Reactive Airway Disease: Anesthetic Perspectives

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This review aims to provide anesthesiologists with a concise physiological and pharmacological background that can minimize the occurrence of bronchospasm in the perioperative period, as well as a guide to recognition and appropriate treatment should airway constriction occur.

The label "reactive airway disease" is usually applied to patients with dyspnea, wheezing, cough, and production of sputum. Almost invariably there is a history of inhaled bronchodilator use. A more specific term "airway hyperreactivity" has been recommended (1) because these patients develop airway narrowing more readily and more intensely than normal in response to a variety of stimuli (Fig. 1).

The mention of such airway hyperactivity immediately focuses on the asthmatic with intermittent bouts of severe airflow obstruction. However, it is important to emphasize that heightened airway reactivity also occurs in patients with chronic bronchitis and emphysema as well as allergic rhinitis and upper and lower respiratory tract infections. The latter patients may actually be more at risk for perioperative bronchospasm than many asthmatics. In the latter, therapy is often optimal, and if not, patients can usually indicate so. Indeed, Warner et al. (2) found a surprisingly low frequency of perioperative bronchospasm in patients with asthma. This contrasted strongly with their observations in smokers with airway obstruction (3).

Mechanisms Of Airway Hyperactivity

When dealing with reactive airways, the goal is to restore the caliber of the airways from their constricted state to their basal resting state. Actually, in this basal state, a mild tonic constriction exists in all normal human airways. This is largely maintained by efferent vagal activity and is readily abolished by antimuscarinics such as atropine. The physiological importance of this normal resting tone is an airway size that provides balance between anatomic dead space and airway resistance to gain efficiency in both gas exchange and work of breathing (Fig. 2).

The exaggerated responses of patients with airway disease have been ascribed to numerous factors including, most simply, reduced resting airway caliber. Because resistance is inversely related to the fourth power of the airway radius, any absolute decrease in the radius of an already constricted airway increases resistance more than the same absolute decrease in the radius of a larger or more dilated airway. However, baseline airway caliber does not account for all of the increase in airway responsiveness. The latter is also influenced by the presence of mucosal edema and inflammation and the volume of airway secretions.

Airway hyperactivity has often been depicted as a simple autonomic imbalance with a relatively increased parasympathetic activity in the lung. Sympathetic innervation in the lung is very limited and difficult to identify. Instead, the major sympathetic influence on airway caliber occurs via circulating catecholamines that act primarily on the β_2-receptors to produce bronchodilation. The parasympathetic nervous system controls both the baseline tone as well as the rapid changes in airway caliber in response to airway stimulation. Within the airway wall sensory receptors alter bronchial smooth muscle tone through the parasympathetic vagal pathways. The most important of these are the rapidly adapting irritant receptors found throughout the mucosa of all the cartilaginous airways but most prominent in the trachea and especially at the carina. They respond to mechanical irritation, thermal stimuli, and irritants such as inhaled particle of gases. Airway edema and histamine reflexes also elicit their activity, which results in reflex cough, bronchoconstriction, and mucus secretion.

The efferent parasympathetic pathways pass down the vagus nerve to synapse in ganglia within the airway walls (Fig. 3). The postsynaptic membranes of these intramural ganglia contain nicotinic-cholinergic receptors (NC). These receptors are activated by acetylcholine (ACH). This activation can be modified by muscarinic receptors (M_1), which are present in these same autonomic ganglia. From this point, short postganglionic fibers pass to airway smooth muscle and submucosal glands. Presynaptic vesicles release ACH on stimulation to produce contraction of smooth muscle and mucus secretion via action on the postjunctional muscarinic (M_3) receptors. The further release of ACH is also attenuated by activation of prejunctional fibers. As such, these M_2 inhibitory receptors may

