招-II PERIOPERATIVE VENTILATORY MANAGEMENT IN CHILDREN

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Characteristics of the developing lungs and thorax

In the human fetus, the development of airways down to the bronchioles occurs as early as 16 weeks of gestation. The development of the alveolus from the primitive terminal saccules, however, starts near term, about 36 weeks of post-conception, and most of alveolar development takes place postnatally.[1] The development and growth of the lungs and surrounding thoracic structures continue with amazing speed during the first year of life. At full-term birth, the number of terminal air sacs (most of which are the saccules) is somewhere between 20-50 million.[2] By 18 months of age, the number reaches the adult level of 300-400 million and most alveolar formations are completed.[3]

In the neonate, static (elastic) recoil pressure of the lung is very low (or the compliance, very high) because the development of elastic fibers in the lung takes place postnatally and continues beyond the first year of life.[4] Alveolar septa are thick with poor capillary development. In addition, the compliance of the chest wall is extremely high (elastic recoil, low) due to the cartilaginous rib cage with poorly developed thoracic muscles. The ratio of chest wall and lung compliance in the adult is approximately 1:1, whereas the ratio in the newborn is 3-4:1. In the premature newborn, the ratio could be 6:1 or higher.[5] These unique characteristics of the thorax and lungs make infants' lungs more vulnerable to collapse and prone to injury by conventional mechanical ventilation (CMV). Throughout infancy and early childhood, static recoil pressure of the lungs increases steadily (compliance, normalized for size, decreases) toward normal values for young adults.[6] The chest wall, on the other had, stiffens and compliance decreases rather rapidly in relation to the lungs during the first year. By 9 to 12 months of age the ratio of thoracic and lung compliance approaches 1:1, although both the chest wall and the lungs continue to stiffen for several more years.[7] This rapid decrease in chest wall compliance may be due to increasing thoracic muscles and connective tissues in preparation for an upright posture.[7]

Functional residual capacity (FRC) is the end expiratory lung volume and is determined by the balance between the outward recoil of the chest wall and inward recoil of the lungs. FRC in the supine position is normally about 40% of total lung capacity (i.e., FRC/TLC ratio: 0.4) in all ages.[8] In young infants, however, FRC is maintained by sustained contractions of inspiratory muscles to compensate for the extremely compliant chest wall against the inward recoil pressure of the lungs.[4]

The effect of general anesthesia on lung mechanics

Under general anesthesia or muscle paralysis, the compensatory outward recoil of the chest wall (by the tonic contractions of inspiratorty muscle) is lost and FRC decreases markedly (as low as FRC/TLC: 0.15), resulting in airway closure and atelectasis.[9] According to a chest CT scan study, atelectasis consistently occurs in the dependent (posterior) portion of the lungs. A positive endexpiratory pressure (PEEP) of 5 cm H_2O restores FRC and avoids the collapse of the lungs.[10] The effect of anesthesia on the reduction of FRC is most significant in young infants less than 8 months of age, when the thoracic structures are not yet developed to sustain the thoracic volume.[11]

How should we ventilate infants and young children who are under general anesthesia with or without muscle paralysis? Based on the anesthetic effect on FRC, a PEEP of 5-6 cm H_2O is essential, especially in those less than one year of age. A tidal volume (V_T) of approximately 10 ml/kg with age-appropriate respiratory rates (12-20/min) should be sufficient, with fine-tuning based on the endtidal PCO_2 ($P_{ET}CO_2$) on a gas monitor.

Most ventilators incorporated in modern anesthetic machines are acceptable for pediatric use whether they are a bellow type (Datex), a piston type (Draeger) or a constant flow interrupter type (Siemens), using either a

volume- or pressure-controlled mode. A volume-controlled mode is problematic, however, when there is a gas leak around the endotracheal tube and when managing infants with a small tidal volume (V_T < 80 ml). The tidal volume on a ventilator monitor is often inaccurate and tends to overestimate V_T, due to the compliance of the anesthesia delivery tubings and gas compression/expansion within the anesthetic circuit.

