

ANESTHESIA IN CHILDREN WITH ASTHMA AND RHINITIS

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The incidence of asthma is increasing worldwide, but morbidity and mortality are decreasing, because of improvements in medical care. Although the incidence of severe perioperative bronchospasm is relatively low in asthmatics undergoing anaesthesia, when it does occur it may be life-threatening. Preoperative assessment of asthma should include a specialized medical history and physical examination as well as pulmonary function testing. Potential trigger agents should be identified and avoided. In many asthmatic patients treatment with systemic corticosteroids and bronchodilators is indicated to prevent the inflammation and bronchoconstriction associated with endotracheal intubation. Nonetheless, acute bronchospasm can still occur, especially at induction and emergence, and should be promptly and methodically managed.

The asthmatic patient undergoing surgery is at risk for a perioperative asthma attack and respiratory complications such as aspiration, bronchospasm, and prolonged mechanical ventilation (1). General anesthesia may trigger asthma exacerbations through several mechanisms, including alteration of diaphragmatic function, impaired ability to cough and decreased mucociliary function. Furthermore, placement of the endotracheal tube itself is a potent airway irritant that may trigger bronchoconstriction in asthmatic patients.

The observation that rhinitis and asthma are often associated and share similar etiological and immunopathological features led to the concept of "united airway disease" (2). Asthma and rhinitis are common clinical conditions, and anesthesiologists need to be familiar with these disorders in order to select anesthetic agents and approaches that will optimize patient status. In many cases, a coordinated "team approach" is required for such patients who require surgery (3).

The aim of this chapter is to underline the need for an accurate clinical and functional evaluation of subjects with

asthma and/or rhinitis undergoing surgical procedures which require general anesthesia, as well as to suggest a preventive pharmacological approach for reducing the risk of perioperative adverse events.

PREOPERATIVE MANAGEMENT

Patients with asthma

In non-emergency situations, the majority of patients with a history of asthma will need to be assessed by pulmonologists or physicians trained in respiratory diseases to assess the severity of the disease and its control. Currently, most internal medicine guidelines focus on cardiac evaluation, but a few include pulmonary function testing or objective assessment of respiratory symptoms as part of a routine preoperative evaluation. Indeed, a preoperative careful clinical and functional evaluation of respiratory system is essential and should be completed at least 1 week before surgery to optimize treatment plans.

- *Medical history* - Recent exacerbations, increased

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use of bronchodilators, emergency visits or hospital admissions for asthma are important risk factors for perioperative bronchospasm. Historical elements include the number of times per week the patient requires a short-acting beta-agonist (SABA), how often oral corticosteroids (OCS) have been used in the previous months and for what duration, and whether the patient currently uses inhaled corticosteroids (ICS) or has used them in the past. Activities of daily living, physical status, presence of infectious symptoms, diagnosed allergies, factors triggering asthma exacerbations, and previous history of reactions during anesthesia must also be investigated.

- *Physical examination* - Physical examination is essential for the early detection of acute respiratory signs. In the absence of an acute episode, physical findings vary with the severity of the disease: patients with mild asthma may have normal findings upon physical examination, but patients with more severe disease are likely to have signs of chronic respiratory distress and chronic hyperinflation (i.e., increased antero-posterior diameter of the chest). Lung examination may reveal prolongation of the expiratory phase, expiratory wheezing and coarse crackles. Clubbing of the fingers is not a feature of straightforward asthma and indicates a need for more extensive evaluation and work-up to exclude other conditions, such as cystic fibrosis.

- *Imaging* - A chest X-ray is rarely useful unless the presence of other pathological conditions in addition to asthma or the presence of atelectasis or pneumothorax following an acute asthmatic attack is suspected.

- *Pulmonary function tests* - A preoperative spirometry is recommended in all subjects with a history of asthma. Spirometric evaluation is essential in individuals suffering from severe bronchospasm, as well as in those patients with uncertain history or who have a limited perception of their respiratory symptoms. Conventional spirometry is often not reliable in patients younger than 5 years; in this age group newer techniques, such as measurement of airway resistance using impulse oscillometry system, are commonly used.

A forced expiratory volume in one second (FEV_1) or forced vital capacity (FVC) lower than 70% predicted, as well as an FEV_1/FVC ratio below 80%, are considered risk factors for perioperative obstructive complications. Documentation of reversibility of airway obstruction (increase of $FEV_1 \geq 12\%$ and 200 mL from baseline) after a standard dose (400 mcg) of salbutamol is central to the diagnosis of asthma. It is important to emphasize that a relevant but "stable" reduction in FEV_1 values with a low degree of reversibility of airway obstruction does not necessarily imply an absolute contraindication to surgical procedures, including those involving endotracheal intubation.