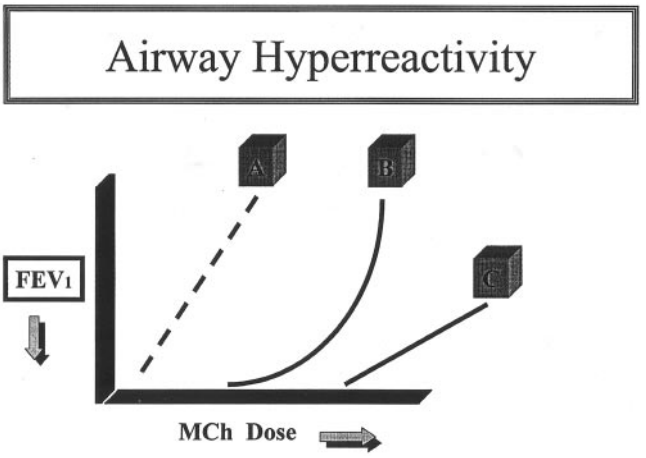

Figure 1. Decreases in forced expiratory 1-s volume with increasing doses of an acetylcholine analog bronchoconstrictor, methacholine (Mch), to illustrate the nature of airway hyperreactivity. The response is provoked more easily (at a lower dose) and is more intense than in normals (c). A = response in an untreated asthmatic; B = response of a treated asthmatic.

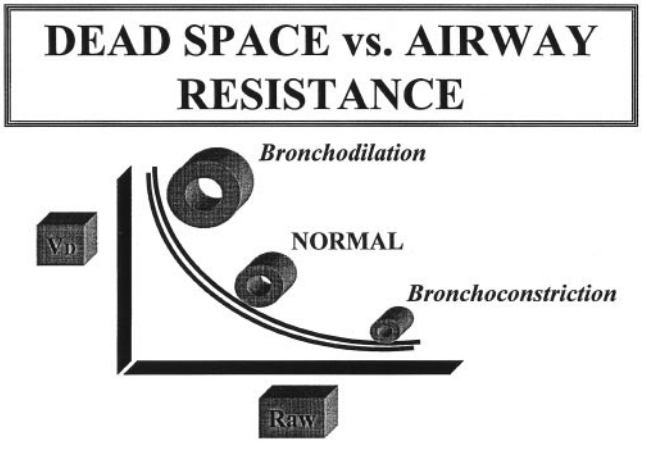

Figure 2. Relationship between anatomic airway dead space (Vd) and airway resistance (R_{aw}) in the normal control state and after bronchodilation and bronchoconstriction. Note that with bronchodilation as R_{aw} decreases Vd increases, whereas with bronchoconstriction Vd decreases as R_{aw} increases.

serve to limit the degree of cholinergic bronchoconstriction by providing a negative feedback to ACH release.

Viral infections appear to be associated with significant decreases in neutral endopeptidase, an airway enzyme responsible for tachykinin degradation, and with increased bronchoconstriction in response to electrical stimulation of the vagus (4). This increased response to afferent stimulation occurs in the face of a normal smooth muscle (M_3) response to ACH. Thus, increased release of ACH is likely from the loss of the inhibitory function of the M_2 receptors on further release of ACH. This absence of negative feedback to ACH release allows cholinergic or neurally mediated bronchoconstriction to be potentiated.

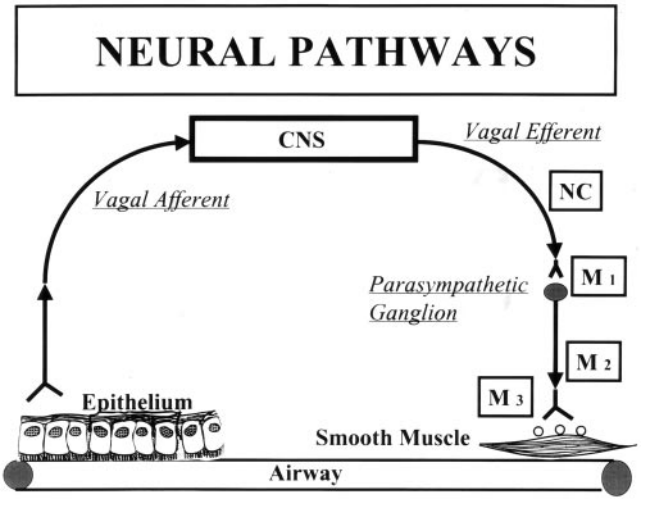

Figure 3. Diagrammatic representation of parasympathetic afferent and efferent neural pathways that affect airway caliber. The afferent fibers arise from the epithelial layer of the airway lumen. CNS = central nervous system; NC = nicotinic cholinergic; M_1 = muscarinic receptors in ganglia within the airway wall; M_2 = prejunctional muscarinic receptors; M_3 = postjunctional muscarinic receptors in airway smooth muscle.