Traditionally, cuffed endotracheal tubes were about recommended for children less than 8 year of age. This was in part due to a concern for an increased flow resistance of a cuffed tube (Usually, a cuffed tube with an ID, 0.5-1.0 mm smaller than an uncuffed tube is used). Also, there have been some reports of tracheal damage from high-pressure cuffs after prolonged intubations. The recent trend, however, is toward the use of cuffed tubes in younger children (and even in infants). The reasons are: 1) spontaneously breathing patients are not usually intubated; 2) the airway injury commonly occurs at the cricoid mucosa by the oversized tube or after repeated intubation attempts with uncuffed tubes; 3) the control of ventilation is better with a cuffed tubes without air leak; and 4) air pollution of the anesthetizing area due to gas leaks, an occupational health concern for anesthesia providers.[12,13]

The effect of general anesthesia on upper airway patency

Infants and young children tend to get upper airway obstruction more often and more severely than older children and young adults under general anesthesia, partly because of their relatively large tongue in relation to a small mandible. The pharynx is surrounded by soft tissues and its patency is maintained by the tonic and phasic contractions of a number of muscles contracting synchronously with the diaphragm. In particular, the genioglossus and geniohyoid muscles move the tongue anteriorly while levator and tensor palatini muscles, among others, maintain the patency of the nasopharynx.[4]

According to Thatch and others, the patency of the pharynx in infants is maintains by a feedback mechanism between the diaphragm and the upper airway muscles.[14] A negative pressure (a suction force) produced in the pharynx during inspiration by the contraction of the diaphragm elicits the increased contraction of the pharyngeal muscles by the feedback reflex and, at the same time, suppresses the intensity of the diaphragmatic contraction, so as to keep the suction force in check and upper airway mucosa from collapsing.[14] This fine balance is lost under general anesthesia because the upper airway muscles are more sensitive to the depressing effect of anesthesia than is the diaphragm.[4,15] Diaphragmatic contraction is then unopposed by the upper airway feedback mechanism and, consequently, the pharynx collapses either at the nasopharynx or at the base of the tongue.

In infants and children, who are breathing spontaneously under general anesthesia, the upper airways can be kept patent by the use of a mask with an insertion of an oral or nasal pharyngeal airway, provided that the ventilatory drive is not severely depressed by the effect of anesthesia and other medications. Alternatively, a properly placed laryngeal mask airway (LMA) is equally effective for the maintenance of the upper airways. In either case, the addition of a low PEEP (5-6 cmH_2O) further improves airway patency and decreases the work of breathing.[16] Spontaneous breathing under a light inhaled anesthetic (1 MAC or less), especially combined with a caudal or low epidural block (for lower abdominal or lower extremity surgery) is, in general, well tolerated (provided that $P_{ET}CO_2$ < 60 mmHg). Infants less than 8 months of age or those with chronic lung disease (such as bronchopulmonary dysplasia [BPD]) are exceptions; they tend to develop thracoabdominal asynchrony, even when the upper airways are patent, and $P_{ET}CO_2$ rises to unacceptably high levels, especially when premedicated with a benzodiazepine derivative or an opioid.

Ventilator-induced lung injury (VILI)

Recent studies have shown that mechanical ventilation with inadvertent lung over distention for a short period of time can cause lasting lung tissue damage and affect the outcome, especially among those who are prematurely born and those with immature and damaged lungs.[17,18] The possibility of VILI is no longer limited to those in the ICU with respiratory diseases, who are chronically ventilated. A recent multi-center study on ventilatory management of patients with ARDS highlighted the issue of VILI and the beneficial effect of the so-called lung protective approach to mechanical ventilation.

Conventional ventilatory management of patients with ARDS has been to maintain near normal V_T (10-15 ml/kg), PaO_2, $PaCO_2$ and pH with minimum PEEP and maximum peak airway pressure as needed. The new

(small tidal volume) approach advocates the use of a small VT (4-6 ml/kg), a high enough PEEP to keep the lungs open and minimize the peak airway pressure to prevent high volume trauma to alveolar and capillary membranes. Hypercapnia is tolerated as long as pH is kept above 7.25.[19-22] The dramatic difference in morbidity and mortality between the control and study groups in favor of the small VT approach forced the multi-center group to stop the investigation midway through the planned study period.[22]

