabetic gastroparesis, or recent oral intake, the need for a secured airway may take precedence.

If endotracheal intubation is deemed necessary, histamine-releasing neuromuscular blockers should be avoided. Vecuronium, rocuronium, and cis-atracurium are safe for use in asthmatics. Succinylcholine, which releases low levels of histamine, has been used safely in asthmatics with little morbidity. Reversal of neuromuscular blockade with acetylcholinesterase inhibitors should be used with caution in asthmatics due to the risk of muscarinic side effects including bronchospasm. Sugammadex, a novel agent that encapsulates steroidal neuromuscular blocking agents without muscarinic side effects, has been proposed as an alternative medication for reversal of neuromuscular blockade. However, a study of sugammadex use in patients with pulmonary disease found a 2.6% incidence of bronchospasm in this population. Thus, sugammadex does not completely eliminate the risk of airway hyperreactivity in patients with underlying disease. Though available in other countries, sugammadex is not yet available in the United States.

Inspired gases should be humidified to avoid airway irritation. Stimulating maneuvers such as airway suctioning should be kept to a minimum and should be performed only while the patient is in a deep plane of anesthesia. Ventilatory strategies such as limiting peak inspiratory pressures and tidal volumes and lengthening the I:E ratio assist in avoiding air-trapping and auto PEEP [65,66]. If not contraindicated, extubation under deep levels of anesthesia may be undertaken to reduce the risk of bronchospasm.

Signs of intraoperative bronchospasm may include wheezing, a change in capnography (upslope on CO2 waveform, or decreased/absent CO2 waveform), decreased tidal volumes, or high peak inspiratory pressures. Clinicians should also investigate alternative diagnoses including ventilator malfunction, endotracheal tube obstruction (e.g. kink, mucous plug, clot), endobronchial intubation, or medical conditions such as tension pneumothorax or pulmonary embolus before making a definitive diagnosis of bronchospasm.

As inadequate depth of anesthesia is a common cause of bronchospasm, initial management steps should include deepening the plane of anesthesia. This may be accomplished by increasing the concentration of volatile anesthetic or by the administration of rapid-acting intravenous bronchodilators such a propofol or ketamine. Subsequently, inhaled β-2 agonists should be administered for further bronchodilation. Unfortunately, delivering inhaled medication through an endotracheal tube may be challenging. As little as 12.3% of albuterol delivered by MDI is delivered to the patient through narrow endotracheal tubes [67,68]. The most effective route of administration is by MDI spacer or nebulizer attached to a ventilator circuit. Other techniques include (1) delivering extra albuterol puffs to account for the medication lost to the endotracheal tubes and (2) placing the albuterol canister inside a 60 ml syringe, attaching the syringe temporarily to the CO2 sampling port on the elbow of the ventilator circuit, and depressing the plunger multiple times. Many resourceful clinicians have fashioned their own delivery systems using common anesthesia items in the operating room (Figure 3) [69].

Other bronchodilating strategies include administering anticholinergics, intravenous steroids, and intravenous or subcutaneous β-agonists such as epinephrine. Terbutaline may be preferable to epinephrine in the pregnant patient due to its tocolytic properties.
Splinting" maintains respiratory muscle function and is associated with pathways from abdominal viscera; this reduces hypoventilation due to earlier hospital discharge [81]. Leading to prevention of further pulmonary complications and allowing gas exchange become possible with early respiratory rehabilitation, throughout the postoperative recovery period as needed for recurrent bronchospasm [35]. It is prudent to readminister ß-agonists prior to emergence and metabolism of neuromuscular blockers without the need reversal agents for further medical management, recovery of airway function, and perioperative strategies for prevention of bronchospasm decrease postoperative pulmonary complications in asthmatics.

In summary, vigilant monitoring and respiratory rehabilitation of the asthmatic patient is of primary importance in preventing perioperative pulmonary complications. Proper preoperative evaluation of disease level and medical compliance with prescribed medication regimens, along with perioperative strategies for prevention of bronchospasm in asthmatics.

**References**

1. Bateman ED, Hurd SS, Barnes PJ, Bousquet J, Drazen JM, et al. (2008) Global strategy for asthma management and prevention: GINA executive summary. Eur Respir J 31: 143-178.

2. Masoli M, Fabian D, Holt S, Beasley R; Global Initiative for Asthma (GINA) Program (2004) The global burden of asthma: executive summary of the GINA Dissemination Committee report. Allergy 59: 469-478.

3. Akinbami LJ, Moorman JE, Bailey C, Zahn HS, King M, et al. (2012) Trends in asthma prevalence, health care use, and mortality in the United States, 2001-2010. NCHS Data Brief: 1-8.

