Review Article

Anesthetic Concerns in Patients with Hyper-reactive Airways

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Abstract

Hyperreactive airway disease occurs due to acute viral or bacterial infections in children, and due to chronic bronchitis, Asthma or Emphysema in adults. Smoking and exposure to allergens may worsen the disease. Anaesthesia in these patients is associated with higher incidence of perioperative bronchospasm, postoperative laryngospam, breath holding, and hypoxia due to maldistribution of Ventilation and Perfusion. Smoking and exposure to allergens may worsen the outcome. Severe bronchospasm is a life threatening emergency. Selective β2 agonists form the main drug of choice for bronchospasm. Corticosteroids should be given early to reduce inflammation and mucosal oedema. For anaesthesia, Propofol, Vecuronium or Rocuronium, Halothane or Sevoflurane and Fentanyl are drugs of choice. Histamine releasing drugs like morphine and atracurium should be avoided. If ventilator support is required, Non invasive Pressure Support ventilation should be used first. However, Intubation and mechanical ventilation may become necessary, which however, may be associated with difficult weaning.

Key words: Anaesthesia, asthma, bronchospasm, chronic obstructive pulmonary disease, corticosteroids, hyperreactive airways, muscarinic receptors, smoking, upper respiratory tract infection, β2 agonist

Introduction

Hyper-reactive airway refers to patients who exhibit heightened airway reactivity to normal or lower level of physical, chemical, or pharmacological stimulus to the airway. Hyper-reactivity is characterized by intermittent bouts of exaggerated airway narrowing clinically manifesting as laryngospasm and/or bronchospasm.

The hyper-reactive airway may occur due to acute or chronic airway diseases. The acute causes include upper and lower respiratory tract infections due to viral or bacterial infections, which commonly occur in children, but may also occur in adults. Chronic diseases such as allergic rhinitis, chronic bronchitis, emphysema, and asthma are common in adults [Table 1]. Smoking is an important factor, which may exaggerate reactive airway. Many of these patients may require anesthesia for simple or day care surgeries. However, anesthesia for these patients with hyper-reactive airway may result in perioperative respiratory complications such as breath holding, coughing, stridor, increased speed of desaturation, laryngospasm, bronchospasm, and sometimes leads to atelectasis and pneumonia.[1]

Mechanism of hyper-reactivity of airways

In the resting condition, the bronchial smooth muscles are in a state of mild constriction, as a result of parasympathetic influence. This state of constriction is necessary to maintain a fine balance between anatomical dead space and airway resistance to maintain optimum balance between gas exchange and work of breathing.[2] Antimuscarinic drugs such as atropine and glycopyrrolate can abolish this muscle tone. The airway resistance is also modified by other factors like amount of airway secretions, presence or absence of mucosal inflammation and edema, in addition to bronchial smooth muscle tone. In patients with chronic bronchitis or asthma, the bronchial smooth muscles may be hypertrophied with narrowing of the bronchioles, even in the resting state. The mucus glands are hypertrophied. They can generate higher tension and higher airway resistance, when exposed to bronchoconstricting stimulus.

The neural supply to respiratory tract includes parasympathetic supply through vagus, which is more prominent, and sympathetic supply, which is less prominent. The mucosa of cartilaginous portion of the respiratory tract has a large number of surface receptors, most prominent in trachea and carina, which respond to physical, chemical, or pharmacological stimuli or irritants such as foreign body, gases, or other inhaled particles [Figure 1]. The impulses from the mucosal receptors are carried along the vagus nerve to the vagal nucleus in the medulla. Once stimulated, the efferents from the vagus nucleus are carried to the parasympathetic ganglia, containing nicotinic-cholinergic receptors, which respond to acetylcholine (Ach). These intramural ganglia also contain

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Table 1: Risk factors for development of perioperative bronchospasm

Recent upper and lower respiratory infection (viral or bacterial)
History of chronic smoking
Chronic bronchitis and emphysema
Bronchial asthma
History of wheezing during previous anesthesia
Allergic rhinitis
Drugs like β-blocking agents

