J Anesth (2013) 27:423–432
DOI 10.1007/s00540-012-1517-0

REVIEW ARTICLE

Postoperative apnea, respiratory strategies, and pathogenesis mechanisms: a review

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Received: 21 June 2012 / Accepted: 28 October 2012 / Published online: 21 November 2012

Abstract Recovery from anesthesia is ideally routine and uneventful. After extubation, the recovering postoperative patient ought to breathe without supportive care or additional oxygenation. It has been demonstrated in previous studies that postoperative pulmonary complications are clinically relevant in terms of mortality, morbidity, and length of hospital stay. Compromised postoperative ventilation can be described as the condition in which the postoperative patient does not have satisfactory spontaneous ventilation support and adequate oxygenation. Causes of impaired ventilation, oxygenation, and airway maintenance can be mechanical, hemodynamic, and pharmacologic. This review describes prevalence and differential diagnosis, including co-morbidities of postoperative apnea. The physiological mechanisms of breathing and prolonged postoperative apnea are also reviewed; these mechanisms include influences from the brainstem, the cerebral cortex, and chemoreceptors in the carotid and aortic body. Causes of prolonged postoperative apnea and management are also discussed.

Keywords Postop apnea · Obesity · Medications · Brain mechanisms

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Introduction

Postoperative apnea in the recovery room is a relatively common occurrence. If this condition is not addressed in a timely and appropriate fashion, it can be life-threatening. Prolonged apnea has been defined as the cessation of breathing for more than 20 s. Prolonged apnea has also been defined typically for infants and children as the cessation of breathing for less than 20 s that is accompanied with either bradycardia or oxygen (O_2) desaturation [1, 2]. Apnea has also been divided into central apnea, obstructive apnea, and mixed apnea. Central apnea is the absence of nasal or oral airflow and chest wall movement. Obstructive apnea is the lack of nasal or oral airflow in the presence of chest wall movement. Mixed apnea is the combination of central and obstructive apnea [1, 2].

Although it is known that 2 percent of women and 4 percent of men in the age group of 30–60 years suffer from symptomatic obstructive sleep apnea during the preoperative stage, the incidence of post operative apnea in the general population is unknown [3]. This review describes the factors that control ventilation. In addition, this review outlines the influence of drugs administered on breathing. This review describes intraoperative ventilation methods

and their contribution to postoperative apnea. The evaluation, causes, and management of postoperative apnea are reviewed.

Review of respiratory physiology and control of ventilation

The control of pulmonary ventilation is complex. A hierarchical system manages the control of pulmonary ventilation. This system includes sensors and effectors that help to exert the influence of the lungs and respiratory muscles. These sensors and effectors coordinate respiration while satisfying the requirements of physiology. These requirements include proper oxygen uptake, carbon dioxide output, and pH (Figs. 1, 2).

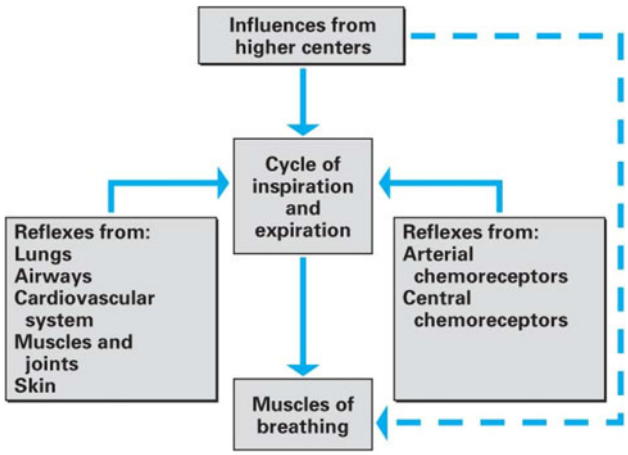

Fig. 1 Elements of control over respiration with permission [44]

Control of ventilation

Under normal conditions, the unconscious control of respiration originates in impulses from the brainstem. The respiratory center, which is located in the pons and medulla, controls the alternation between inspiration and expiration. Inspiration is an active process in the spontaneously breathing individual. Inspiration is executed by the signaling that results in the contraction of inspiratory muscles (Figs. 1, 2). Expiration is passive in normal individuals during quiet breathing due to relaxation of the chest wall. However, expiration may become active during exercise. In some cases, expiration is active under anesthesia [4].

Historically, the apneustic center in the pons is thought to stimulate inspiration (Figs. 1, 2). Studies have shown that the interruption of signaling from the apneustic center leads to periods of prolonged inspiratory gaps [5]. The pneumotaxic center, also in the pons, functions to inhibit inspiration. This inhibition allows the regulation of inspiratory volume and respiratory rate. The signaling for ventilation is further modulated by input from the vagal and glossopharyngeal nerves. Voluntary control of breathing is regulated by the cortex. The cortex is able to override signals from the brainstem [4].