4. Eder W, Ege MJ, von Mulus E (2006) The asthma epidemic. N Engl J Med 355: 2226-2235.

5. Kuehni CE, Davis A, Brooke AM, Silverman M (2001) Are all wheezing disorders in very young (preschool) children increasing in prevalence? Lancet 357: 1821-1825.

6. Fanta CH (2009) Asthma. N Engl J Med 360: 1002-1014.

7. Warner DO, Warner MA, Barnes RD, Offord KP, Schroeder DR, et al. (1996) Perioperative respiratory complications in patients with asthma. Anesthesiology 85: 460-467.

8. Orestes MI, Lander L, Vergheses S, Shah RK (2012) Incidence of laryngospasm and bronchospasm in pediatric adenotonsillectomy. Laryngoscope 122: 425-428.

9. Liccardi G, Salzillo A, Sofia M, D’Amato M, D’Amato G (2012) Bronchial asthma. Curr Opin Anaesthesiol 25: 30-37.

10. Johnson M (2001) Beta2-adrenoceptors: mechanisms of action of beta2-agonists. Paediatr Respir Rev 2: 57-62.

11. Johnson M (2006) Molecular mechanisms of beta(2)-adrenergic receptor function, response, and regulation. J Allergy Clin Immunol 117: 18-24.

12. Pedersen SE, Hurd SS, Lemanske RF Jr, Becker A, Zar HJ, et al. (2011) Global strategy for the diagnosis and management of asthma in children 5 years and younger. Pediatr Pulmonol 46: 1-17.

13. Wolfe JD, Shapiro GG, Ratner PH (1991) Comparison of albuterol and metaproterenol syrup in the treatment of childhood asthma. Pediatrics 88: 312-319.

14. Hozawa S, Haruda Y, Terada M, Yamakido M (2009) Effects of the addition of Beta2-agonist tulobuterol patches to inhaled corticosteroid in patients with asthma. Allergol Int 58: 509-518.

15. Katsunuma T, Fujisawa T, Nagao M, Akasawa A, Nomura I, et al. (2013) Effects of transdermal tulobuterol in pediatric asthma patients on long-term leukotriene receptor antagonist therapy: results of a randomized, open-label, multicenter clinical trial in Japanese children aged 4-12 years. Allergol Int 62: 37-43.

16. National Asthma Education and Prevention Program (2007) Expert Panel Report 3 (EPR-3): Guidelines for the Diagnosis and Management of Asthma—Summary Report 2007. J Allergy Clin Immunol 120: S94-S138.

17. Barnes PJ, Adcock IM (2003) How do corticosteroids work in asthma? Ann Intern Med 139: 359-370.
18. Drazen JM, Israel E, O’Byrne PM (1999) Treatment of asthma with drugs modifying the leukotriene pathway. N Engl J Med 340: 197-206.

19. Mitsuta K, Shimoda T, Fukushima C, Obase Y, Ayabe H, et al. (2001) Preoperative steroid therapy inhibits cytokine production in the lung parenchyma in asthmatic patients. Chest 120: 1175-1183.

20. Kabalin CS, Yamold PR, Grammer LC (1995) Low complication rate of corticosteroid-treated asthmatics undergoing surgical procedures. Arch Intern Med 155: 1379-1384.

21. Korsgaard J, Ledet M (2009) Potential side effects in patients treated with inhaled corticosteroids and long-acting beta2-agonists. Respir Med 103: 566-573.

22. Rodrigo GJ, Castro-Rodriguez JA (2005) Anticholinergics in the treatment of children and adults with acute asthma: a systematic review with meta-analysis. Thorax 60: 740-746.

23. Plotnick LH, Ducharme FM (2000) Combined inhaled anticholinergics and beta2-agonists for initial treatment of acute asthma in children. Cochrane Database Syst Rev 4: CD000060.

24. Vestbo J, Hurd SS, Agusti AG, Jones PW, Vogelmeier C, et al. (2013) Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. Am J Respir Crit Care Med 187: 347-365.

25. Weinberger M, Hendeles L (1996) Theophylline in asthma. N Engl J Med 334: 1380-1389.

26. Ream RS, Loftis LL, Albers GM, Becker BA, Lynch RE, et al. (2001) Efficacy of IV theophylline in children with severe status asthmaticus. Chest 119: 1480-1488.

27. Liccardi G, Salzillo A, De Biasio F, D’Amato G (2009) Control of asthma from reducing the risk of bronchospasm in asthmatics undergoing general anesthesia and/or intravenous administration of radiographic contrast media. Curr Med Res Opin 25: 1621-1630.

