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The Perioperative Management of Asthma

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Abstract

Anesthesiologists encounter asthmatic patients routinely. This common disease frequently complicates the peri-operative 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 adenylyl 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 bronchodilation 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

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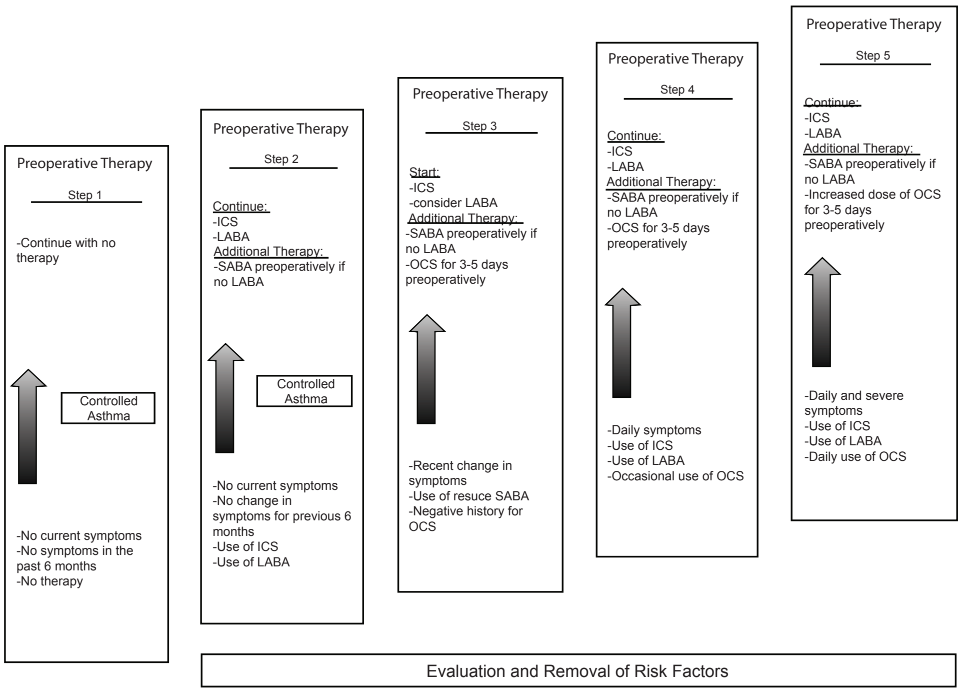

Figure 1: A stepwise approach to the preoperative treatment of asthmatic patients based on their degree of asthma control.

ICS: Inhaled Corticosteroids; LABA: Long-Acting Beta-2 Agonist; OCS: Oral Corticosteroids; SABA: Short-Acting Beta-2 Agonist. Modified with permission [9].

proliferation through a non-histamine mechanism [18]. Inhibition of these mediators can lead to mild bronchodilation via a pathway distinct from β-agonists suggesting an additive effect. Leukotriene pathway modifiers (e.g. montelukast) are used as second-line controller agents. They are thought to be very useful in specific asthma environments such as exercise-induced, viral-induced (intermittent), and aspirin-induced asthma [1,18].

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 reflexive bronchoconstriction by targeting airway muscarinic cholinergic 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 the 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