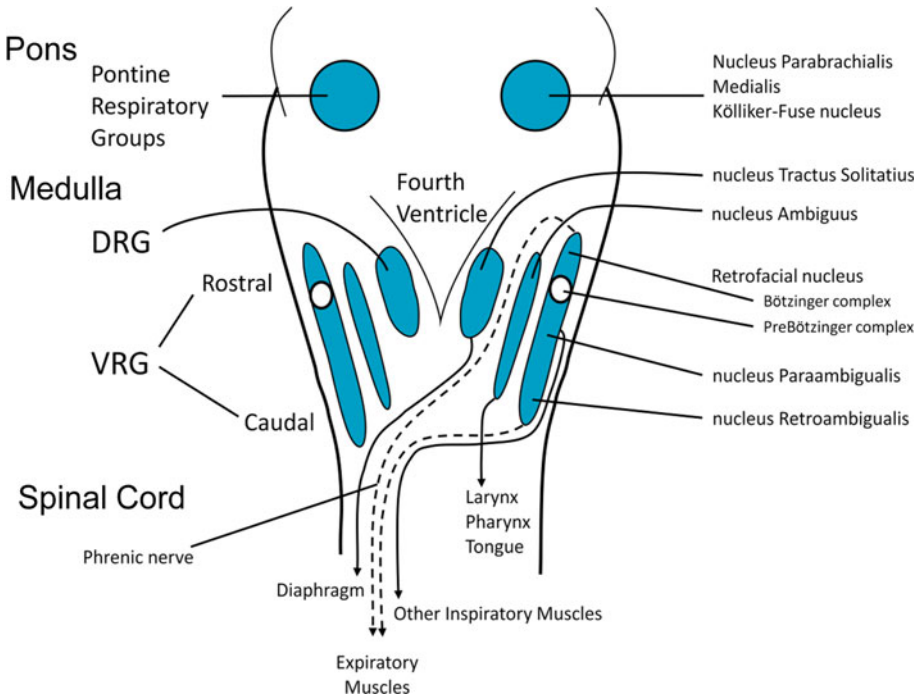

Fig. 2 Key anatomical structures involved in respiration with permission [44]

Current understanding of medullary and pontine mediated influences of respiration is complex. There are two dense bilateral aggregations of respiratory neurons, described as dorsal and ventral respiratory groups. The dorsal is mainly inspiratory neurons, initiates the phrenic nerve, projects to the contralateral spinal cord, and is located bilaterally in the nucleus of the tractus solitarius. The nucleus tractus solitarius transfers arterial PO_2, PCO_2, and pH from the carotid and aortic arterial chemoreceptors and systemic arterial blood pressure from the carotid and aortic baroreceptors. The ventral respiratory group is located bilaterally in the retrofacial nucleus, the nucleus ambiguous, and the nucleus retroamibigualis, consisting of both inspiratory and expiratory neurons that innervating critical muscles involved in breathing and in maintaining airway patency (Figs. 1, 2). Thus, both inspiratory and expiratory neurons co-exist in these regions. Of note, the retrofacial nucleus within the ventral respiratory groups primarily contains expiratory neurons in the Bötzinger complex, which has been shown to inhibit inspiratory cells in the dorsal root ganglion and some phrenic neurons. It should be noted that some research in different animal models almost two decades ago identified this site as being influenced by barbiturate agents.

Chemoreceptors within the body provide reflexic homeostatic control over breathing. Chemoreceptors sense arterial PO_2, PCO_2, and pH changes, which can result in alterations in ventilation (Figs. 1, 2). This process helps to ensure that breathing satisfies the current metabolic demands in an ever changing body. Under normal conditions, the arterial PCO_2 is the most important factor in the control of ventilation. Chemoreceptors are extremely sensitive to arterial PCO_2. Even a 1 mm Hg rise in arterial PCO_2 has the ability to increase ventilation 2–3 L/min. Increases in PCO_2 trigger a signal for increased ventilation at any level of PO_2. Low PCO_2 levels in the blood reduce ventilation.

Central chemoreceptors, peripheral chemoreceptors, and receptors in the lungs provide input into the brain and modulate respiration (Figs. 1, 2). Although the blood brain barrier is relatively impermeable to hydrogen ions and to bicarbonate, the blood brain barrier is easily permeable to CO_2. Once in the cerebral spinal fluid, CO_2 liberates hydrogen ions. This liberation of hydrogen ions causes a focal acidification. The focal acidification initiates a chemoreflex. The chemoreflex stimulates breathing [6].