28. Triunfalasetty J, Grammer LC (2006) Asthma, surgery, and general anesthesia: a review. J Asthma 43: 251-254.

29. Zachary CY, Evans R 3rd (1996) Perioperative management for childhood asthma. Ann Allergy Asthma Immunol 77: 468-472.

30. Bousquet J, Khattarv N, Cruz AA, Denburg J, Fokkens WJ, et al. (2008) Allergic Rhinitis and its Impact on Asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). Allergy 63 Suppl 86: 139-148.

31. von Ungern-Sternberg BS, Boda K, Chambers NA, Rebmann C, Johnson 8-160.

32. Kil HK, Rooke GA, Ryan-Dykes MA, Bishop MJ (1994) Effect of prophylactic bronchodilator treatment on lung resistance after tracheal intubation. Anesthesiology 81: 169-172.

33. Silverman MT, Groeben H, Peters J (2004) Corticosteroids and inhaled salbutamol in patients with reversible airway obstruction markedly decrease the incidence of bronchospasm after tracheal intubation. Anesthesiology 100: 1052-1057.

34. von Ungern-Sternberg BS, Habre W, Erb TO, Heaney M (2009) Salbutamol premedication in children with a recent respiratory tract infection. Paediatr Anaesth 19: 1064-1069.

35. Maslow AD, Regan MM, Israel E, Darvish A, Mehrzad M, et al. (2000) Inhaled albuterol, but not inhaled lidocaine, protects against intubation-induced bronchoconstriction in asthma. Anesthesiology 93: 1198-1204.

36. Kil N, Zhu JF, VanWagenen C, Abdulhamit I (2003) The effects of midazolam on pediatric patients with asthma. Pediatr Dent 25: 137-142.

37. Chetta A, Tzani P, Marangoi E, Carborgnoli P, Bobbio A, et al. (2006) Respiratory effects of surgery and pulmonary function testing in the preoperative evaluation. Acta Biomed 77: 69-74.

38. Rodgers A, Walker N, Schug S, McKee A, Kehlet H, et al. (2000) Reduction of postoperative morbidity and morbidity with epidural or spinal anesthesia: results from overview of randomised trials. BMJ 321: 1493.

39. Adamzik M, Groeben H, Farahani R, Lehmann N, Peters J (2007) Intravenous lidocaine after tracheal intubation mitigates bronchoconstriction in patients with asthma. Anesth Analg 104: 1109-1115, tables of contents.

40. Bulut Y, Hirschman CA, Brown RH (1996) Prevention of lidocaine aerosol-induced bronchoconstriction with intravenous lidocaine. Anesthesiology 85: 853-859.

41. Wu RS, Wu KC, Sum DC, Bishop MJ (1996) Comparative effects of thiopentone and propofol on respiratory resistance after tracheal intubation. Br J Anaesth 77: 735-738.

42. Plizov R, Brown RH, Weiss YS, Baranov D, Hennes H, et al. (1995) Wheezing during induction of general anaesthesia in patients with and without asthma. A randomized, blinded trial. Anesthesiology 82: 1111-1116.

43. Eames VO, Rooke GA, Wu RS, Bishop MJ (1996) Comparison of the effects of etomidate, propofol, and thiopental on respiratory resistance after tracheal intubation. Anesthesiology 84: 1307-1311.

44. Brown RH, Wagner EM (1999) Mechanisms of bronchoconstriction by anesthetic induction agents: propofol versus ketamine. Anesthesiology 90: 822-828.

45. Pedersen CM, Thrstrup S, Nielsen-Kudsk JE (1993) Smooth muscle relaxant effects of propofol and ketamine in isolated guinea-pig trachea. Eur J Pharmacol 238: 75-80.

46. Harmsen CA, Edelstein G, Pooett S, Wayne R, Downes H (1982) Mechanism of action of inhalational anaesthesia on airways. Anesthesiology 56: 107-111.

47. Rooke GA, Choi JH, Bishop MJ (1997) The effect of isoflurane, halothane, sevoflurane, and thiopental/nitrous oxide on respiratory system resistance after tracheal intubation. Anesthesiology 86: 1294-1299.

48. Nyktari V, Papaioannou V, Volakakis N, Lappa A, Margaritisanaki P, et al. (2011) Respiratory resistance during anaesthesia with isoflurane, sevoflurane, and desflurane: a randomized clinical trial. Br J Anaesth 107: 454-461.
62. Nyktari VG, Papaioannou AA, Prinianakis G, Mamidakis EG, Georgopoulos D, et al. (2006) Effect of the physical properties of isoflurane, sevoflurane, and desflurane on pulmonary resistance in a laboratory lung model. Anaesthesiology 104: 1202-1207.