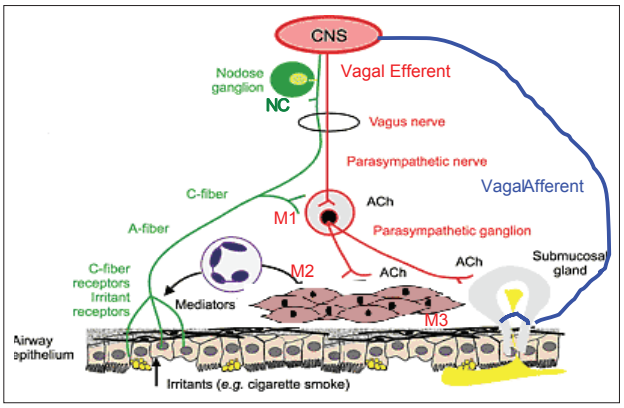

Figure 1: Parasympathetic pathways affecting bronchoconstriction. NC = Nicotinic receptors; M1, M2, M3 = Muscarinic receptors

muscarinic receptors (M1 receptors). The postganglionic fibers from the parasympathetic ganglia are short processes which supply efferents to the submucosal glands and smooth muscles of the trachea, and bronchi (M3 receptors), and they increase the mucosal secretions and bronchoconstriction. In between these two receptors, the prejunctional fibers contain M2 receptors, which are inhibitory to M3 receptor action. These M2 fibers tend to regulate the smooth muscle tone and secretions in the bronchi, and regulate the bronchoconstriction by negative feedback mechanism to Ach release.[3]

The sympathetic innervations to the respiratory tract are very limited. However, they respond very well to catecholamines and sympathomimetic drugs.[2] The β2 receptors of the respiratory tract produce bronchodilatation on stimulation. Airway hyper-reactivity has been attributed to autonomic imbalance between the sympathetic and parasympathetic responses, with relative overactivity of the parasympathetic system. These result in the following: (a) Over-reactivity of surface receptors; (b) stimulation of M3 receptors resulting in bronchial constriction, increased airway resistance; and (c) increased mucosal secretions. Irritant stimuli or inflammation may also result in mucosal edema, which further tends to increase airway resistance.

The viral infections, particularly in children, and allergens when exposed to the respiratory tract produce immunological and inflammatory response. There is increased IgE production, pro-inflammatory cytokines, and antigen–antibody complexes.[4] The effect of these complexes on bronchial mucosal receptors results in release of histamine, leukotrienes, and other proconstrictive metabolites, and extensive loss of epithelial cells. The epithelial damage results in exposure of sensory nerve endings to direct contact with the irritants.[5] There is increase in tachykinins (which produce bronchoconstriction with cholinergic transmission) and decrease in neutral endopeptidases, enzymes responsible for degradation of tachykinins (and produces bronchodilatation with ACh). The epithelial cell loss may also be responsible for decrease in epithelial relaxing factors such as Prostaglandin E2 (PGE 2) and Prostaglandin I2 (PGI 2) I2 (PGI2).[6] Some viruses also decrease β2 receptors. In such a situation, an increased afferent response of M3 smooth muscle receptors results in increased ACH release from loss of inhibitory response to the release of ACH. The absence of negative feedback mechanism leads to bronchoconstriction, resulting in increased airway resistance, increased mucosal secretions, and mucosal inflammatory edema.[4]

Diagnosis

Acute upper or lower respiratory tract infection may exaggerate the reactivity of airway in susceptible patients. Such patients show higher incidence of stridor, laryngeal spasm, coughing, and breath holding during anesthesia.[7,8] Laryngospasm and bronchospasm alters the ventilation–perfusion ratio leading to rapid desaturation. Endotracheal intubation and anesthesia reduce the Forced Vital Capacity (FVC), which may further add to desaturation. It is crucial to identify these high-risk patients who have hyper-reactivity. Patients receiving multiple medications, requiring repeated hospitalization, and having the need for increasing therapy should raise the suspicion of hyper-reactivity. However, no definite sign or symptom can be identified as pathognomonic of hyper-reactivity.

Clinically, patients with nocturnal dyspnea, chest tightness on awakening, feeling breathless, and wheezing on exposure to cold air or other respiratory irritants have a high tendency to develop bronchospasm intraoperatively.[2] Pulmonary function tests (PFT) may show airway constriction and its reversibility. Spirometric measurement of Forced Vital Capacity in 1 sec (FEV1) gives the degree of constriction and its reversibility with bronchodilators. However, the variation of FEV1 is so large even in normal patients that only those values less than 15% should be considered as suggestive.[9] Improvement in FEV1 value after treatment with bronchodilators, however, definitely suggests presence of airway obstruction and reversibility. Measurement of peak expiratory flow rate (PEFR) shows less variability, and can be performed with small hand-held equipment. From 15 to 20% decrease in morning PEFR reading definitely suggests hyper-reactive airway.[10] Recent viral respiratory infections increase the bronchial reactivity, which may persist for 4–6 weeks, particularly in pediatric population.[7,8] In such patients, decrease in PEFR suggests the possibility of development of intraoperative or postoperative laryngospasm and bronchospasm.