Blood CO_2 changes the pH of the cerebral spinal fluid. As a result, pH changes may trigger chemoreceptors to signal a change in ventilation. Higher levels of CO_2 signal the respiratory control center to increase the drive to breathe. The decreased pH stimulates chemoreceptors. Central chemoreceptors appear to be widely distributed in the brainstem, allowing for a high sensitivity to changes in the systemic PCO_2 level. Central chemoreceptors have also been localized to the orexin group of neurons in the hypothalamus (Figs. 1, 2). Orexin, also known as hypocretin, is a neurotransmitter that targets specific receptors and regulates among other things, arousal and wakefulness. A reduction of orexin producing cells in the brain can lead to narcolepsy. These particular central chemoreceptors have been shown to initiate an arousal response both to CO_2 and to acid loads [6].

Peripheral chemoreceptors also provide input to the brainstem. Peripheral chemoreceptors are located in the bifurcation of the common carotid arteries, the aortic bodies, and the carotid bodies, which are thought to be highly sensitive. These receptors respond to extremely small decreases in arterial PO_2. Peripheral chemoreceptors are responsible for increased ventilation in response to arterial hypoxemia.

There are still further elements of control over respiration, including sensors in the lung. Pulmonary stretch receptors in airway smooth muscle can provide feedback during periods of low respiratory frequency. Pulmonary stretch receptors can provide feedback when irritant receptors between epithelial cells induce bronchoconstriction. Pulmonary stretch receptors may provide feedback when J receptors in the alveolar walls participate in rapid shallow breathing and dyspnea (Figs. 1, 2) [4].

The muscles of respiration are sometimes referred to as the effectors of ventilation. These muscles include the diaphragm, intercostal muscles, abdominal muscles, and accessory muscles such as the sternocleidomastoid and scalene muscles (Figs. 1, 2). The brainstem signals coordination among these muscles in order to execute inspiration and expiration [7].

Arterial CO_2 serves as the main signal that affects respiratory drive. However, the physiologic response to CO_2 can be blunted or altered by sleep, age, genetic factors, and other determinants such as physical fitness. With a stable PCO_2, the arterial PO_2 can be reduced to around 50 mmHg before the occurrence of any noticeable increase in ventilation. This observation demonstrates the reduced role of hypoxic stimulus in the control of normal breathing. Hypoxia takes on a larger role in patients with chronic lung disease. The larger role of hypoxia in patients with chronic lung disease is often due to the chronic retention of CO_2. The chronic retention of CO_2 may eventually lead to hypoxia, serving as the chief stimulus to ventilation [4].

Cardiovascular physiology and its role in ventilation

Ventilation exerts its complex effect on the hemodynamics of the cardiovascular system through various mechanisms.

For instance, breathing may be considered work, or exercise, and patients who are very weak or ill may struggle to mount this effort. The main impact that ventilation has on the cardiovascular system is based on lung volumes and intrathoracic pressures [7]. Hyperinflation of the lungs may compress the cardiac fossa. Hyperinflation also leads to increased pulmonary vascular resistance. Increased pulmonary vascular resistance increases the load on the heart. Conversely, lower lung volumes predispose to atelectasis and to hypoxia. Hypoxia triggers pulmonary vasoconstriction. The cardiovascular system and respiration are also intertwined by the impact of intrathoracic pressures. The decrease in intrathoracic pressure from inspiration influences hemodynamics. The result of the decrease of intrathoracic pressure from inspiration is a simultaneous decrease in right atrial pressure and an increase venous pressure in the abdomen. An increase in intrathoracic pressure decreases the pressure gradient for systemic venous return to the heart and also decreases left ventricular afterload. Both of these resultant decreases improve cardiac output [8].

Differential diagnosis and pathophysiology of compromised postoperative ventilation

Postoperative pulmonary complications can result in morbidity and mortality. Obviously, depressed postoperative ventilation requires an immediate response dictated by the evaluation of the airway, breathing, and circulation. There are many causes for prolonged postoperative apnea or failure of ventilation after the administration of general anesthesia. The pathophysiology of apnea is characterized by the specific situation. The causes of compromised postoperative ventilation may be grouped into pharmacologic, mechanical, and physiologic etiologies (Table 1) [9, 10].

Table 1 Differential diagnosis of failed ventilation postoperatively

Pharmacologic	Mechanical	Physiologic/hemodynamic
Residual anesthetic	Increased resistance	V/Q mismatch
Residual narcotic/sedative	Decreased compliance	Trauma/nerve damage
Neuromuscular blockade	Skeletal/neuromuscular	Acidemia or electrolyte imbalance
Unexpected drug reaction	Pain	Unstable CNS/cardiovascular systems
Pharmacogenetic disease	Weakness	Atelectasis

Pharmacologic causes of compromised postoperative ventilation

The comprehensive evaluation of the patient with depressed postoperative ventilation compels one to consider pharmacologic causes. Depressed respiratory drive and decreased ability to ventilate are documented side effects of many anesthetics. Residual anesthetic, opioid, sedative, or muscle relaxant should be initially suspected and ruled out in the evaluation of a patient with prolonged postoperative apnea. In many cases, one of these pharmacotherapies is the culprit for the apnea.