Identifying Patients with Reactive Airways

Careful preoperative identification of patients at risk for perioperative bronchospasm is important in planning a rational approach for anesthetic care. Clinical assessment is hampered by the fact that no single best test exists for identifying or evaluating the airway hyperresponsiveness. Respiratory symptoms, which in young adults appear highly predictive of increased bronchial reactivity, consist principally of nocturnal dyspnea and chest tightness on awakening and an associated breathlessness and wheezing in response to various respiratory irritants such as cold air. Such symptoms are typically present in patients referred for pulmonary function testing to identify the degree of airway constriction and its reversibility.

Values obtained with forced exhalation during clinical spirometry, such as forced expired volume in one second (FEV_1), reflect airway resistance and help to estimate the degree of variability. Unfortunately, the normal day-to-day variability is exaggerated in patients with airway obstruction. Thus, increases in FEV_1 with bronchodilators must exceed 15% to be considered evidence of significant bronchodilation or reversibility of airway obstruction (5). Bronchodilation as reflected by forced expiration seems to be dependent on the baseline degree of constriction. The most dramatic responses are observed with moderate degrees of airway obstruction, whereas very mild or very severe disease is associated with far smaller changes. In addition, the reduction of dyspnea with bronchodilation seems better associated with improvements in forced inspiration. It appears that expiratory airway

collapse during the forced maneuver hampers detection of smooth muscle relaxation (6).

Often, precise testing is impractical preoperatively, and clinicians must instead rely on a careful history to identify factors suggesting an increased likelihood for perioperative bronchospasm. One of the most important is a history of a recent upper respiratory infection. It is well recognized that the clinical state of asthmatic and bronchitic patients often deteriorates markedly when they suffer viral respiratory tract infections. In normal subjects, viral upper respiratory infections cause a striking increase in bronchial reactivity that appears to persist for 3 to 4 wk after infection (7). Because clinical studies suggest much of the bronchoconstriction occurs thorough vagal reflexes, pretreatment with vagal blocking doses of atropine (2 mg) or glycopyrrolate (1 mg) before induction of general anesthesia may be valuable if surgery must be performed immediately.

In patients with a prominent smoking history, the desirability of discontinuing smoking is usually raised. Cessation of smoking is followed by a decreased volume of airway secretions, less airway reactivity, and improved mucociliary transport, but these benefits take several weeks to develop (8). In the short term (48–72 h) there may actually be increased reactivity and secretions such that the only actual benefit may be the decrease in carboxyhemoglobin content and thus better oxygen delivery to the tissue (9).

Pharmacologic Therapy

Parasympathetic innervation provides the major influence on airway smooth muscle by releasing acetylcholine onto muscarinic receptors and causing contraction and an increase in airway secretions. The process results from a sequence of intracellular events involving phosphoinositide hydrolysis and calcium release in contrast. Sympathetic innervation of airway is sparse and difficult to identify. Nevertheless, the major therapeutic efforts for dealing with bronchial reactivity have employed drugs with sympathetic activity.

β-Adrenergics

These drugs form the cornerstone of therapy for prophylaxis as well as reversal of bronchospasm. The classic catechols have been replaced by longer acting resorcinols and saligens with greater receptor "selectivity." At present, albuterol is still the most popular because of its marked β_2 selectivity, i.e., bronchial smooth muscle relaxation occurs with little or no undesirable β_1 effects such as tachyarrhythmias. Much of the β_2 selectivity results from the aerosol route of administration and the local deposition in the airways to produce bronchodilation. If given IV, albuterol is less effective as a bronchodilator, and the plasma concentrations needed effectively abolish β_2 selectivity (10).

The important role of β-adrenergic agonists in the therapy of bronchoconstriction causes concern for the use of β-adrenergic antagonists (β-blockers) in the presence of reactive airway disease. The treatment of tachycardia, hypertension, or angina pectoris with such drugs can precipitate or worsen bronchoconstriction. The replacement of propranolol with more cardioselective β-blockers can reduce, but not eliminate, the risk. When given in small oral doses, β_1-selective drugs such as atenolol or metoprolol do not seem to produce clinical deterioration of airway function. Other observations in cardiac patients with airway obstruction (11) indicate that an effective IV therapy can be achieved with the short-acting compound esmolol without incurring any adverse increase in airway reactivity.

