Recent Advances on Pediatric Ventilation

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Abstract

The prevention of ventilator-induced lung injury and diaphragmatic dysfunction is now a key aspect in the management of mechanical ventilation, since these complications may lead to higher mortality and prolonged length of stay in intensive care units. Different physiological measurements, such as esophageal pressure, electrical activity of the diaphragm, and volumetric capnography, may be useful objective tools to help guide ventilator assistance.

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Introduction

Respiratory failure is the leading cause of admission to pediatric intensive care units (PICUs).(1-3) Mechanical ventilation (MV) is a lifesaving therapy which improves gas exchange and decreases the work of breathing. MV consists of a pressurized volume of gas delivered by either an invasive (tracheal tube or tracheostomy) or a non-invasive interface. MV is particularly challenging in children because of the heterogeneity of this population in terms of age, weight, and pathophysiology. Mechanical ventilation is a cornerstone in the management of patients with acute respiratory distress syndrome (ARDS). We now know that mechanical ventilation per se can aggravate lung injury, a process referred to as ventilator-induced lung injury (VILI), through several mechanisms including volutrauma, barotrauma and biotrauma.(1-4) Dynamic lung distension and repeated opening and closing of recruitable lung units are considered the two main mechanisms contributing to lung injury (132 full pdf).

In this brief review, we aim to discuss the current clinical challenges of pediatric ventilation. We will also focus this discussion on recent advances regarding-

1. Optimization and individualization of patient–ventilator interactions during MV to prevent ventilator induced lung injury,
2. Application of high-frequency oscillatory ventilation (HFOV), and
3. The role of non-invasive ventilation (NIV)

Advances in the management of mechanical ventilation to limit ventilator-induced lung injury (VILI)

Dynamic lung distension and repeated opening and closing of recruitable lung units are considered the two main mechanisms contributing to lung injury. These days there is use of a global lung-protective ventilatory strategy, referring to low tidal volume and high levels of positive end-expiratory pressure (PEEP), in order to prevent ventilator-induced lung injury (VILI) which improved survival in patients with acute respiratory distress syndrome (ARDS).(4-8) The only way to assess the respiratory mechanics and the effects of MV on the lung itself are the ventilatory pressure, flow, and volume measured by the ventilator. But these recording variables reflect the respiratory system as a whole and do not take into account important pathophysiological features (e.g. chest wall compliance, intrinsic inspiratory/expiratory respiratory effort, heterogeneity of lung disease, etc.).

Current challenge is to optimize and individualize MV by monitoring at the bedside for avoiding barotrauma, volutrauma, atelectrauma, and biotrauma.(9) To do so, transpulmonary pressure and capnography monitoring are helpful. The transpulmonary pressure is defined by the difference between the airway pressure and pleural pressure and is considered as the lung-distending pressure. This pressure measurement is closely correlated with lung strain and risk of VILI.(13) Measurement of oesophageal pressure (Poes) as a surrogate for pleural pressure helps to determine the lung mechanics and separate the effect of the chest wall.(10) In addition, the assessment of lung recruitability may be of great help to individualise the settings for mechanical ventilation and choose the level of positive end-expiratory pressure (PEEP) needed to keep the lung sufficiently open to minimise the risks of repeated opening and closing of alveoli. Despite controversies regarding the interpretation -of absolute values of esophageal pressure, a recent paper reviewed the usefulness of this tool in ventilation management.(14) When a given amount of pressure is delivered, it is of great importance in some situations to better know which percentage is distending the lung (potentially harmful to the lungs) and which amount is distending the chest wall. In ARDS, at the end of expiration, transpulmonary pressure can be negative (when pleural pressure exceeds end-expiratory airway pressure) which induces collapse of the alveoli and expose these parts of the lungs to being repeatedly reopened and recollapsed at each breath. A balance between protecting aerated units from over-distension and recruiting unstable units must be obtained for the prevention of VILI.