History of smoking is another important factor predisposing to bronchospasm. Cessation of smoking decreases the amount of airway secretions and improves mucociliary transport and airway reactivity. Cessation of smoking even a few days before surgery has been found to be beneficial. Within 8 h of stopping smoking, the carbon monoxide level in the blood decreases and the oxygen carrying capacity of hemoglobin improves. In 48–72 h, there is bronchodilatation. In about 1–3 months, ciliary growth occurs and the mucociliary function improves. Cessation of smoking also improves the circulation and decreases the possibility of coronary artery spasm.[11]

Pharmacological Control

Treatment of bronchoconstriction mainly depends on sympathomimetic drugs which cause bronchial smooth muscle relaxation. They have additional advantage of being able to be administered as spray. Methylxanthines and corticosteroids have been traditionally used, even though they are less effective in acute conditions.

Sympathomimetics

β-Adrenergic agonist compounds like isoproterenol and epinephrine have both β1 (cardiac) and β2 (bronchial) effects. These drugs are superseded by more specific β2 agonists which do not produce tachyarrhythmias due to β1 effect.

Salbutamol (Albuterol) is a classic example of β2 agonist. Given in nebulized aerosol metered dose inhaler, most of the drug is deposited on the bronchial mucosal surface for local action and very little is absorbed systemically. Administration of Salbutamol intravenously or in large dose may result in abolition of β2 selectivity and may produce tachyarrhythmia.[12]

Levoalbuterol is a selective R-enantiomer of Albuterol (Salbutamol). This has more specific β2 agonist effect and may be more effective in reducing the long-term effects of Salbutamol, such as reduction in PFT, which are due to the S-enantiomer which does not bind with the β2 receptors.

Terbutaline is another selective β2 agonist which can be given by inhalation. Subcutaneous and intravenous preparations are also available.

Salmeterol is a long-acting selective β2 agonist. Available as dry powder of 50 μg packets, it is used for the prevention and maintenance of asthma, prevention of bronchospasm due to chronic obstructive pulmonary disease (COPD), and treating exercise-induced asthma. It takes about 30 min to show its effects and, hence, cannot be used in acute emergency treatment.

Adrenaline is a non-selective adrenergic agonist agent having both α and β2 agonist effects. β2 effects are responsible for bronchodilatation and positive chronotropic and inotropic effects. It is given subcutaneously in the dose of 0.01 mg/kg. It is mainly used in the treatment of severe bronchospasm in status asthmaticus. The α effect causes increased peripheral vascular resistance and increased vascular permeability.

Using β-adrenergic antagonists in the treatment of cardiovascular disorders like angina and tachycardias may have adverse impact on hyper-reactive airways, causing bronchoconstriction. Use of cardioselective β1 agonist reduces, but does not abolish bronchoconstriction. Use of short acting drugs like esmolol and metaprolol has not shown to produce adverse bronchospasm.[13]

Theophylline

Methylxanthines like theophylline and aminophylline produce smooth muscle relaxation by inhibition of the enzyme phosphodiesterase and by reduced degradation of cyclic AMP. They do not have any selective action, but produce both cardiac and bronchial smooth muscle relaxation. Aminophylline has been shown to activate tyrosine hydroxylase with increased synthesis of catecholamine, which may be responsible for bronchodilatation. Theophyllines have anti-inflammatory and immune-modulatory activities and down-regulate the inflammatory and immune cell function, which potentially contributes to the efficacy of the drug used in prophylaxis of bronchial asthma. Theophyllines are no longer recommended in the treatment of acute bronchospasm.[14]

Aminophylline has narrow therapeutic range and toxicity is common in the treatment of acute exacerbation of chronic obstructive airway diseases.[15] Administration of theophyllines for bronchospasm arising during halothane anaesthesia, has been shown to increase arrhythmias, whereas deepening anaesthetic depth with halothane and β2 adrenergic agonists were much more effective in abolishing bronchospasm, than aminophylline.[16]

Anticholinergic drugs

Ipratropium is an anticholinergic quaternary compound related to atropine. It acts at the muscarinic receptor of the parasympathetic system, causing bronchodilatation. The drug is administered by aerosol nebulization and has no systemic side effects of atropine. Ipratropium is used as an adjunct to β2 agonist.