Methylxanthines

The compounds, which include theophylline and its relatives, are the mainstays of chronic bronchodilator therapy. Aminophylline, the ethylene-diamine water-soluble salt of the theophylline, is roughly 80% theophylline. Despite speculations about theophylline's action including adenosine antagonism and phosphodiesterase inhibition, data in subjects with normal airways suggest that bronchodilation occurs largely as a result of catecholamine release (12). Indeed, IV aminophylline produces a dose-related increase in catecholamines in humans (13). Interestingly, amrinone, another compound with phosphodiesterase-inhibiting activity, is not associated with this catecholamine release, but seems to attenuate methacholine-induced bronchoconstriction, presumably by direct action on airway smooth muscle (14).

Despite its rather narrow therapeutic range, aminophylline is considered the standard maintenance therapy in patients with airflow obstruction. Its role in treating acute bronchospasm has been increasingly questioned. Meta-analysis has underscored the scarcity of data supporting the rational use and efficacy of aminophylline for treatment of acute bronchospasm in the emergency setting (15). The role of aminophylline is treating or preventing bronchospasm during anesthesia also sorely lacks objective efficacy data as compared with β agonists.

Corticosteroids

Although their precise mechanisms remain unclear, parenteral steroids are important adjuncts in preoperative preparation of patients with reactive airway disease and treatment of intraoperative bronchospasm. Dosage equivalents of 1–2 mg/kg hydrocortisone are usually recommended for good clinical response. In

patients treated with steroids these are usually doubled because lower plasma corticoid levels often result from usual doses. Steroids suppress airway inflammation, mucous secretion, and the release of activity of mediator substances, all of which tend to decrease the maximal bronchoconstrictive response. They also appear to enhance and prolong the therapeutic effects of the β-adrenergic agonists. Preoperative administration is particularly important because the airway effects require some time to develop. In mechanically ventilated patients with airflow obstruction, methylprednisolone (0.8 mg/kg) improved respiratory mechanics 90 min after IV injections (16).

Other Anti-Inflammatory Agents

Although bronchodilators are the mainstays of symptom control, the role of chronic inflammation in reactive airway disease cannot be ignored. Steroids, especially in the inhaled form, address the latter to some extent. Other agents, such as cromolyn and nedocromil, that inhibit mast cell release of histamine and other substances are important, particularly in asthmatics. These drugs, however, have no actual bronchodilating effect. They merely inhibit bronchoconstriction.

Mast cells, as well as macrophages, produce other bronchoconstrictive substances, leukotrienes, via the lipoxygenase pathway of arachidonic acid metabolism. Antileukotriene drugs take two approaches, either direct inhibition of the enzyme by drugs such as zyleuton (Zyflo) or antagonism of the receptor by montelukast (singular) or Zakfurast (Accolate). Blockade of leukotriene activity does not seem to improve airflow obstruction in a manner comparable to that achieved by β adrenergics or steroids. The emergence of side effects may eventually limit their use (17).

Anticholinergic Agents

The anticholinergic (antimuscarinic) compounds have provided limited therapy because of the troublesome systemic side effects such as dry mouth, blurred vision, and tachycardia so common with atropine. Atropine's quaternary ammonium congeners are poorly absorbed as aerosols and produce significant prolonged bronchodilation with few side effects. They offer an alternative or complementary therapy for airway obstruction, especially in patients who experience tremor or tachycardia with β-adrenergic drugs despite an incomplete bronchodilator response. Presently, only ipratropium bromide is available as metered dose aerosol, but its rather low concentration per puff (20 μg) renders adequate therapy somewhat awkward for adults.

Another quaternary compound now in Phase III clinical trials is Tiotropium Bromide. Given once daily as an inhaled powder it is more effective than ipratropium inhaled three times daily. In addition to its long duration, Tiotropium appears to have little effect on the M_2 muscarinic receptors and a much more profound blockade of M_3 receptors (18). Thus episodes of paradoxical bronchospasm, as reported with ipratropium, are not likely.