Asthmatics with reversible airway obstruction and those with high degree of bronchial hyperresponsiveness (BHR) are at higher risk of perioperative/postoperative obstructive complications. For this reason, individuals suffering from symptoms of a suspected asthmatic etiology (e.g. persistent cough) or diseases often associated with BHR (e.g. allergic rhinitis, exposure to passive smoking) should undergo spirometry and, in selected cases, nonspecific bronchial provocation tests to quantify the degree of their BHR (4).

- *Markers of inflammation* - Markers of inflammation can be determined in blood, urine and expired gas. Peripheral blood eosinophilia is a simple measure which correlates poorly with the severity of asthma. Other serum markers, as the eosinophilic cationic protein, have some correlation with asthma severity. Currently, the only non-invasive direct measure of airway inflammation is expired nitric oxide (ENO). ENO is a sensitive indicator of airway inflammation in children, and ENO levels more than 20 parts per billion are a reliable and sensitive screening tool to diagnose asthma in high-risk untreated patients (5). ENO levels do not correlate with asthma severity, but serial measurements are useful in monitoring the activity of the disease, assessing asthma control and evaluating compliance and response to therapy.

- *Categorization of asthma severity* - Asthma severity is defined as "the intensity of the disease process prior to initiating therapy" and may help in determining the treatment in a patient who is not on any controller medication. Asthma severity is classified according to the impairment and risk related to disease, which are measured by frequency and severity of symptoms, including nocturnal symptoms, characteristics of acute episodes, pulmonary function and exacerbations prior to initiating treatment. Assessment of asthma severity should help to both stratify patients for risk of pulmonary complications and alert the anesthesiologist to the choice of preoperative therapy. According to severity, asthma can be divided into four categories (6):

- *Mild intermittent*: patients with mild symptoms and who typically use SABA on an as needed basis.

- *Mild persistent*: patients with clinical and functional severity to require a daily controller medication, such as a low-dose ICS, or a leukotriene receptor antagonist (LTRA).

- *Moderate persistent*: patients with clinical and functional severity to require a low or medium-dose of ICS together with a long-acting beta-agonist (LABA) or LTRA.

- *Severe persistent*: patients who have established daily symptoms and typically are on multiple medications (such as high-dose ICS, bronchodilators, OCS).

The characteristics in this classification system should

not be considered fixed because asthma severity widely varies and may change over time.

- *Assessment of asthma control* - The importance of the relationship between asthma severity and asthma control is essential in children undergoing surgical procedures. The goals of asthma control are: minimal or no symptoms during the day or night, full physical activity including exertion, decreased use of rescue beta2-agonist medication, prevention of exacerbations, maintenance of normal pulmonary function, and minimal or no adverse effects from medications. An optimal control of asthmatic symptoms constitutes the gold standard if the patient is to be considered as having a "reasonably low" risk for perioperative bronchospasm. The most frequent causes of uncontrolled asthma are poor compliance to treatment, inadequacy of the inhalation technique, or wrong diagnosis. Only some children truly have asthma poorly sensitive to treatment with steroids (7). The role of asthma control in reducing the risk in asthmatics undergoing general anesthesia is showed in Fig. 1.

A simple questionnaire can identify children with poorly controlled asthma who suffer from asthma symptoms that limit their daily activities. A panel of asthma specialists developed two questionnaires (Childhood Asthma Control Test, C-ACT score), one for children aged 4-11 years and another for those aged >11 years. Each question offers several answers, which are scored on a scale from 0 to 5. Patients are classified into one of 3 groups on the basis of their C-ACT score: very poorly controlled (score of ≤ 2), not well controlled (score of 13-19) or well controlled (score ≥ 20) (8).

A small group of children suffering from asthma is in life-threatening conditions. These children may have "unstable" asthma, with sudden onset and rapid developing asthmatic attacks. History of serious or life-threatening attacks, especially if admission to intensive care unit was required, is indicative of high-risk for perioperative bronchospasm.

- *Avoidance of risk/complicating factors* - Risk factors for pulmonary complications identified in subject with asthma are obesity, stress, perioperative aspiration, upper abdominal surgery and thoracic surgery near the diaphragm. Preoperative control of factors known to trigger asthma, such as allergens, passive smoking, infections and gastro-esophageal reflux, is important.