Both glycopyrrolate and atropine have significant bronchodilatation properties.[17] Glycopyrrolate has longer duration of action than atropine, and has better bronchodilating properties than atropine. However, their therapeutic action takes 20–30 min and, hence, is more useful in preventing bronchospasm than in its treatment. Both glycopyrrolate and atropine are mainly used in premedication for their antisecretory and bronchodilation effect.

Anticholinergic drugs have been considered to render more viscous respiratory secretions and, hence, there is difficulty in their elimination. However, many studies have shown that these drugs reduce the amount of secretion and do not change any chemical composition or viscosity. Further, bronchoscopic examination has not shown any inspissated secretions blocking the bronchi in many of these studies.[2] They, in fact, improve the ventilation–perfusion ratio and improve gas exchange.

Corticosteroids

Corticosteroids are anti-inflammatory agents, reduce airway inflammation, inhibit mucus secretion, decrease the release of mediator substance responsible for bronchoconstriction, and decrease airway hyper-reactivity. They are now recommended for prevention, acute treatment, and maintenance therapy. Hydrocortisone in a dose of 1–2 mg/kg has been used in the treatment of bronchospasm. Corticosteroids are also helpful in preventing bronchospasm since they act by reducing the mediator substance and not by direct smooth muscle relaxation.[18] They should be given 2–4 h before anesthesia as preoperative preparation. Patients on chronic corticosteroid therapy should be given two to three times their regular dosages. Corticosteroids have also been found to increase the therapeutic effect of β2 agonist.[18,19] Sylvanus[20] has shown that use of methylprednisolone with Salbutamol inhalation improves the lung function and decreases the incidence of wheezing after tracheal intubation. Various preparations of steroids are available. Inhaled steroids are becoming popular, as there is significant improvement in the hyper-reactive state and pulmonary functions and they increase the sensitivity for β2 agonist in the respiratory tract.[21] Dexamethasone has both glucocorticoid and mineralocorticoid effects. It stabilizes cell and lysosomal membranes, inhibits prostaglandins, and prevents the liberation of proinflammatory kinins. It also increases surfactant synthesis, decreases inflammation by reversing the increased capillary permeability occurring with the liberation of kinins, and improves microcirculation. It is most commonly used intravenously for acute treatment of bronchospasm. It is given orally for maintenance therapy.

Hydrocortisone has major glucocorticoid and minimum mineralocorticoid effects. It is mainly used as an emergency drug in the treatment of bronchospasm.

Prednisolone is used both for acute and maintenance therapy in chronic asthma. Continuous usage results in adrenocortical suppression and, hence, the dosage should always be tapered.

Methylprednisolone has been used in acute control of bronchospasm. Given parenterally, it has rapid onset of action. It reduces ongoing inflammation and capillary permeability. It increases the response of β2 agonists by increasing the sensitivity of β2 receptors.

Budenoside produces direct smooth muscle relaxation, in addition to its anti-inflammatory effect. It inhibits bronchoconstriction, and decreases airway inflammation and hyper-reactivity. It is available as a suspension for nebulized inhalation.

Other drugs

Mast cell stabilizer Cromolyn, inhibits the release of histamine and slow reacting substances from the mast cells. It is given in nebulized form. Leukotriene inhibitors such as Zileuton, Zafirlucast, and Montelucast inhibit aspirin-induced, cold air–, and exercise-induced asthma. These drugs are used for prevention and cannot be used in acute asthmatic attacks.

Magnesium sulfate decreases the release of Ach at the neuromuscular junction and decreases the smooth muscle tone. It causes bronchodilatation by inhibiting calcium-mediated smooth muscle contraction. It is recommended in the treatment of asthma as an adjuvant to other drugs.

Anesthetic Agents and Airway Reactivity

Intravenous anesthetic agents

Thiopentone *per se* has not been shown to induce bronchospasm. However, induction dose of thiopentone generally leaves respiratory reflexes more active, and instrumentation at light level of anesthesia may induce bronchospasm. Thiopentone is, therefore, not contraindicated in bronchial asthmatic patients; however, it should be used with other inhalational agents and with adequate depth of anesthesia.

Propofol has been shown to have mild bronchodilatation property by inhibition of vagal response. Propofol has been used for sedation in intensive care units, and has been shown to reduce the airway resistance.[22] Further, it depresses airway reflexes and tolerates airway instrumentation very well.