Glycopyrrolate, another quaternary compound familiar to anesthesiologists, produces prolonged bronchodilation when injected IV (18) or inhaled as an aerosol (19). Large doses of glycopyrrolate are required to prevent or reverse reflex bronchospasm although maximal bronchodilation occurs with considerably lower doses in normal patients (20). The maximum bronchodilating action of the anticholinergics is somewhat slow in onset (20–30 min) whether by inhalation or parenteral administration. Thus, they are more useful as prophylaxis than as treatment for active episodes of bronchospasm (21). Such prophylaxis can be readily accomplished by IV administration, ideally 20 to 30 min before induction of anesthesia. This will assure adequate time to achieve maximal effect while minimizing the time during which patients must endure the dry mouth sensation. Subsequent administration of glycopyrrolate solution may be accomplished by direct injection into the trachea. The latter limits problems with systemic side effects because the drug is not readily absorbed across the airway mucosa.

Airway Effects of Anesthetic Drugs

Inhalation anesthetics such as halothane produce bronchodilation and appear to prevent the development of bronchospasm. The major effect on airway caliber is the result of blocking airway reflexes and direct relaxing effects on airway smooth muscle (22).

Halothane has long been considered the agent of choice but its myocardial depressant action and arrhythmic effects in the presence of circulating catecholamines are limitations. Both enflurane and isoflurane equally prevented vagally medicated bronchoconstriction at equal multiples of MAC (23). Because such anesthetic levels (>1.5 MAC) may be difficult to achieve in some patients because of cardiovascular depression, other adjunct therapy for bronchospasm must be considered. Laboratory evidence (23) suggests that at lower doses of anesthetic (<1.0 MAC), halothane may be the most effective agent in reversing airway constriction. On the other hand, more recent clinical observations in humans indicate that sevoflurane at 1.1 MAC may be the most effective agent (24), especially in the presence of airway instrumentation. Desflurane, on the other hand, has little utility and may elicit bronchoconstriction in smokers (25).

IV Induction Agents

Customary hypnotic doses of thiopental leave airway reflexes largely intact, and bronchospasm may occur if

instrumentation of the airway is attempted. It has long been recognized that thiopental per se was not the cause of bronchospasm and is therefore not contraindicated in patients with airway disease. Actually, thiopental infusions (1.5 to 2.0 mg $\cdot$ kg^{-1} $\cdot$ h^{-1}) have been used during mechanical ventilation for status asthmaticus (26).

The bronchodilating actions of ketamine have been touted since its early clinical use and are largely attributed to release of endogenous catecholamines because the effects are eliminated by β-adrenergic blockade (27). Actual clinical data identifying bronchodilating actions of ketamine in humans are rather scant and largely subjective. The apparent inhibition of muscarinic receptors by ketamine suggests that some of the clinical effects may result from this mechanism as well (28).

Brown and Wagner (29) most recently showed in sheep that the bronchoprotective effects of both ketamine and propofol result from a neurally mediated mechanism, i.e., a diminished response to vagal stimulation. Direct effects on airway smooth muscle occur as well but only at concentrations well above those of clinical relevance.

Propofol, another short-acting anesthetic, has undergone extensive hemodynamic investigation but scant clinical study of its effects on airway functions. In patients requiring ventilation for acute respiratory failure, consistent decreases in airway resistance were noted after propofol administration (30). These results suggest that propofol may be useful for induction of anesthesia in the patient at risk for bronchospasm. Preliminary observations in asymptomatic asthmatics (31) also suggest that this might indeed be the case largely because of profound depression of airway reflexes with propofol. Etomidate, however, is as ineffective as thiopental in blunting airway reflexes (32).

Local Anesthetics

IV local anesthetics such as lidocaine have occasionally been suggested as part of the treatment of airway reactivity and intraoperative bronchospasm. It was long assumed that the major mechanism whereby lidocaine prevented bronchospasm was by blockade of the airway reflex response to irritation (33). However, recent observations also suggest a direct smooth muscle action on the basis of the ability to attenuate responses to ACH (34). Aerosol therapy offers little or no advantage over IV administration and may itself provoke bronchospasm because of direct airway irritation. Pretreatment with IV lidocaine may blunt this constriction response and enhance subsequent bronchodilation as well (35).