- *Preoperative treatment* - Over the past decade, there has been increasing evidence to support efficacy and safety of pharmacologic treatment of asthma before surgery. However, the role and benefits of preoperative medication to limit pulmonary complications in asthmatic patients have not been determined. A stepwise approach to preoperative treatment of asthmatics undergoing general anesthesia based on their level of control of asthma

symptoms is suggested (9).

First step: Patients who, at the time of their visit, show no symptoms, no need for regular anti-asthma medications, no symptoms in the past 12 months, normal spirometry, and a high C-ACT score (>20 points), are included in this step. These individuals do not require a preoperative therapy.

Second step: Includes patients that are not on regular treatment with ICS, but use SABA and show clinical and functional data suggesting incomplete control of their disease. In these conditions, the associated use of LABA/ICS for at least 1 week is suggested, as well as an additional treatment with oral prednisone (0.5 mg/kg/day) for 5 days before surgery.

Third step: Patients who are using a regular anti-inflammatory therapy are included here. Patient who are controlled (C-ACT score >20 points) should continue their usual therapy and do not require additional treatment before surgery. Patients who are not controlled (C-ACT score <20 points) require an additional short-term treatment with prednisone (0.5 mg/kg/day) for 2-3 days before surgery.

Fourth step: Includes patients with compromised (obstructive) respiratory function, despite adequate doses of ICS+LABA and occasional use of OCS. These patients show persistent symptoms, compromised (obstructive) spirometric values ($FEV_1 < 80\%$ predicted) and a low C-ACT score. In these clinical conditions, continuing the use of ICS+LABA and a preoperative/postoperative treatment with prednisone (0.5 mg/kg/day) is suggested.

Fifth step: Includes severe asthmatics with persistent and severe symptoms who use regular therapy with ICS+LABA and need daily administration of OCS to maintain an acceptable respiratory function. Spirometric values are compromised ($FEV_1 < 80\%$ predicted) and the ACT score is very low. These individuals are at the highest risk of perioperative complications, including life-threatening bronchospasm. Preoperative treatment includes continuing ICS+LABA, an increased dose of already used OCS for at least 5 days before surgery, and hydrocortisone (100 mg/i.v. every 8 h) before and soon after the surgical procedure to take into account patient's fasting.

Patients with rhinitis

The most important nasal disorders that should be assessed during the preoperative visit are allergic rhinitis, upper respiratory infections (URI), obstructive sleep apnea syndrome (OSAS). All these conditions have a high prevalence in pediatric anesthesia practice, therefore it is crucial for the pediatric anesthesiologist to anticipate, recognize, and treat them.