Ketamine produces bronchial smooth muscle relaxation directly and also by inhibition of muscarinic receptors.[23] It also releases endogenous catecholamine, and causes bronchodilatation which can be blocked by β-adrenergic blocking agents.[23] Ketamine has been used in asthmatic patients and also to treat resistance bronchospasm during surgery or in the intensive care.

Inhalational anesthetic agents

Halogenated hydrocarbon anesthetic agents have potent bronchodilatation property. They inhibit bronchoconstriction by inhibiting airway reflexes, and also produce bronchodilatation by direct bronchial smooth muscle relaxation and by augmenting β-adrenergic response.

Halothane has been considered the drug of choice for bronchospastic diseases, even though enflurane and isoflurane also cause bronchodilatation in a dose-dependent manner. But they also cause myocardial depression, and arrhythmias in the presence of circulating catecholamine.[24] Isoflurane requires higher concentration (Minimum Alveolar Concentration (MAC) >1.5) for significant bronchodilatation, and may produce significant myocardial depression.[25] Halothane and sevoflurane produce bronchodilatation at an MAC of 1.0. Desflurane has irritant effect on respiratory tract and may induce bronchoconstriction during induction, when given alone. However, when given in higher concentration, it produces bronchodilatation.

Muscle relaxants

Muscle relaxants act directly at muscarinic receptors of the neuromuscular junction (M3 receptors). However, they also act at the parasympathetic ganglia (M1 receptors), producing unwanted side effects. They may also release histamine, which induces bronchospasm. Atracurium is known to release histamine. However, they do not produce bronchoconstriction

in normal patients, even though they may do so in patients with hyper-reactive airways. Cisatracurium does not release histamine and has been used in asthmatic patients. Drugs like pancuronium and atracurium have been shown to block M2 receptors at the ganglion level, which inhibit reflex Ach release. This loss of M2 inhibition may result in reflex vagal-mediated bronchoconstriction. Such M2 blockade has not been demonstrated with vecuronium.[26]

Neostigmine is used to reverse the muscle relaxant effect. Cholinesterase inhibitors increase bronchial secretions and cause bronchospasm. This effect may be exaggerated in patients with hyper-reactive airways.[27] This effect can be prevented by prior use of atropine or glycopyrrolate. In patients with severe bronchospasm, better alternative would be to use short acting muscle relaxants and avoid reversal with neostigmine.

Narcotic analgesics and sedatives

Use of narcotic analgesics in chronic respiratory diseases is controversial. They cause respiratory depression and carbon dioxide accumulation. They depress the cough reflex and decrease secretions through neural pathways. They are also shown to depress vagal-mediated reflex bronchospasm.

Morphine is contraindicated in patients with asthma or hyper-reactive airway disease. It has been shown to depress cough and bronchial reflexes; however, it releases histamine and produces bronchospasm. This response, however, is short-lived and very often mild. Infusion of histamine has a similar effect and does not produce clinically significant bronchospasm. These effects can be modified by concomitant administration of β-adrenergic agents, atropine, or with antihistaminics such as chlorpheniramine maleate. Eschenbacher *et al*.[28] have shown that in patients with mild asthma, morphine inhibits vagally mediated bronchospasm and produces bronchodilatation.

Pethidine with its atropine-like action suppresses vagus-induced bronchoconstriction and is preferred over morphine. Fentanyl has been shown to increase airway resistance in susceptible patients, though the effect can be reversed with atropine and, hence, is thought to be mediated through vagal stimulation.[29]

Among the various sedative drugs, phenothiazines like promethazine have bronchodilating properties by suppression of reflex vagal response. Benzodiazepenes like diazepam and midazolam have no effect on bronchial smooth muscles and can be used safely. However, they may cause respiratory depression.

Lidocaine

Hunt *et al*. have shown that nebulized lidocaine solution reduces the requirement of corticosteroids in mild to moderate asthma, improves FEV1 and decreases the eosinophil count osinophil count.[30] Lidocaine has also been shown to promote apoptosis of eosinophils and has been found to be effective in steroid-resistant asthma.[31] It may produce smooth muscle relaxation and suppress mediator release in high doses, resulting in toxic concentration. However, in clinically used dosage of 1.5–2 mg/kg, lidocaine seems to act by blocking the airway reflexes to tracheo-bronchial irritation.[32] Lidocaine has been used in the treatment of intraoperative bronchospasm. Adamzick *et al*.[33] have shown that intravenous lidocaine given before or after tracheal intubation mitigates bronchoconstriction in asthmatic patients. Intravenous administration has been found to be more effective than local aerosol spray, which sometimes may be less effective or may even produce irritation of bronchial tree. Nishino *et al*.[32] measured lidocaine concentration in blood and found that a blood level of 3 μg/ml is capable of suppressing the cough response to tracheal irritation. Such concentration may also be achieved during epidural analgesia and intravenous arrhythmia treatment. Hence, lidocaine may be used in patients with bronchospasm, when adequate depth of anesthesia cannot be obtained with inhalation agents, without much cardiovascular depression.