The titration of PEEP based on esophageal pressure measurement[15-17] has been proposed in patients with ARDS. Talmor et al[12] showed that oxygenation and lung compliance were significantly improved in patients managed by a ventilator strategy including esophageal pressure measurement. This recent interest in transplumonary pressure has contributed to the development of such monitoring in several advanced ventilators. Unfortunately, such ventilators are not available in all units in India. We believe that the use of transpulmonary pressure has to be developed and more research in this field is needed to validate the best strategy to quantify esophageal pressure in children and to confirm its utility in ventilation titration.

Volumetric capnography (Vcap) is also a novel tool which allows the measurement of physiological and alveolar dead space at the bedside.[21-23] In this technique, expired CO_2 is plotted against the tidal volume for each breath. Vcap analysis gives index of ventilation/perfusion (V/Q) mismatch, containing shunt and indices of lung efficiency (physiological and alveolar dead space). Vcap can help to set PEEP to obtain the lowest physiological and alveolar dead space, the lowest arterial to end-tidal CO_2 gradient ($PaCO_2$–$ETCO_2$ gradient), and the optimal alveolar plateau slope (SIII) that reflect V/Q heterogeneity.[24-27] We believe that Vcap will help clinicians to set PEEP routinely in the near future.

There are increasing evidence on the role of diaphragmatic functions which suggests that MV is associated with diaphragmatic dysfunction and atrophy, also known as ventilator-induced diaphragmatic dysfunction.[29-31] To limit such consequences on the diaphragm, specific efforts should be addressed to reduce the duration of MV and to optimize ventilator settings. Improving individualized MV at bedside to limit diaphragmatic weakness is a great challenge but is essential to successfully wean patients from MV and decrease poor outcomes.[30,32,33] Monitoring of the electrical activity of the diaphragm (EAdi) provides new information to clinicians in order to assess diaphragm function and the impact of ventilation on the diaphragm muscle that can lead to rapidly progressive diaphragmatic weakness.[30.32] EAdi has been shown to reflect the patient ventilatory drive, and it is well correlated with work of breathing based on short-term physiological studies.[34,35] EAdi permits the detection of periods of blunted drive secondary to over assistance,[36] which likely favour the risk of diaphragm dysfunction. It therefore may be used as a tool to adjust ventilatory support,[37] to detect tonic activity of the diaphragm (which reflects the effort of the patient to increase the lung volume),[38] and to assess patient–ventilator asynchrony.[39] When combined with pressure or volume delivered, EAdi measurements permit the assessment of diaphragm neuroventilatory (VT/EAdi) or neuromechanical (ΔP/EAdi) efficiency.[40] In the only pediatric study on this topic to date, Wolf et al[41] observed that the ability to generate a higher diaphragmatic activity for the same tidal volume in pressure support ventilation (PSV) was a predictor of successful extubation.

This technology requires a specific nasogastric catheter equipped with distal electrodes connected to a dedicated ventilator. The main clinical application of EAdi monitoring is the neurally adjusted ventilatory assist mode (NAVA), a mode of ventilation which uses the EAdi to trigger and cycle-off breathing efforts and determine the amount of ventilator assistance. NAVA has many advantages compared to conventional MV, including improved patient–ventilator synchrony[39,42-45] the potential for a reduction in barotrauma (secondary to a decline of inspiratory pressure and tidal volume)[23,39,42,44,46] a possible decrease in atelectrauma,[47] and finally, improved diaphragmatic efficiency.[40] Moreover, NAVA improves unloading of the respiratory muscles and prevents the risk of over-assistance through down regulation of EAdi induced by increased assistance.[37] A recent randomized trial[48] was conducted in children to test the clinical impact of NAVA and found that the feasibility of NAVA in clinical practice was confirmed, and it was associated with lower FiO_2 requirements and lower inspiratory pressures. A trend for shorter duration of ventilation was observed, but it did not reach statistical significance. Now a days NAVA mode is used in difficult-to-wean children, in children who have undergone cardiac surgery, or any case in which the promotion of assisted ventilation and avoidance of diaphragm rest is important. EAdi is also routinely used to detect diaphragm contractility recovery in children with neuromuscular disease (e.g. botulism, Guillain-Barré syndrome, and cervical trauma).