Narcotic Analgesics

Opioids are known to alter the activity of various neural pathways. Although they serve to modulate cholinergic transmission somewhat, they are also antitussive and provide some inhibiting effect on mucus secretion and neurally mediated microvascular leakage (36). Thus, they may serve to inhibit bronchoconstriction as well. Indeed, in patients with mild asthma morphine administration has been shown to inhibit vagally mediated bronchoconstriction (37).

Morphine in patients with airway obstruction gives rise to concern about increases in plasma histamine on airway function. Indeed, rapid IV histamine injection produces a decrease in static compliance and an increase in airway resistance as a result of direct effects of smooth muscle of alveolar ducts and bronchioles as well as a reflex vagal component (38). The response is of small magnitude and is very short lived ($<$1 min). This helps to explain the virtual absence of bronchospasm during countless histamine infusion studies and in patients with systemic mastocytosis (39).

The concern about histamine is heightened in the asthmatics, who are supposedly more sensitive to its bronchoconstricting effects than are healthy subjects. This has only been demonstrated with inhalation of histamine aerosols; there are no actual data with parenteral histamine administration. More importantly, pretreatment with β-adrenergic, atropine, or chlorpheniramine renders the response to histamine aerosols in asthmatics similar to those of normal subjects (40).

Concerns about histamine could be eliminated by choosing opioids that cause almost no histamine release, such as fentanyl and its derivatives. Fentanyl, by producing truncal muscle rigidity, would be expected to decrease respiratory system compliance and also to increase total respiratory resistance. These effects on the chest wall, however, can easily be offset by muscle relaxation to eliminate any confusion with bronchospasm.

It is important to note that fentanyl probably causes some degree of bronchoconstriction. Administration of fentanyl (5 mg/kg) to two groups of normal anesthetized paralyzed patients produced increases in respiratory resistance (41,42). Administration of atropine reversed a portion of this increased resistance, which thus appears to be the result of vagally induced contraction of airway smooth muscle.

Muscle Relaxants

Relaxants may produce unwanted autonomic nervous system effects, and can theoretically affect airway caliber and reactivity by promoting histamine release or by interacting with muscarinic receptors as structural analogs of acetylcholine. Because of their structure, neuromuscular blockers may block muscarinic receptors. Gallamine, for example, has been shown to block

muscarinic M_2 receptors. These receptors activate smooth muscle (M_2) receptors to produce contraction but also function as a negative feedback mechanism by limiting continued ACH release during further stimulation. Thus, with M_2 receptor block, there may be a removal of this inhibition to further ACH release and a potentiation of vagally mediated (usually irritant-induced) bronchoconstriction. Such M_2 blocking properties have also been reported for atracurium and pancuronium, but not vecuronium (43). The latter may also explain the mechanism of the bronchospasm resulting from rapacuronium (44).

Perhaps, a more important factor with regard to the use of muscle relaxants concerns the need to reverse their actions. By inhibiting the destruction of endogenous ACH, cholinesterase inhibitors such as neostigmine may increase airway secretions and can precipitate bronchospasm. These effects can be prevented by muscarinic antagonists, and it seems prudent to use larger than the customary doses of glycopyrrolate (0.5 mg) or atropine (1.0 mg) to minimize the possible muscarinic side effects of reversal. An alternate approach would be to avoid the need for reversal by infusing short acting relaxants. If reversal is necessary, it can be accomplished with edrophonium, a drug of much less muscarinic qualities and less tendency to constrict airway smooth muscle (45). Edrophonium appears to be antimuscarinic in doses used to reverse muscle relaxants (46).

Choice of Anesthesia: Regional Versus General

Whenever feasible, regional anesthesia constitutes an ideal choice in the patient with reactive airway disease because it eliminates the need for airway instrumentation and the possibility of eliciting airway reflexes. However, if high levels of sensory and motor block are required they may produce severe anxiety and actually incite bronchospasm. Also, the loss of expiratory muscle power may functionally limit some patients with airway obstruction not only in their ability to cough but also because of their need for active exhalation. Such patients may have even further difficulties because of surgical positioning.

Another concern with the high sensory and motor blockade with regional anesthesia is the associated blockade of sympathetic input to the lungs. Some case reports have speculated about a resultant increase in airway resistance. Groeben et al. (47) dispelled this notion and actually provided evidence that systemic levels of the local anesthetic associated with epidural anesthesia actually attenuated airway hyperreactivity.