Anesthetic Management

The goal in the anesthetic management is to prevent reflex airway reactivity. This involves specific management plan. Patients with acute viral or respiratory infections or obvious bronchospasm should have all routine surgeries postponed. Routine surgery should be postponed in the following patients.[34]

- Children less than 1 year of age who have or had acute viral infection in the last 3 weeks can develop severe laryngospasm and bronchospasm during anesthesia or postoperatively. Symptoms can be severe with longer duration of infection. In such patients, it may be wise to undertake surgery 4–6 weeks later
- Patients with pre-existing pulmonary diseases such as chronic obstructive airway disease and asthma should be treated with bronchodilators; respiratory secretion should be reduced and chest physiotherapy needs to be done before surgery
- Patients presenting with positive major signs such as fever, mucopurulent nasal secretions, elevated white cell count, rhonchi or crepitations on auscultation, and radiographic findings definitely have high risk of developing severe laryngo-bronchospasm.

Laryngospasm is less common in children beyond 6 years of age. For children between 1 and 6 years of age, the risk/benefit ratio must be evaluated vis-à-vis surgery.[35] Hyper-reactivity persists 4–6 weeks after respiratory tract infection.

Regional anesthesia

Whenever and wherever possible, regional anesthesia is ideal. It avoids endotracheal intubation and does not induce bronchospasm. Central axial blocks often tend to produce bronchodilatation. However, if high-level sensory–motor blockade is necessary, difficulty in respiration may produce

anxiety and bronchospasm. Further, such high motor blockade abolishes expiratory muscle power, and in patients with bronchospasm, who depend on these accessory muscles of respiration, respiratory failure may occur. There is high incidence of hypoxia, retention of secretions, laryngospasm, and bronchospam in such patients.[36] Such patients may be better managed with general anesthesia with muscle relaxants.

General anesthesia

All patients should be managed with a specific protocol. β2 Agonists like Salbutamol can be given by inhalation just before induction. Premedication should always be given. Anticholinergics like atropine or glycopyrrolate help in preventing reflex vagal-induced bronchospasm; however, they may also cause inspissations of secretions. They should be given 20–30 min before induction. This also reduces the bronchial secretions. Alternatively, ipratropium bromide can be given by inhalation. Propofol is perhaps the drug of choice. However, ketamine may also be used in emergency situations or with unstable hemodynamics. The choice among inhalational agents is halothane, though isoflurane can be used depending on the hemodynamic and associated cardiac condition. Sevoflurane can also be used for rapid induction of anesthesia. Use of laryngeal mask airway may help in reducing the incidence of bronchospasm. Endotracheal intubation should be carried out only under deep anesthetic level. Intravenous lidocaine 1.5–2 mg/kg helps in depressing airway reflexes. Vecuronium may be preferred over other muscle relaxants. It is short acting, has no effect on bronchi. Neostigmine may be avoided for reversal, in frank bronchospastic patients. Total intravenous anesthesia with propofol may also be used instead of inhalational agents.

Intraoperative bronchospasm

Olsson[37] performed a computer-aided study of more than 1 lakh patients undergoing anesthesia. The general incidence of bronchospasm was 0.17%. However, in patients with hyper-reactive airways, the incidence was 0.88%. In children with respiratory infection, the incidence of bronchospasm was 4.1%. With endotracheal intubation, the incidence was 0.9%. Recent studies, however, have shown lower incidence of complications. In a study by Warner *et al*.,[36] the incidence of intraoperative bronchospasm was only 1.7% and that of overall respiratory complications was 2%. The incidence, however, was higher in children. In a study by Budic and Simic,[38] the incidence of airway complications was 5.71%, laryngospasm was 2.1%, and breath holding was 1.4%. While bronchospasm is common, other conditions that mimic bronchospasm may occur [Table 2].