- *Allergic rhinitis* - BHR, a characteristic feature of

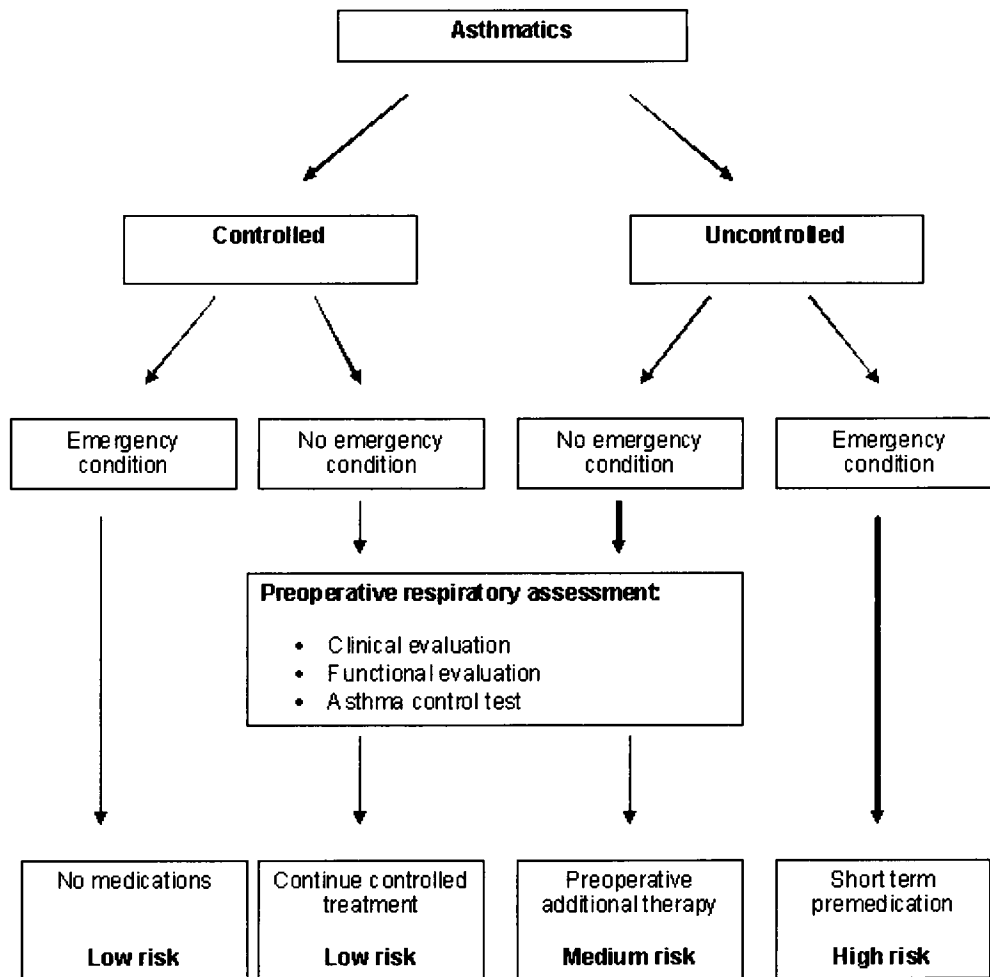


Fig. 1. The role of asthma control in reducing the risk of perioperative bronchospasm in asthmatics undergoing general anesthesia (adapted from ref. 9)

asthma, is frequent in patients with allergic rhinitis (10–40% of cases) and 30–40% of patients with allergic rhinitis have coexisting asthma (10). Patients with BHR are at risk for severe bronchospasm during general anesthesia, that may readily be precipitated by instrumentation, a variety of drugs and perioperative problems such as aspiration, infection, or trauma (11). Although there are no studies demonstrating that patients with allergic rhinitis without symptoms of asthma are at risk for perioperative respiratory complications, investigating the presence of BHR in the preoperative period is recommended. In patients with high degree of BHR, a preoperative antiasthmatic treatment should be considered.

- *Upper respiratory infections* – URI are the primary reason for cancellation of elective surgery in children. The rationale for this practice is based on data suggesting an association between the administration of anesthesia to a child with URI and the appearance of respiratory complications. Although some studies suggest that anesthesia for a patient with URI increases the risk of laryngospasm, bronchospasm, atelectasis, and arterial oxygen desaturation in the perioperative period, others suggest that children with an acute, uncomplicated URI have no increased morbidity (12). Moreover, since children suffer an average of 6 URI per year, if all recent URI were a reason for postponing surgery, there will be