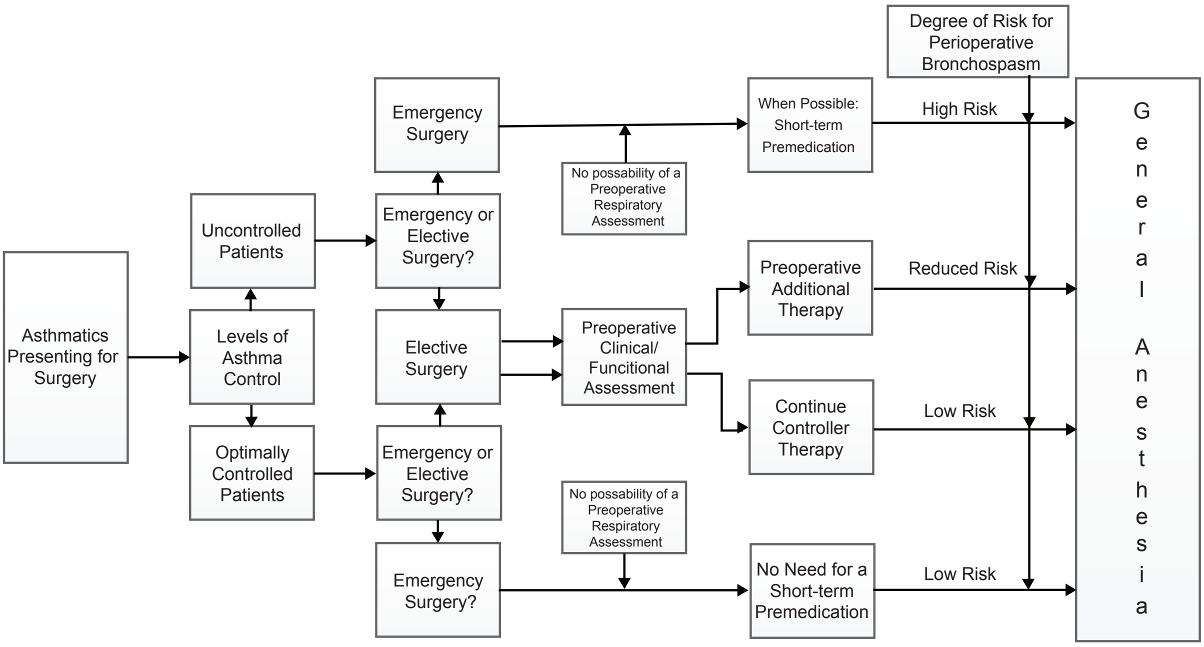

Figure 2: A pre-anesthetic assessment and plan can reduce the risk for perioperative bronchospasm in asthmatics undergoing general anesthesia. Modified with permission [9].

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 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 oscillation 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 β-2 agonist just prior to surgery. Moderately controlled patients should add inhaled corticosteroids to their β-2 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]. Anti-muscarinics such as glycopyrrolate and atropine may decrease secretions and provide additional bronchodilation 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 bronchodilation without decreasing arterial pressure or systemic vascular resistance. However, ketamine-induced bronchodilation 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, suggamadex does not completely eliminate the risk of airway hyperreactivity in patients with underlying disease. Though available in other countries, suggamadex 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 CO_2 waveform, or decreased/absent CO_2 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 CO_2 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 tocolyticproperties

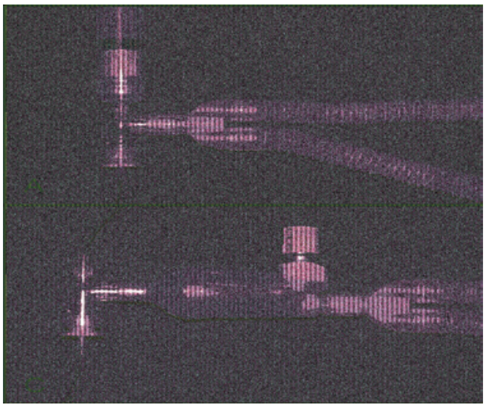

Figure 3: Options for the delivery of inhaled medications to intubated children. **A:** Metered dose inhaler (MDI) actuated inside a 60 ml syringe and connected to the gas-sampling port of the circuit elbow. **B:** Delivery via a 19G intravenous catheter advanced out of the end of the endotracheal tube. **C:** Valved MDI spacer positioned between the circuit "Y" and the endotracheal tube. **D:** Jet nebulizer positioned in the inspiratory limb of an intensive care unit ventilator circuit. Used with permission [69].

[57,70-73]. Theophylline (or intravenous aminophylline) may be added for refractory bronchospasm [26,74].

Magnesium has been used in children with severe asthma who were unresponsive to traditional treatment with β-agonists and corticosteroids [75]. Inhaled magnesium sulfate has been suggested as a useful treatment for severe asthma exacerbations in adults as well [76,77]. Although meta-analysis does not conclusively support a benefit of *inhaled* magnesium given to adults with acute asthma exacerbations, it does support the addition of *intravenous* magnesium to treat both adults and children with acute asthma [78,79]. Intravenous magnesium sulfate administration may attenuate tachycardia associated with β-agonist treatment [76]. Extracorporeal membrane oxygenation (ECMO) is reserved for patients with severe bronchospasm refractory to maximal medical therapy. ECMO has been used successfully with good neurological outcomes to treat status asthmaticus in children [80].

Postoperative Management

The postoperative care of the asthmatic patient is often dictated by the intraoperative course. If the surgery was uneventful, and pain, nausea, and respiratory status are well-controlled, asthmatics may safely be discharged either to home or to an appropriate inpatient unit without further intervention. However, in the setting of significant intraoperative complications such as severe bronchospasm, special care must be taken to ensure patient safety during the postoperative period. Postoperative ventilation should be considered, allowing time for further medical management, recovery of airway function, and metabolism of neuromuscular blockers without the need reversal agents [35]. It is prudent to readministerβ-agonists prior to emergence and throughout the postoperative recovery period as needed for recurrent bronchospasm. Maintaining a head of the bed up position is preferable for prevention of atelectasis. Recovery and maintenance of ventilatory gas exchange become possible with early respiratory rehabilitation, leading to prevention of further pulmonary complications and allowing for earlier hospital discharge [81].

Postoperative epidural anesthesia is useful to block afferent pain pathways from abdominal viscera; this reduces hypoventilation due to "splinting", maintains respiratory muscle function and is associated with improved pulmonary outcomes in addition to superior pain control [82]. The use of epidural anesthesia with local anesthetics increases tidal volume and vital capacity and preserves diaphragmatic function following thoracotomy or laparotomy. Systematic review supports use of either epidural or nerve block analgesia following thoracotomy [83]. At present, no consensus has been reached regarding systemic opioid administration or drugs for use in the epidural space, however there is no doubt that appropriate postoperative analgesia increases patient quality of life [84,85].

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 decrease postoperative pulmonary complications in asthmatics.

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