During the initial recovery from anesthesia, the effects of any lingering anesthetics cause a central nervous system depression. This depression may blunt the natural drive to breathe normally, and the depression may be exacerbated by both hypercarbia and hypoxemia. The decrease of alveolar concentration of an inhaled anesthetic directly depends on the rate of alveolar ventilation, the blood and lipid solubility of the anesthetic drug, the metabolism of the drug, and the duration of anesthesia [11]. These factors must be analyzed simultaneously in order to determine whether the residual anesthetic is compromising respiration. The administration of anesthetics themselves may predispose to hypoxemia. Anesthetics change pulmonary function and reduce functional residual capacity. These changes lead to compromised gas exchange and to a widened alveolar-arterial oxygen gradient. The reduced capacity merits increased concern when the functional residual capacity (FRC) is below awakened closing capacity. FRC decreases below awakened closing capacity commonly in the elderly, the obese, and those with lung disorders. However, FRC is often normal in patients with normal lungs.

Sedatives, such as opioids, are known to exert direct depressant effects on central ventilatory drive and on volitional control of breathing. The most opioid sensitive aspect of respiration is rhythm generation. At lower opioid doses, there are more changes in the respiratory pattern than changes in tidal volume. Higher opioid doses cause a reduction in tidal volume. This reduction is related to the decreased tonic inputs from opioid sensitive chemoreceptors [12]. Residual sedatives in the patient may augment the respiratory depression of a patient through the reduction of the conscious drive to ventilate. This reduction usually manifests itself in lower respiratory rates and reduced minute volume. Simultaneously, the depression of the medullary centers by opioids can lead to disregulation of the sympathetic nervous system. This disregulation of the sympathetic nervous system may lead to other effects. Disregulation of the sympathetic nervous system may mask acidosis. Also, this disregulation may also cause the blunting of indicators of hypoxemia such as tachycardia,

hypertension, and agitation. Disregulation of the sympathetic nervous system may further conceal hypoventilation from the clinician. Respiratory depression is of the most concern for risk and limitation of opioid use. Intravenous naloxone may be needed to reverse respiratory depression. However, naloxone administration is not without consequence because patients given naloxone will experience decreased pain control. Obvious clinical signs of opioid overdose are miosis, central nervous system depression, and decline in respiratory function. New experimental approaches to opioid reversal are currently being studied and may help prevent respiratory compromise without the suppression of analgesia. These approaches include the use of non-opioid drugs such as serotonin agonists, ampakines, and the antibiotic minocycline [13]. Currently, naloxone infusion is the only treatment that may reverse the respiratory depressive effects that opioids induce.

The primary and most salient risk of residual neuromuscular relaxants is the paralysis of respiratory muscles, which leads to decreased ventilation. Residual neuromuscular relaxants decrease the ability to execute the hypoxemia-driven signal for ventilation. This signal is normally transmitted during hypoxemia. The lack of signal transmission may increase the risk of postoperative complications. The mechanism of decreased signaling is related to the flaccid paralysis of respiratory muscles. This flaccid paralysis leads to the depression of the cholinergic component of the signal that is carried by the vagus nerve from the peripheral chemoreceptors. It has been shown that even a minimal residual neuromuscular blockade can significantly increase upper airway closing pressures and collapsibility [14]. The residual activity from administered neuromuscular drugs may be assessed with a peripheral nerve stimulator. The peripheral nerve stimulator guides clinical decisions and is related directly to the percentage of neuromuscular receptor blockade. In this regard, electrical twitch monitors, standard in anesthesia practice, are limited in that 4/4 twitches can still correspond to up to a blockade of 2/3 of neuromuscular receptors. As a result, clinical signs such as the 5 s head lift and the 4/4 hand grip are essential in the definition of the degree of recovery from neuromuscular blockers. It is also important to note that hypothermia has been shown to reduce muscle strength. A decrease of even 2 °C has been shown to prolong the duration of action of neuromuscular blocking agents. A long list of drugs and electrolyte disturbances can also potentiate neuromuscular blockade and delay motor strength recovery. As a result, the potentiated blockade and delay and recovery may diminish respiratory function [15]. The pharmacodynamics and pharmacokinetics of sedatives and analgesics are altered by hypothermia. Hypothermia may potentiate the neuromuscular blockade. Neuromuscular blockade may be potentiated by pathological states that include: hyponatremia, hypokalemia, acidosis, hypocalcemia, and hypermagnesemia.