Table 2: Conditions mimicking bronchospasm during anesthesia

Endobronchial intubation
Coughing and straining
Mechanical obstruction of endotracheal tube
Tension pneumothorax
Pulmonary gastric aspiration
Pulmonary embolism
Pulmonary edema

Endobronchial intubation or endotracheal tube touching the carina may stimulate the receptors that are present in high concentration in these areas, which may reflexly produce bronchospasm. They may cause coughing and straining, particularly in patients breathing spontaneously. Muscle relaxants abolish the coughing and straining. Endobronchial intubation produces fall in oxygen saturation and high inflation pressures. Auscultation of chest shows absence of ventilation on the opposite side. Mechanical obstruction of endotracheal tube by kinking, foreign body, or inspissated secretion produces high inflation pressures and high pitch sounds which are heard both during inspiration and expiration. Passing a suction catheter through the endotracheal tube may encounter the obstruction. Obstruction may be suspected if peak airway pressure is high, but plateau pressure during inspiration is low. Development of pneumothorax due to high inspiratory pressures may also mimic bronchospasm. With the collapsed lung causing bronchiolar compression, rhonchi may be heard on the side. Hypoxia, tachycardia, and hypotension may be present. Definitive diagnosis is made by demonstrating gas escape through the thoracic cavity by inserting a 16 or 14 G needle at the second intercostal space into the thoracic cavity. Pulmonary aspiration of gastric contents produces severe bronchospasm due to acid and also produces irritation and hypoxia. The spasm is often unilateral, on the side of aspiration. Pulmonary embolism produces similar clinical signs of bronchospasm, but if accompanied by hypotension and bradycardia. Wheezing probably occurs because of release of mediators causing bronchospasm. Similarly, in early stages of pulmonary edema, accumulation of fluid in the interstitial spaces causes constriction of bronchioles leading to bronchospasm. Cooperman and Price[39] have demonstrated that wheezing is the earliest sign of pulmonary edema developing during anesthesia.

Management of bronchospasm

When bronchospasm occurs during anesthesia, it may be necessary to increase the depth of anesthesia by increasing the inhaled concentration of halothane or other inhalational agent. With bronchospasm, the alveolar concentration is much less than the inspired concentration and not effective to achieve adequate depth of anesthesia.[40] Increasing the inhaled concentration will increase the depth and often relieves the bronchospasm. However, one should be aware of the fact that with the relief of bronchospasm, sudden cardiovascular depression may occur due to high alveolar concentration of anesthetic gases and high PaCO2 levels. In patients breathing spontaneously, paralyzing the patient with a muscle relaxant would suppress reflex bronchoconstriction by abolishing coughing and straining. Paralyzing and ventilating the patients also help in deepening the depth of anesthesia. Another effect of bronchospasm is maldistribution of gases. Under-ventilated alveoli (low v/p ratio) lead to hypoxemia. Pulmonary

vasodilatation produced by bronchodilating agents increases this maldistribution and worsens hypoxemia. Hence, higher concentration of and, sometimes, 100% oxygen needs to be administered to maintain adequate oxygenation. Adequate analgesics have to be supplemented in place of nitrous oxide. Untreated bronchospam results in severe hypoxia, cardiovascular collapse, and arrest.

The mainstay in the treatment of bronchospasm is β2-adrenergic drugs. Salbutamol aerosol preparation should be given by inhalation. The drug, at a dosage of 200–400 μg, should be nebulized into the breathing circuit or into the endotracheal tube, and ventilated with FiO2 necessary to maintain an oxygen saturation of 90%. Most of the drug may get deposited into the circuit or endotracheal tube. Hence, three to four times of the normal dosage may be needed to reach adequate concentration in the bronchi. The drug could be administered directly into the lower end of endotracheal tube or trachea by connecting a long catheter to the metered dose aerosol canister preparation.[41] Such high concentration of drug, however, may produce tracheo-bronchial epithelial lesions due to oleic acid present in the aerosol preparation. An alternative effective method to administer aerosol preparation would be to insert a reservoir and a nebulizing chamber between the Y-piece and the inspiratory circuit.[42] The nebulizing chamber is actuated during inspiration, though a separate gas flow device, carrying the drug as micro droplets. micro droplets. However, the drug is more useful if given 20–30 min before anesthesia, as a preventive measure. If the patient is already premedicated with glycopyrrolate, direct instillation of 1 mg of glycopyrrolate into the trachea is useful in suppressing bronchoconstriction. Lidocaine at a dosage of 1.5–2 mg/kg may also be helpful which can be given intravenously, though this is more beneficial if given early. Corticosteroid supplement may be useful if the patient is already on treatment. Hydrocortisone at a dosage of 100–200 mg helps in abolishing the attack. Even if the patient has not been on corticosteroids, supplementing hydrocortisone helps in reversing bronchoconstriction by neutralizing tachykinin's effects. This action may be delayed, but tries to sustain the bronchodilation. Corticosteroids may also be given by aerosol route for immediate local action.