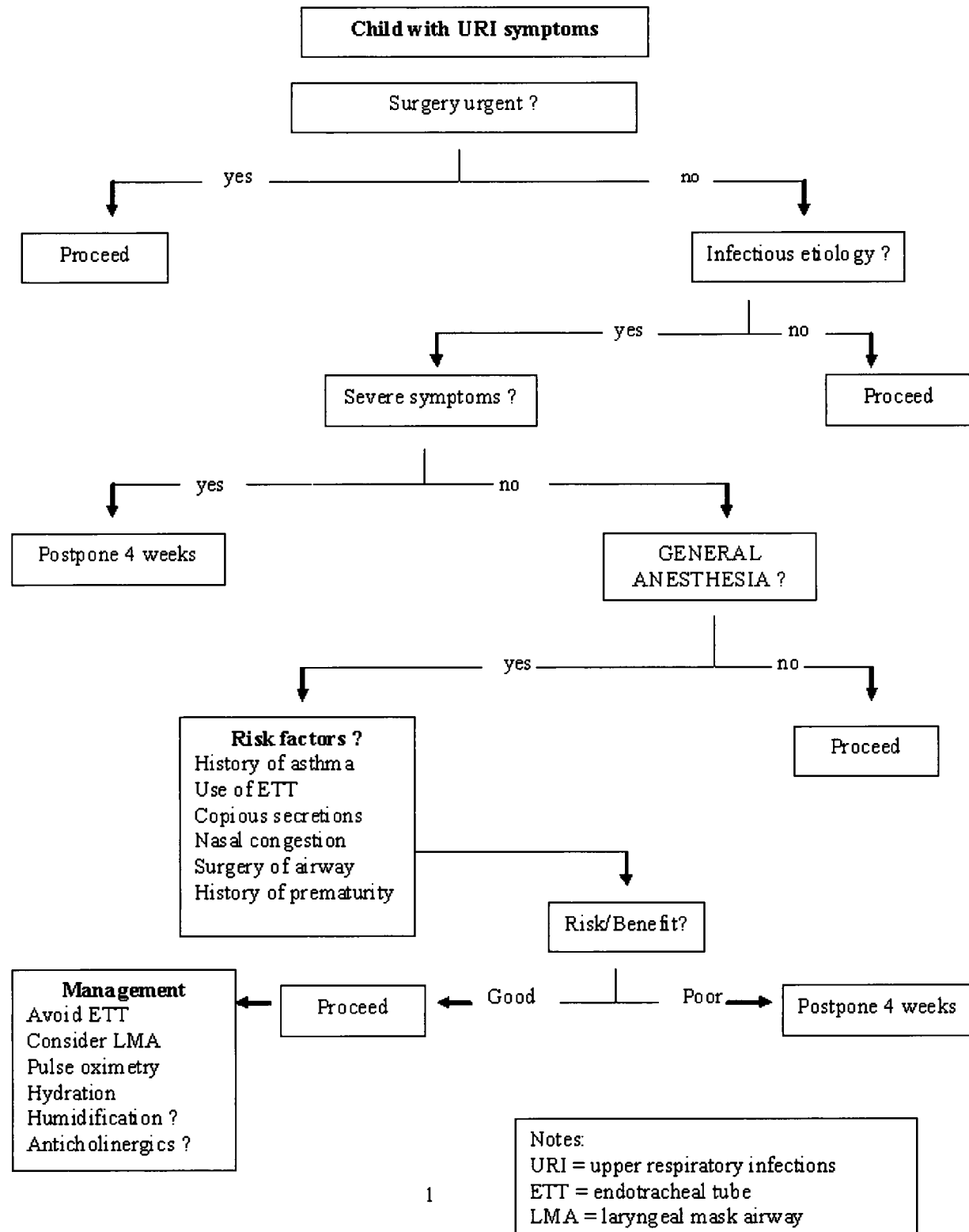


Fig. 2. Suggested algorithm for the assessment and anesthetic management of the child with an upper respiratory infection (adapted from ref. 14)

only a few weeks in which the child is asymptomatic and considered fit for surgery.

Some risk factors are identified for development of respiratory complications in patients with URI. These are related to the patient (children under 1 year of age, presence of fever, nasal congestion, history of prematurity or bronchopulmonary dysplasia, parental smoking, congenital abnormalities of the airways), the type of surgery (surgical procedure involving the airway) or anesthesiological procedure (tracheal intubation).

It is important to consider that, although most viral URI are self-limiting, they may produce BHR that persist for at least 6 weeks after infection. This may have important implications for children requiring anesthesia in the acute and convalescent periods, particularly if intubation is required (13). A suggested operative algorithm in patient with URI presenting for elective surgery is reported in Fig. 2 (16).

- *Chronic nasal obstruction with OSAS* – OSAS is a breathing disorder characterized by a repeated collapse of the upper airway with periods of apnea. In children, the major cause of OSAS is adenotonsillar hypertrophy; in some cases, OSAS is part of other diseases, such as obesity, craniofacial syndromes (e.g. S. Down, S. Pierre-Robin, S. Apert), cranial base disorders (S. Arnold-Chiari, achondroplasia), neuromuscular disorders (cerebral palsy), and infiltrative disorders (mucopolysaccharidoses). Patients with OSAS are at increased risk of developing arterial hypoxemia during the postoperative period, both in the early (first 24 hours) and late phase (2-5 days). Children with severe OSAS have depressed responses to hypoxia and hypercarbia which can be aggravated by inhalational and intravenous anesthetics. The frequent hypoxic events lead to increased levels of endogenous catecholamines, hypoxic vasoconstriction of the pulmonary artery, and eventually to pulmonary hypertension. This chain of events increases the risk of life-threatening episodes in the perioperative period. For these reasons, children with history of OSAS should perform preoperative polysomnography and be closely monitored in a pediatric intensive care unit postoperatively (15).

INTRAOPERATIVE MANAGEMENT

- *Premedication* – Stress is closely related to the development of asthma. In patients with asthma and preoperative anxiety, the use of sedatives can decrease tidal volume and should therefore be avoided. The administration of atropine is supported by its inhibitory effects on vagal reflexes, but some experts advise against using this drug, because of the risk of increased viscosity of airway secretions. In the future, preoperative

inhalation of anticholinergic agents that are highly selective for M3 receptors may play a more prominent role in premedication. Although commonly used to treat intraoperative tachycardia, beta blockers may cause smooth muscle contraction and should be avoided in asthmatics.