There exist other pharmacologic causes of postoperative apnea and respiratory compromise in the context of pre-existing disease. Any patient with pre-existing respiratory pathology and altered physiologic responses to PCO_2 and pH is likely to express greater sensitivity to pharmacologic respiratory depression. This includes patients with disorders, including: obstructive sleep apnea, obesity, and chronic obstructive lung disease [12]. One ought also to consider the rare possibility of an unexpected reaction to any of the medications used perioperatively. One of these medications could express varied pharmacodynamics and pharmacokinetics in a person with either a genetic abnormality or a disease that could compromise ventilation. Malignant hyperthermia, an inherited disorder of skeletal muscle, is induced by pharmacologic agents in almost all cases and is known to complicate postoperative ventilation. The pathophysiology is based on biochemical changes induced in skeletal muscle. The pathophysiology often results in hypermetabolism and hyperkalemia. An unexpected rise in end-tidal CO_2 is a sensitive and specific sign of malignant hyperthermia.

Other diseases may cause compromised postoperative respiratory function. Examples include occult myopathies and known myopathies including Duchenne's muscular dystrophy. The administration of anesthetics in these patients with muscular disorders may result in hyperkalemia. Hyperkalemia may compromise cardiac function and respiratory function. Another pharmacogenetic disorder that complicates anesthesia administration is pseudocholinesterase deficiency. Exposure to succinylcholine or other exogenous choline esters may paralyze the patient for an extended period. This paralysis may include the preclusion of normal ventilation, and this preclusion itself may further limit drug metabolism.

Rare factors that can lead to respiratory depression following anesthesia

In the consideration of respiratory depression, after the elimination of the usual causes, the clinician considers additional rare factors. One example is the Lambert-Eaton myasthenic syndrome. Lambert-Eaton myasthenic syndrome is a paraneoplastic syndrome linked to small cell lung cancer. In the Lambert-Eaton myasthenic syndrome, patients have been reported to exhibit increased sensitivity to depolarizing relaxants and to non-depolarizing muscle relaxants. This heightened sensitivity contributes to prolonged postoperative neuromuscular weakness [16]. Patients with mitochondrial myopathies, which are often caused by defects in oxidative phosphorylation, also are

known to experience respiratory depression following anesthesia [17]. In addition, porphyrias are a group of genetic disorders which can lead to central, peripheral, and autonomic nervous system dysfunction. Porphyria may also lead to electrolyte disturbances. Also, porphyria may lead to life threatening respiratory muscle paralysis [17].

Evaluation of patients at risk of postoperative apnea

It is of utmost importance to identify with precision the patients in need of post-operative respiratory support. During the preoperative evaluation period, it would be well advised to discuss the potential role of regional techniques for patients who face the risk of respiratory dysfunction. Non-opioid analgesic strategies offer potential benefits in certain situations [18]. It has been noted that the exclusive administration of opioids has been challenged because of their side effects [18]. An important predictor of post operative pulmonary complications is the surgical site with upper abdominal procedures. Thoracic and aortic procedures each pose a greater risk for post operative pulmonary complications [19].

Any mechanical failure that increases the work of breathing may cause prolonged postoperative apnea, acute ventilation failure, or insufficient air exchange. During inhalation, the inspiratory muscles must generate a pressure gradient sufficient to draw in volume. This process may be impeded by mechanical causes such as: increased airway resistance, decreased compliance, neuromuscular and/or skeletal problems, pain on breathing, or muscular weakness. Respiratory acidosis ensues when alveolar ventilation cannot match CO_2 production.

An increase in airway resistance increases the mechanical work of breathing; an increase in airway resistance increases the pressure gradient to be surmounted. Airway obstruction is a common postoperative problem. The upper airway is often constricted in the pharynx. This constriction stems from obstruction or soft tissue collapse in the larynx by either laryngeal edema or laryngospasm. Large upper airway resistance can be increased by either extrinsic compression, such as from a hematoma or tumor, or an internal problem such as tracheal stenosis [12]. Stronger resistance to the upper airway may be increased by either extrinsic compression or internal factors [12]. Examples of extrinsic compression include hematoma or tumor. Internal factors include tracheal stenosis and related conditions. The reduced central drive to breathe decreases the muscle tone of the respiratory system. This decreased muscle tone obstructs the upper airway. This obstruction leads to pharyngeal narrowing. Upper airway obstruction demands the clinician to clear the airway. Options for airway clearance include: chin lift, mandible elevation, and artificial airway placement [20, 21]. It is important to note that airway edema is a potential complication of airway instrumentation.

In order to clear the airway, clinicians may also consider increasing the level of consciousness of the patient. Increasing the level of consciousness of the patient improves the patency of the airway and decreases the resistance to breathing. Neuromuscular diseases such as Guillain–Barre syndrome, myasthenia gravis, or muscular dystrophy also compromise the mechanical ability of the respiratory muscles during ventilation [22].