Laryngospasm is common in children, particularly after viral infections.[36,37] This is common during induction of anesthesia. This can be easily treated with muscle relaxants and endotracheal intubation. However, laryngospasm may still occur after extubation. Patients should receive humidified warm oxygen through facemask. Hydrocortisone supplement may be useful in abolishing the stimulus for laryngospasm. The l-adrenaline aerosol may be helpful in reducing severe spasm. However, in small children, it may produce severe tachycardia and arrhythmias, particularly in hypoxic condition. In uncontrolled laryngospasm with falling oxygen saturation, reintubation with muscle relaxant may be necessary to achieve adequate ventilation and oxygenation. Extubation should only be carried out after the patient is adequately oxygenated with good humidification. Return of laryngospasm may still occur. All patients who have had bronchospasm intraoperatively should be extubated only when the patient is totally awake. Humidified oxygen supplement should be given, as desaturation can occur very easily in these patients. Atelectasis may develop easily in these patients, and therefore, patients should undergo physiotherapy.

Mechanical ventilation

Acute asthma is characterized by severe reduction in expiratory flow, requiring prolonged expiratory period and increase in airway resistance, resulting in premature closure of airways, hyperinflation, and auto positive end-expiratory pressure (PEEP). This results in abnormal ventilation–perfusion ratio due to diversion of blood flow to normally ventilated zones, increased risk of barotraumas, high airway pressure resulting in impediment to venous return, hemodynamic instability, and circulatory collapse.[43] The indications for mechanical ventilation in these patients include severe respiratory acidosis and altered level of consciousness, unresponsiveness to medical management, and severe respiratory distress leading to severe fatigue and exhaustion.

An approach to pulmonary ventilation in these patients is controversial. Because of high airway resistance, adequate tidal volume can be achieved only with high peak inspiratory pressures. Concerns have been expressed regarding barotraumas with high peak pressures. To avoid high peak pressures, lower tidal volume with higher rate and lower inspiratory flow rate[44] has been suggested to maintain minute ventilation. In bronchospastic condition, the inspiration is achieved with mechanical ventilation by generating high pressures as necessary. However, the expiration, being passive, is slow in the presence of high expiratory resistance. If prolonged expiratory phase is not provided, adequate exhalation may not occur, resulting in dynamic hyperinflation, barotraumas, and circulatory depression. Tuxane and Lane[45] have demonstrated that increase in the tidal volume or decrease in the expiratory time (by increasing the rate) was associated with increase in the end inspiratory volume (VIe). The increase in VIe was associated with increase in alveolar, central venous, and esophageal pressures and hypotension. Peak airway pressure (Ppk) was predominantly related to inspiratory flow and did not reflect changes in lung volume.

Many patients with asthma may require respiratory support. Non-invasive ventilation may be tried in patients with mild to moderate respiratory failure. Non invasive Positive Pressure Ventilation (NPPV) should be started with low pressure support level and increased gradually till the respiratory rate is below 25 and peak inspiratory pressure is less than 25 cm.[46] Intubation in an asthma patient is indicated if there is progressive increase in PaCO2 or patient is exhausted. A strategy of mechanical ventilation includes increase in expiratory time by decreasing the rate, limiting the tidal volume and decreasing the inspiratory time. Permissive hypercapnia may be used to prevent lung hyperinflation and auto PEEP effect and barotrauma. Achieving normocapnia in such patients

may be dangerous and PaCO2 levels should be brought down slowly. Intubated and mechanically ventilated patients should be aggressively sedated. Paralytic agents should be used only if adequate control of the cardiopulmonary status cannot be achieved by sedation alone.

Conclusion

Hyper-reactivity diseases are common and require a definite protocol for their management. Medical management is the mainstay in the treatment of acute spasm. However, respiratory support may be necessary. With proper understanding of the mechanism involving bronchospasm and the therapeutic action of various drugs, even severe bronchospasm can be treated with low morbidity or mortality.

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