63. Dikmen Y, Eminoglu E, Salihoglu Z, Demiroluks S (2003) Pulmonary mechanics during isoflurane, sevoflurane and desflurane anaesthesia. Anaesthesia 58: 745-748.

64. Kim E, Bishop MJ (1999) Endotracheal intubation, but not laryngeal mask airway insertion, produces reversible bronchoconstriction. Anaesthesiology 90: 391-394.

65. Mesiano G, Davis GM (2008) Ventilatory strategies in the neonatal and paediatric intensive care units. Paediatr Respir Rev 9: 281-288.

66. Oddo M, Feihl F, Schaller MD, Perret C (2006) Management of mechanical ventilation in acute severe asthma: practical aspects. Intensive Care Med 32: 501-510.

67. Taylor RH, Lerman J (1991) High-efficiency delivery of salbutamol with a metered-dose inhaler in narrow tracheal tubes and catheters. Anaesthesiology 74: 360-363.

68. Crogan SJ, Bishop MJ (1989) Delivery efficiency of metered dose aerosols given via endotracheal tubes. Anaesthesiology 70: 1006-1010.

69. Lauer R, Vadi M, Mason L (2012) Anaesthetic management of the child with co-existing pulmonary disease. Br J Anaesth 109: i47-47i59.

70. Sellers WF, Messahel B (2003) Rapidly repeated intravenous boluses of salbutamol for acute severe asthma. Anaesthesia 587: 680-683.

71. Chiang VW, Burns JP, Ritali N, Lipshultz SE, Adams MJ, et al. (2000) Cardiac toxicity of intravenous terbutaline for the treatment of severe asthma in children: a prospective assessment. J Pediatr 137: 77-77.

72. Smith D, Reel J, Tilley I, Kino R, Lis J, et al. (2003) Intravenous epinephrine in life-threatening asthma. Ann Emerg Med 41: 706-711.

73. Bogie AL, Towne D, Luckett PM, Abramo TJ, Wiebe RA (2007) Comparison of intravenous terbutaline versus normal saline in pediatric patients on continuous high-dose nebulized albuterol for status asthmaticus. Pediatr Emerg Care 23: 355-361.

74. Wheeler DS, Jacobs BR, Kenneigh CA, Bean JA, Hutson TK, et al. (2005) Theophylline versus terbutaline in treating critically ill children with status asthmaticus: a prospective, randomized, controlled trial. Pediatr Crit Care Med 6: 142-147.

75. Cheuk DK, Chau TC, Lee SL (2005) A meta-analysis on intravenous magnesium sulphate for treating acute asthma. Arch Dis Child 90: 74-77.

76. Sellers WF (2013) Inhaled and intravenous treatment in acute severe and life-threatening asthma. Br J Anaesth 110: 183-190.

77. Rogers L, Reitman J (2011) Pharmacologic approaches to life-threatening asthma. Ther Adv Respir Dis 5: 397-408.

78. Powell C, Dwan K, Milan SJ, Beasley R, Hughes R, et al. (2012) Inhaled magnesium sulfate in the treatment of acute asthma. Cochrane Database Syst Rev 12: CD003898.

79. Shan Z, Rong Y, Yang W, Wang D, Yao P, et al. (2013) Intravenous and nebulized magnesium sulfate for treating acute asthma in adults and children: a systematic review and meta-analysis. Respir Med 107: 321-330.

80. Coleman NE, Dalton HJ (2009) Extracorporeal life support for status asthmaticus: the breath of life that's often forgotten. Crit Care 13: 136.

81. Yamakage M, Iwasaki S, Namiki A (2008) Guideline-oriented perioperative management of patients with bronchial asthma and chronic obstructive pulmonary disease. J Anesth 22: 412-428.

82. Manion SC, Brennan TJ (2011) Thoracic epidural analgesia and acute pain management. Anaesthesiology 115: 181-188.

83. Joshi GP, Bonnet F, Shah R, Wilkinson RC, Camu F, et al. (2008) A systematic review of randomized trials evaluating regional techniques for postthoracotomy analgesia. Anesth Analg 107: 1026-1040.

84. Jayr C, Thomas H, Rey A, Farhat F, Lasser P, et al. (1993) Postoperative pulmonary complications. Epidural analgesia using bupivacaine and opioids versus parenteral opioids. Anesthesiology 78: 666-676.

85. Ballantyne JC, Carr DB, deFerranti S, Suarez T, Lau J, et al. (1998) The comparative effects of postoperative analgesic therapies on pulmonary outcome: cumulative meta-analyses of randomized, controlled trials. Anesth Analg 86: 598-612.