The comparison of small airways and large airways compels one to note recurring patterns. The total cross sectional area of small airways may be several orders of magnitude greater than the total cross sectional area of large airways [23]. The resistance of smaller airways forms an aggregate impact on the effort of breathing. This resistance may be increased by bronchoconstriction related to: secretions, histamine release, and/or aspiration. Patients with chronic obstructive pulmonary disease, obesity, excessive lung water or splinting have decreased lung volume. The decreased lung volume is related to decreased traction. Traction is a property that is necessary in the support of small airways. The reduction of the cross sectional area of small airways is proportional to the significant increase in airway resistance. Smokers and patients with allergies or reactive airway disease may present with chronic inflammation. Inflammation is suspected to predispose to bronchospasm and to airway remodeling [24]. The management of small airway resistance depends on the underlying etiology. Strategies include: the reduction of the irritating stimulant, use of incentive spirometry in the improvement of lung volumes, and/or the administration of bronchodilators. Increased dead space in the airway also contributes to increased airway resistance.

Decreased pulmonary compliance increases the work of breathing. This increased work directly leads to respiratory muscle fatigue. The increased work of breathing eventually leads to hypoventilation and to respiratory acidosis. Any change that compresses the lung parenchyma, decreases elasticity, or causes alveolar collapse results in the attenuation of pulmonary compliance. The attenuation of pulmonary compliance leads to an increase in the pressure gradient that the inspiratory muscles must work harder to overcome. Certain conditions may compress the lung tissue and increase the work of breathing. These conditions include: hemothorax, pneumothorax, pulmonary contusion, restrictive lung diseases (e.g., sarcoidosis, pulmonary fibrosis), and/or intrathoracic masses (e.g., cardiomegaly). Compliance is decreased by pulmonary edema. Pulmonary edema adds to the weight of the lung parenchyma. Pulmonary edema also interferes with the surfactant activity, and in effect increases surface tension. Anesthesia itself has also been shown to affect pulmonary compliance.

Specifically, deep anesthesia may decrease pulmonary compliance by one-third [25].

Skeletal abnormality (e.g., scoliosis) serves as another mechanical etiology of the increased work of breathing. Extrathoracic factors such as tight dressings, ascites, or increased abdominal pressure also increase the work of breathing. These factors may increase the pressure gradient required for breathing. Also, these factors may decrease the functional residual capacity. Optimization of breathing mechanics forces one to consider patient position. Gravity exerts influence on ventilation mechanics. Trendelenburg positions have been shown to decrease the alveolar–arterial oxygen tension difference. The reverse Trendelenburg position is suspected to improve oxygenation and to improve respiratory compliance. Trendelenburg positions are thought to lower airway pressures [26]. Obesity has a significant impact on the mechanics of respiration. Obesity reduces compliance and functional residual capacity. Furthermore, obesity may increase the airway resistance of upper and lower airways [27]. Pain and weakness influence the mechanics of breathing. Pain may come from factors such as a preexisting condition. Weakness may stem from other factors. Pain and weakness may prevent the patient from generating the necessary mechanical force for proper ventilation. Pain may be minimized with suitable pharmacotherapies. Weakness may be ameliorated with improved positioning.

Physiologic/hemodynamic causes of prolonged postoperative respiratory depression

Physiology and hemodynamics may provide the root cause of prolonged postoperative apnea. Ventilation and perfusion mismatch (V/Q mismatch) may be responsible for postoperative acute respiratory failure. Common causes of V/Q mismatch include: partial airway obstruction, inadequate tidal volumes, and atelectasis. Atelectasis may appear in up to 90 % of patients who are anesthetized. Atalectasis may contribute to postoperative complications. The major causes of anesthesia related atelectasis include: use of high oxygen concentration gases, decreased functional residual capacity, reduction of peak air flows during anesthesia, and intraoperative compression of lung tissues [28]. More severe V/Q mismatch prevents proper oxygenation and complicates the efforts of the patient to receive oxygen. Examples of factors that may cause V/Q mismatch include: decreased cardiac output, adult respiratory distress syndrome (ARDS), intraoperative pulmonary embolism, pneumonia, or pulmonary edema.

Positive end expiratory pressure (PEEP) and perioperative recruitment maneuvers may be utilized in the prevention of progressive atelectasis. Recruitment maneuvers re-expand collapsed alveoli. Recruitment maneuvers may be executed intraoperatively by the application of PEEP [29]. These maneuvers prevent the de-recruitment and collapse of alveoli. Effective PEEP occurs when the applied pressure exceeds the critical opening pressure of the affected lung. Excessive PEEP can result in barothorax disorder [30].

In some cases, the interruption to the normal physiology of respiration may cause apnea. An unstable central nervous system or trauma to the head or neck may damage the brain, nerves, and/or other components of the nervous system. A possible consequence of this damage includes the ablation of the central control of respiration. Damage to the peripheral nerves that innervate the diaphragm and respiratory muscles will prevent the proper coordination of the muscles of respiration. Operative damage to the carotid bodies sometimes occurs in cases such as bilateral endarterectomy and may destroy the peripheral hypoxic drive to ventilate.