Currently, ventilator-induced lung injury is believed to occur in two principal ways: (1): high volume trauma or volu-trauma and (2): low volume trauma or shear stress trauma.[21] High volume trauma is the consequence of hyperdistention of the alveolar and capillary membranes with consequent release of proinflammatory cytokines activation of the alveolar macrophages and neutrophils, and a subsequent inflammatory cascade, plasma leakage and surfactant inactivation, leading to further lung damage and ARDS.[21] Low volume trauma is caused by the cyclic opening and closing of the small airways and alveoli with each positive pressure ventilation and the consequent stress and damage of cell membranes between the static and moving tissue segments, and the resulting inflammatory cascade as described above.[21,23] In order to prevent high and low volume lung injury, the airspace should be kept open with appropriate PEEP and conventional mechanical ventilation (CMV) needs to be set within the "safe zone" of lung volumes, avoiding the too high peak pressure and the too low endtidal volume with adequate PEEP while PCO_2 is allowed to float upward (permissive hypercapnia).[5,21]

Ventilatory strategies in the Pediatric ICU (PICU)

Ventilatory management in the PICU should be planned according to the pathophysiological nature of the patients. They can be divided into several categories:

1. Primary ventilatory failure
   - Postoperative patients
   - Neuromuscular disorders
   - Brain injury
2. Parenchymal lung disease
   - Acute lung injury, ARDS, IRDS
   - Pneumonia
3. Lower airway disease
   - Bronchial asthma, bronchiolitis
4. Cardiac failure

Primary ventilatory failure is managed with conventional mechanical ventilation:

1. Volume controlled ventilation
2. Physiologic PEEP (5-6 cmH_2O)
3. Normocapnia
4. Avoid hypercapnia in case of brain injury
5. For ventilatory support for weaning:
   - Synchronized intermittent mandatory ventilation (SIMV)
   - Pressure support ventilation
   - CPAP

Parenchymal lung disease is characterized by decreased lung compliance, increased tissue viscoelastic resistance (whereas airway resistance may or may not be affected), and airway closure and atelectasis with ventilation-perfusion imbalance and increased intrapulmonary shunting. The primary goals of ventilatory management are the recruitment of atelectatic air spaces and the maintenance of FRC, and to prevent or minimize VILI. The therapeutic approach is the so-called lung protective approach to maintain acceptable gas exchange, as has been described above.[5,21]

The pathophysiology of lower respiratory tract disease consists of central and/or peripheral airway obstruction due either to airway constriction/spasm (asthma) or inflammation and swelling of airways and surrounding lung parenchyma with intraluminal debris, resulting in hyperinflation, air trapping, auto PEEP and inadequate lung emptying at end-expiration. Ventilatory strategy includes the pharmacological approach, including bronchodilators, cortocosteroids and diuretics. The expiratory time on CMV is increased to accommodate slow expiration and to minimize auto PEEP. A higher PEEP may be used to prevent premature airway closure to facilitate lung emptying. Helium-oxygen mixture (Heliox) with lower gas density decreases airflow resistance and facilitates lung emptying, although this practice, once popular for the treatment of emphysema, has not been commonly practiced. In severe cases of air trapping and hypercapnia, high-frequency oscillatory ventilation is useful to facilitate CO_2 elimination. In infants and children with heart failure, especially those with right ventricular failure and who are preload dependent, the reduction in mean airway pressure is important to minimize the effect of CMV on cardiac output and blood pressure.

High frequency oscillatory ventilation (HFO)

High frequency oscillatory ventilation or high frequency oscillation (HFO) in children was developed by a group of

investigators at the Hospital for Sick Children in Toronto in the late 1970s, about the same time as the development of its counterpart in adults by investigators in Boston and elsewhere.[24,25] Unlike its predecessors, high frequency positive pressure ventilation (Oberg and Sjostrand, 1967)[26] and high frequency jet ventilation (Klain and Smith, 1977)[27], in which expiration was achieved by passive exhalation, in HFO both the inspiratory and expiratory phases are accomplished actively. In the early models of HFO, the waveform was sinusoidal with a 1:1 inspiratory and expiratory ratio.[28] In the newer models of HFO generators, both the waveform and I/E ratio can be altered. With HFO, unlike CMV, the efficiency of oxygenation and CO_2 elimination are not directly linked. Gas exchange under HFO is achieved by the combination of bulk flow and agitated diffusion. With the HFO generator, the mean airway pressure (PEEP) is set by the bias flow and amplitude. In our clinical practice (Sensormedics 3100A), we normally use 8-10 Hz for infants and 5-6Hz for children up to 30 kg. In the premature lungs, HFO is found to be lung protective in comparison to CMV. This is particularly true when neonatal resuscitation at delivery with a high volume IPPV is avoided.[5,17]