When general anesthesia is required, the primary goal is the prevention of reflex airway constriction. This is best accomplished by avoiding mechanical stimulation of the airway in the presence of inadequate anesthesia. If wheezing occurs, it is important to identify the potential causes to limit the extent of the bronchospasm and render it more readily reversible with therapy. The inhaled anesthetics can accomplish this, but only after a significant depth of anesthesia as established. In such a setting it appears that sevoflurane may be the most effective (24). Ideally, tracheal intubation should not be attempted early, but the significant ventilation/perfusion mismatch characteristic of most patients with airway obstruction often delays the onset of anesthesia. In this situation, IV lidocaine (1–2 mg/kg) and cholinergic antagonists such as glycopyrrolate (0.5–1.0 mg) are helpful therapeutic adjuncts to prevent reflex airway constriction. β-adrenergic aerosols such as albuterol are also very effective when inhaled before the induction of general anesthesia (48). If rapid induction and tracheal intubation are essential, ketamine (1–2 mg/kg) or propofol (2–3 mg/kg), are logical preferences to thiopental or etomidate.

Intraoperative Bronchospasm

Diagnosis

In his extensive retrospective analysis of bronchospasm during anesthesia, Olssen (49) noted an incidence of one case per 634 anesthetics or 1.7 per 1000 patients. He confirmed the increased incidence in the presence of preexisting airway obstruction, particularly in the face of airway instrumentation. Bronchospasm was diagnosed by ventilatory difficulties characterized by increased peak airway pressures and expiratory wheezing. Although the simplest explanation for increased peak airway pressure is increased airway resistance caused by airway smooth muscle constriction, many other factors may be responsible (Fig. 4), any of which may lead to confusion with bronchospasm.

Some other less likely conditions that may present with clinical signs suggestive of bronchospasm include pulmonary edema, tension pneumothorax, aspiration of gastric contents, and pulmonary embolism. Therapy in these cases must center on correcting the mechanical problem or gas exchange abnormalities rather than the bronchospasm itself.

Therapy

The initial therapy may consist simply of increasing anesthetic depth. The use of profound levels of inhaled anesthesia may not be practical in severe bronchospasm because of difficulty delivering the drugs to the airways and the severe hypotension that may occur before achieving the desired bronchodilatation.

The key treatment for intraoperative bronchospasm is inhalation of sympathomimetics such as albuterol

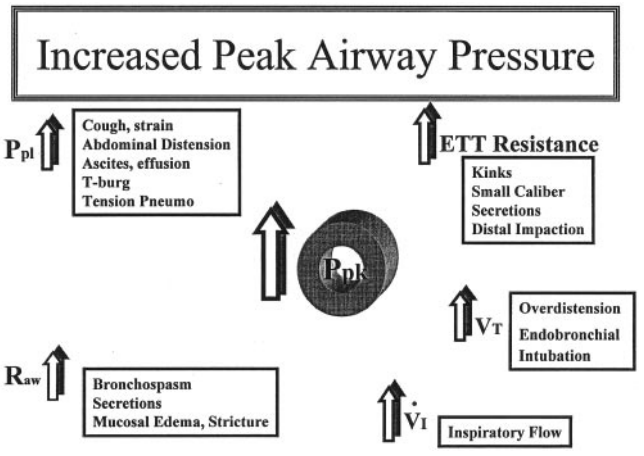

Figure 4. Increases in peak pressure (P_{pk}) may be because of increases in pleural pressure (P_{p1}), airway resistance (R_{aw}), endotracheal tube (ETT) resistance, tidal volume (Vt), or inspiratory flow (V_I).

(200–400 μg). These drugs can be administered conveniently and produce more rapid and effective bronchodilatation than IV aminophylline, an often incorrectly listed therapy. Although aerosols can be generated from a solution and delivered by driven nebulizers to the anesthetic circuit, factors of cost and convenience favor the use of metered-dose inhalers. Delivery of bronchodilator aerosols through these canister-style metered dose inhalers to anesthetized intubated patients was made possible by a variety of commercial elbow adapters many of which are markedly inefficient. Enhanced aerosol delivery to the anesthetized patient involves the use of a reservoir chamber or spacer devices. Such spaces can be conveniently inserted in the anesthetic circuit between the inspiratory limb and patient Y-piece. A port with a removable cap allows convenient canister placement. The spray is actuated just before an inspiratory cycle begins to provide optimum aerosol delivery to the airway. As much as 30%–50% of the administered dose can reach the airways with this technique.