An unstable cardiovascular system precludes quality ventilation. Compromised delivery of blood to the lungs for gas exchange reduces the quality of ventilation. Electrolyte imbalances, including derangements of sodium, calcium, and potassium, may compromise neuromuscular and cardiovascular function. These imbalances may be identified as a physiologic cause of difficulty with postoperative ventilation.

The abrupt diminution of a painful stimulus may alter ventilation. For example, the removal of an endotracheal tube may lead to airway obstruction and hypoventilation. The abrupt diminution of a painful stimulus may alter the medicated responses to arousal, discomfort, and result in respiratory depression [12]. Another physiologic cause for the decreased drive to breathe includes chronic respiratory disease. An example of chronic respiratory disease is chronic obstructive pulmonary disease. The adaptation of the central nervous system to chronic acidosis decreases the sensitivity of the peripheral chemoreceptor to PCO_2. A result of this decreased sensitivity is an attenuated stimulus to breathe. The blunted response to increased PCO_2 may lead hypoxia to become the dominant influence for respiration. This influence may be inadequate for proper ventilation.

Evaluation of patients with prolonged postoperative respiratory depression

The preoperative evaluation includes both the review of the patient history and also the physical examination of the patient. The evaluation is conducted in order to screen for possible complications. Critical respiratory events, including hypoxemia, hypoventilation, and airway obstruction

have been estimated to occur in 1.3 % of patients who are administered general anesthesia [31]. Previous histories of anesthetic experiences and records of prior anesthesia serve as valuable sources of information. Impaired pulmonary function is expected in patients with prior conditions that include: chronic lung disease, smoking history, obesity, and/or neuromuscular or spinal conditions. A pre-operative chest radiograph, arterial blood gas analysis, and screening spirometry may be ordered depending on the patient history. Unfortunately, it appears that pulmonary function test results are poor predictors of postoperative complications [32]. The most important patient risk factors for postoperative pulmonary complications are age and the American Society of Anesthesiologist (ASA) risk classification. In general, chronic obstructive lung disease and smoking have been shown to be less reliable predictors of complications [19].

Intraoperative positioning may exert an impact on patient physiology. As a result, the surgical team must consider and decide patient position during the procedure. Pharmacotherapy influences patient physiology. Patient needs must be considered during the use and selection of the induction sequence, the use of muscle relaxants, and the course of pharmacologic management. The course of treatment must be monitored and adjusted for maximum efficacy. The management of intraoperative events may determine the outcome of the case. Vigilance is imperative.

Postoperatively evaluation of the ventilation in patients is done with capnography and oxygen saturation, but also clinically by examining patients for chest wall rise, tachypnea, labored ventilation, and anxiety which may be signs of respiratory compromise. Evaluation of acid–base status both in respiration and in metabolism may help to determine the cause of difficulty in postoperative ventilation.

Management of postoperative sleep apnea

There are several causes for prolonged postoperative apnea [33, 34]. Higher doses of opioids that are administered preoperatively and intraoperatively cause prolonged postoperative apnea. Careful titration of naloxone, in doses of 0.1–0.4 mg, administered i.v., can readily reverse opioid-mediated effects. As described earlier in this review, opioids may reduce the respiratory drive. Further, opioid administration may decrease tidal volume and respiratory rate. The effects of lower tidal volume and respiratory rate include: hypercarbia, hypoventilation, and hypoxemia.

Anesthetic agents such as nitrous oxide, benzodiazepines, induction agents, hypnotics, and muscle relaxants may cause pharyngeal collapse [32, 35–43]. The effects of benzodiazepenes may be reversed rapidly with flumazenil. Normally flumazenil is administered in doses of 0.1–1.0 mg i.v. The respiratory depression from muscle relaxants are typically reversed in the operating room with neostigmine and with glycopyrrolate. Larger doses of neostigmine and glycopyrrolate, or in certain conditions, calcium, in doses of 100–500 mg administered i.v. may facilitate reversal of neuromuscular blockade.

Prolonged postoperative apnea is often seen in obese patients. This postoperative apnea may be related to prolonged partial upper airway obstruction, intermittent airway obstruction, or complete airway obstruction. These cases result in the disruption of normal ventilation. Obese patients should not be left flat as this impairs the breathing mechanics of the obese patient. The flat positioning of the obese patient may result in mechanical apnea. Pharyngeal airway tissue is enlarged in obese patients and can cause apnea during sleep. Enlarged pharyngeal airway tissue is considered one of the classical signs of obstructive sleep apnea. As many as 80–90 % of individuals with obstructive sleep apnea are undiagnosed [35]. Increased neck circumference has also been associated with obstructive sleep apnea [36, 37]. The correct transport from the operating room to the recovery room of patients who have obstructive sleep apnea should emphasize proper positioning, supplemental oxygen, and vigilant monitoring of the patient.