Liquid assisted ventilation

Total liquid ventilation (TLV) was originally described in animals by Clark and Golan (1966),[29] but it was not clinically applied until relatively recently. Liquid ventilation is most useful for ventilating the stiff lungs, due to a loss of or inactivated pulmonary surfactant with increased surface tension, by eliminating the gas-liquid interface in the alveoli. By using a liquid perfluorochemical (PFC) with extremely high gas solubility, a sufficient quantity of oxygen can be delivered to the lungs, although, because of high airway resistance and slow liquid movement, CO_2 elimination is problematic. In a clinical setting for the newborn, using a special liquid ventilator or exchanger, the respiratory rate of 3-8/min with relatively large V_T (15 ml/kg) has been used.[30]

Partial liquid ventilation (PLV) has been developed in part to eliminate the problem of CO_2 accumulation with TLV. With this system, the lungs are partially filled with PFC, usually 30 ml/kg, with several different methods of instillation. Ventilation is achieved by means of a conventional mechanical ventilator.[31] The safety of liquid ventilation with possible decreases in inflammatory process in the lungs, has been demonstrated in a number of experimental and pilot clinical studies in adults with ARDS,[32] as well as in newborn infants with prematurity, congenital heart disease, diaphragmatic hernia, and meconium aspiration syndrome.[33,34] Although the results of early studies in infants have been encouraging, only a multi-center clinical trial for PLV in adult patients with ARDS has so far been underway.

Ventilatory strategy in infants and children with acute respiratory insufficiency

Up to the present time, the ventilatory strategies in the pediatric, neonatal or adult ICUs have been to begin with conventional mechanical ventilation (CMV) with the ventilator settings, F_IO_2 and the level of PEEP adjusted as needed. High frequency oscillation (HFO) is used only when the patient fails to improve on CMV. An additional treatment, such as exogenous surfactant and inhaled nitric oxide, may be added. Extracorporeal membrane oxygenation (ECMO) (and possibly partial or total liquid ventilation in the future) is added to the list as the last resort only when everything else has failed. With the increased understanding and awareness of ventilator-induced lung injury over the last few years, it may be the time to critically reevaluate this "serial approach" of ventilatory management.[5] Instead, the choice of the initial ventilatory management should be based on the pathophysiology and potential outcome of respiratory insufficiency and, in some cases, such as the neonate with congenital diaphragmatic hernia, ventilatory management should be started with HFO rather than CMV.[5]

In summary, pedidatric anesthesiologists, surgeons and intensivists should know the special characteristics of the developing lungs and thorax for a better understanding and management of infants and young children during the perioperative period. During the first year of life and beyond:

- The lungs are extremely compliant and are prone to airway closure and injury
- The chest wall is extremely compliant; FRC is maintained with tonic inspiratory muscle contractions.
- General anesthesia and paralysis abolish the muscle tone; FRC decreases, the airways collapse and atelectasis ensues
- A low PEEP (5-6 cmH_2O) maintains the FRC and prevents atelectasis
- The patency of the pharynx depends on the tonic and

cyclic muscle contractions.

- The upper airway muscles are disproportionately sensitive to general anesthesia and this results in upper airway obstruction in the patients breathing spontaneously under general anesthesia
- A low CPAP (5-6 cmH_2O) diminishes upper airway obstruction
- The lungs of infants and young children are especially vulnerable to injury by mechanical ventilation even during the perioperative period
- Ventilatory management in the pediatric ICU should be adjusted according to respiratory pathophysiology
- In patients susceptible to VILI, the lung protective strategy should be exercised with a small tidal volume, appropriate PEEP and permissive hypercapnia

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