In anesthetized patients skeletal muscle relaxation is essential because vigorous expiratory efforts may further increase airway pressures. Paralysis also helps to determine whether the increased airway pressure and difficulty in ventilating are caused by actual bronchospasm or merely straining and coughing on the endotracheal tube. (Fig. 4).

The decreased airway caliber associated with bronchoconstriction profoundly affects the distribution of gases within the lung. The major effect is underventilation of many lung units whose low ratio of ventilation relative to perfusion results in arterial hypoxemia. The pulmonary vasodilating properties of many bronchodilators further worsen these low ventilation perfusion ratios. Thus, it is important in the anesthetized patient to increase the inspired oxygen concentrations to 100% in the presence of bronchospasm. This will not only minimize the degree of atrial hypoxemia but will also assure an increased oxygen tension in the alveoli. The latter is important because regional alveolar hypoxia appears to intensify nonspecific bronchial reactivity.

Therapy with IV glycopyrrolate up to 1 mg may be helpful in reversing some of the reflex bronchoconstriction but is more valuable as prophylaxis because its delay in onset. Direct instillation of glycopyrrolate through the endotracheal tube incurs a similar delay but has the advantage of avoiding systemic side effects. IV lidocaine (1.5–2 mg/kg) is also likely to be more effective if given before the stimulus, as would corticosteroids (hydrocortisone 4 mg/kg or its equivalent).

Episodes of bronchospasm may be accompanied by arterial hypotension, often as a consequence of the high airway pressures necessary to achieve ventilation. In such cases IV ephedrine, an old reliable vasopressor is very useful because of its bronchodilating qualities. Similarly, IV epinephrine in doses of 10–20 mEq may be appropriate, especially if delivery of β-adrenergic aerosols is difficult. A common example of the latter is with a double-lumen tube in place.

Ventilatory Management

Patients who require pharmacological treatment of bronchospasm present problems to mechanical ventilation because of their marked increase in airway resistance. Approaches to ventilating such patients have been controversial, largely because of a misunderstanding of differences between peak airway pressure and mean airway or alveolar pressure. The latter is the true pressure responsible for airway expansion and hence ventilation. The peak airway pressure as measured distally in the breathing circuit usually far exceeds actual airway or alveolar pressure. Such peak pressure if high, raises alarm about barotrauma, but at times may actually produce inadequate alveolar pressure for lung inflation. Attempts to deliver adequate ventilation while avoiding high peak airway pressure (P_{pk}) have largely been based on the use of low inspiratory flow rates (V_I).

Support for the time-honored recommendation to minimize P_{pk} by limiting or reducing V_I seems to be lacking. Much of the increased P_{pk} that occurs in these patients as a result of V_I reflects that expended on the resistance of the proximal airways and, in particular, the endotracheal tube. Thus, P_{pk} does not reflect the true alveolar or distending pressure, which is more closely approximated by the plateau pressure during an inspiratory pause.

One of the major benefits of an increased V_I is the ability to deliver tidal volume in a shorter time and thus maximize the time available for expiration (50).

With airway obstruction, expiratory flows are extremely slow, and a much longer expiratory time is necessary for adequate exhalation. If exhalation time is inadequate, dynamic hyperinflation will occur and lead to barotrauma or at least circulatory depression. This is best avoided if V_I is increased and respiratory frequency is decreased (<10) in an effort to provide an adequate expiratory time as well as adequate ventilation (51).

In summary, this review has considered the many factors that modify and contribute to airway hyperactivity. It also has attempted to provide an update of the actions of anesthetic as well as nonanesthetic medications on the airways. The goal has been to provide the anesthesiologist with the tools to administer a safer smoother anesthetic to the patient with hyperreactive airways. The anesthetic management of such patient at risk, of necessity, must focus on prevention on airway constriction, as well as its prompt reversal, and ventilatory management.

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