Proper positioning, supplemental oxygen, pulse oximetry, capnography, arterial blood gas analysis, and electrocardiogram monitoring are important for the avoidance of postoperative hypoxemia. The utilization of paralytics requires judgment. An additional adjuvant agent to consider is steroids. Steroids may be used to decrease the amount of airway swelling [38]. The administration of steroids depends on the appropriate clinical situation.

Certain requirements must be met before extubation. The development of a rescue airway management plan is necessary before extubation. It is imperative to ensure that neuromuscular function has returned completely before one considers extubation. The upper airway must be intact before extubation.

The ventilation must be monitored for negative pressure. The prevention of negative pressure pulmonary edema in cases of spontaneous ventilation is important. Negative pressure pulmonary edema that presents in an obstructed airway requires reintubation [39, 40]. Other clinical important measures against negative pressure include: blood pressure control that reduces the edema of the upper airway, reduction of deep vein thrombosis, the use of continuous positive airway pressure (CPAP), and the use of bi-level positive airway pressure (BIPAP).

CPAP stabilizes the partial pressure of O_2 (PaO_2) by several mechanisms. These mechanisms include: sustained opening of upper airways, influence on the stretch receptors that regulate respiration timing and increase of FRC. CPAP is effective in the treatment of obstructive and mixed

apnea. CPAP is not effective against central apnea. CPAP may be delivered by a variety of methods. In the setting of the recovery room, a nasal or face mask with a water pressure of 3–6 cm or specialized nasal prongs utilize CPAP effectively.

Gastric distension and use of the nasogastric tube aid the management of post-operative ventilatory impairment. Chest X-rays taken in the post-operative period assist in the examination of lower airway symptoms. These symptoms include: post feeding regurgitation or wheezing. Upper airway obstruction is evaluated by head and neck 3-dimensional tomography, lateral neck radiography, and fiberoptic assessment. Fiberoptic examination of the larynx via the nose in the presence of spontaneous ventilation is useful. In general, assistance from the otolaryngeal service often proves to be a valuable post operative resource [41].

Sound technique prevents post-operative complications. One such technique is the delivery of warm and humid inspired gases from the start of anesthesia. Another technique is use of the lowest concentration of oxygen that is compatible with acceptable oxygen saturation. Furthermore, another technique is the vigilant monitoring against conditions such as denitrogenation and atelectasis. Emergency tracheotomy or scheduled tracheotomy may manage severe airway obstruction.

The use of elastic or compression stockings and subcutaneous heparin may decrease both deep venous thrombosis and pulmonary embolus formation. Each individual case must be thoroughly evaluated and the needs unique to each case must be satisfied. Intubation, extubation, and control of pain must be performed in the presence of prolonged postoperative apnea. Patients with obstructive sleep apnea present a higher risk of airway compromise during the postoperative period [42].

Causes of airway bleeding should be ruled out. Airway bleeding ought to be treated immediately with surgical help. Pain may be a serious concern in the postoperative period. The postoperative management of pain is important. Both post operative complications and morbidity may be decreased through the appropriate management of post operative pain [43].

Electronic monitoring and visual monitoring of regional/local anesthesia can facilitate satisfactory and safe postoperative analgesia. It is important to use sedatives and opiates for pain control with judgment in the postoperative period in order to prevent aspiration, especially in high risk patients. High risk patients merit special care.

Summary

Patients who emerge from anesthesia experience mild hypoxemia, hypercapnia, atelectasis, airway obstruction, and even minor bronchospasm. These complications may be prevented with proper prophylactic therapy. It is essential to monitor postoperative ventilation and pulse oximetry in patients. Before any procedure, every patient should learn of possible adverse potential outcomes in the perioperative period, including the risk of postoperative apnea. It is essential in the preoperative stage to identify those high risk patients who will require postoperative respiratory support. The administration of all postoperative sedative agents in these patients ought to be discontinued. These patients should be evaluated for narcosis depth and for muscle relaxation. The administration of reversal agents may be needed. Inadequate respiration that causes hypoxemia could persist in spite of oxygen administration, airway management, and bronchodilator administration. In the case of this persistent hypoxemia, it may be prudent to use supportive measures such as positive airway pressure [19]. Pulmonary edema, pneumothorax, pulmonary embolism, and obstruction of airways should be considered. Techniques including the proper determination of the arterial blood gas values and the sound adjustment of the ventilator support the recovery of the patient. Anesthesiologists must simultaneously monitor the circulatory status and provide support during changes. In severe cases, the administration of sedatives and the use of mechanical ventilation may be required and maintained to recovery. Emergency tracheostomy or scheduled tracheostomy may be necessary in order to manage severe airway obstruction in the post operative period.

Successful care of the patient with apnea demands: understanding of the unique needs of the patient, control of pain, consideration of opiate and/or neuromuscular blocker effects.

Conflict of interest The authors have no relationships with pharmaceutical companies or products to disclose, nor do they discuss off-label or investigative products in this lesson.

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