- *Airway management* – Many procedures commonly performed during anesthesia (e.g. laryngoscopy, intubation, suctioning of the airway) are potent stimuli which can potentially lead to bronchospasm. Preoperative combination of SABA and systemic corticosteroids can significantly prevent increased airway resistance or postoperative respiratory complications (16). In addition, the combination of intravenous lidocaine and salbutamol in patients with BHR is much more effective than either agent alone (17).

- *Ventilator setting* – Pressure control ventilation is essential to avoid an increase in airway pressure. In patients with severe respiratory acidosis, excessive ventilation decreases PaCO₂ and causes alkalosis. This can lead to bronchoconstriction and cardiovascular complications such as arrhythmia.

- *Choice of anesthetics* – Many inhalational anesthetics have bronchodilator effects, mediated by the regulation of calcium channel activity. Sevoflurane and isoflurane are appropriate for use in patients with obstructive lung disease and are sometimes used for status asthmaticus refractory to other medical therapies. However, some inhalational anesthetics, such as desflurane, are unsuitable for anesthesia in patients with BHR for their irritative action on the respiratory tract (18).

Propofol has a protective effect against increased airway resistance during tracheal intubation, due to involvement of direct or vagal mediated relaxation of airway smooth muscles. Barbiturates, as compared to propofol, produce a weaker inhibition of airway contraction and may induce airway smooth muscle contraction when used alone. Ketamine has bronchodilator effects and is suitable in asthmatic patients (19). Opioids should be administered to suppress the cough reflex and to achieve deep anesthesia, but prolongation of these effects can cause postoperative respiratory depression. The use of opioids during intubation can prevent increased airway resistance, but muscle rigidity can decrease lung compliance and functional residual capacity, thus impairing ventilation. Opioid induced muscle rigidity can be decreased by the combined use of intravenous anesthetics and neuromuscular blocking agents (NMBA). Morphine displays histamine releasing effects and can cause bronchoconstriction (20).

NMBA with greater affinity for M2 than M3 receptors (pipecuronium and rapacuronium) can induce and worsen bronchoconstriction. However, NMBA with more affinity

for M3 receptors (vecuronium, rocuronium, pancuronium) can be safely used. Atracurium and mivacurium display dose-dependent histamine releasing effects and can cause bronchoconstriction. Anticholinesterase drugs (neostigmine or physostigmine) that inhibit NMBA also increase airway secretions and induce bronchospasm (21).

- *Treatment of intraoperative bronchospasm* - Bronchospasm is recognized by polyphonic, bilateral expiratory wheeze, prolonged expiration, active expiration with increased respiratory effort, increased airway pressures, rising end-tidal CO₂, and possibly hypoxemia. Hypoxemia may become manifest more quickly in the child where the respiratory drive has been blunted by anesthesia. Bronchospasm may usually be treated effectively by inhaled beta₂-agonists, either nebulized or through a metered-dose inhaler with a spacer via the tracheal tube. Intravenous salbutamol or aminophylline may be used to treat severe bronchospasm, and the evidence to favor one over the other in children is scanty. Hypokalemia is a side-effect of almost all anti-asthmatic drugs and carries a theoretical risk of arrhythmia which is fortunately rare in practice. Other options include intravenous magnesium or increasing concentrations of volatile anesthetics. Children who have anything other than minor bronchospasm should also receive corticosteroids if they have not already done so (22).

POST-OPERATIVE CARE

Non steroidal analgesic anti-inflammatory drugs are frequently used in pediatric surgery, often administered immediately after induction of anesthesia. The association of use of analgesics with a sudden worsening of asthma is object of discussion. Although asthma due to aspirin is much less frequent in children than adults, this may occur anyway. Ibuprofen and diclofenac are used more frequently than aspirin in children, but studies on the safety of these drugs are limited by the small number of patients involved.

CONCLUSIONS

Children with asthma or rhinitis frequently receive anesthesia safely and without incidents. A surveillance on possible risks, careful preoperative assessment and preparation together with good preoperative control of asthma can reduce the incidence of life-threatening perioperative complications. Anesthesiologists should also be aware of recent guidelines for the proper management of patients with airway hyperresponsiveness.

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