Advances in weaning from mechanical ventilation

Because of MV's potential complications, such as VILI[49] and severe diaphragmatic atrophy[30,32] so it must be discontinued as soon as the patient is capable of sustaining spontaneous breathing.

On the other hand, premature extubation may also be problematic, as higher mortality rates have been reported in patients with extubation failure.[2,50] Consequently, when and how to perform MV weaning are key questions in critically ill patients. The identification of extubation readiness is usually based on clinical judgement, according to the respiratory, neurological, and hemodynamic status.

Clinical and research efforts have focused on early identification of weaning readiness. The development of the closed-loop system (CLS) (computerized protocol implementing recommendations regarding extubation without caregiver intervention) optimizes ventilatory support on a continuous basis according to the patient's respiratory condition. CLS offers consistent orders that constrain interpretation variations among caregivers, potentially resulting in a more efficient application of protocols. The use of CLS leads to a quicker adjustment of ventilator settings assessed by a reduction of time between the assessment of patient status and medical order, and medical order and clinical execution.[53]

Two CLSs are commercialized for respiratory weaning: Smart- Care/PS® (Dräger Medical, Lubeck, Germany) and IntelliVent® (Hamilton Medical, Bonaduz, Switzerland). These systems automatically reduce the level of support when the patient's respiratory rate, tidal volume, and end tidal CO2 (EtPCO2) are within acceptable ranges. In adults, these systems reduced the weaning time without increasing adverse events.[54] Currently, only two trials, one for each of these two technologies, have been conducted in children, and their findings regarding safety and duration of weaning process are encouraging.[28,53] A significant limitation of these systems remains the minimal weight/age required (15 kg for Smartcare/PS ® and 7 kg with Intellivent®) and they cannot be used in case of significant leaks around the endotracheal tube. These automated systems will improve the management of MV and therefore the outcome of patients, allowing the customization of ventilator support according to each child's condition. However, companies and researchers should now focus their efforts on algorithms adapted to our pediatric population.

During the weaning process, identifying whether or not patients will be able to breathe spontaneously after extubation is a significant challenge. The recent consensus conference on pediatric ARDS (PALICC) has addressed this question and recommended that spontaneous breathing trials (SBTs) or extubation readiness tests should be performed.[55] Determining inclusion criteria for SBT initiation has been a difficult challenge because of the broad patient population, different modes of ventilation, and lack of consensus for acceptable SBT parameters.

Another limitation is appropriate timing for starting SBT. For these reasons, some patients who qualify for SBTs may not be recognized, which may result in a prolonged ventilation course. Some institutions are now using electronic data pooled from ventilators and electronic medical records to develop explicit software rules and algorithms (decision support) to help identify patients who may be ready for SBT. Assuming a patient has met certain parameters for SBT criteria (EtCO2, SpO2, tidal volume, respiratory rate, inspiratory pressure, etc.), the electronic medical record can provide visual cues to help remind clinicians that their patient is ready for SBT. In adults undergoing SBT, the use of an inspiratory pressure of 5 to 8cm H_2O is recommended.[56] In children, very few data exist regarding the optimal method to conduct a SBT. Interestingly, a physiologic study conducted by Khemani et al, comparing a SBT with a continuous positive airway pressure (CPAP) of 5 cm H_2O versus pressure support of 10cm H_2O, concluded that pressure support significantly underestimates the potential for post extubation breathing efforts.[57] According to this recent study, we recommend performing a SBT in CPAP mode or with a T-tube. However, it should be noted that respiratory efforts observed during CPAP trial will be reflective of the efforts observed after extubation but will be larger than during SBT with PSV. Therefore, it is not surprising to observe increased efforts during CPAP, which should not lead to delay in extubation unless they appear to be objectively poorly tolerated.

During weaning, esophageal pressure measurement can be a useful tool to assess the work of breathing. A robust parameter which can be derived from esophageal pressure and transdiaphragmatic pressure, i.e. the difference between esophageal pressure and gastric pressure, is the pressure-time-product. This parameter was used as a tool to assess work of breathing and optimize ventilation support in children with different diseases.[18,20] Jubran et al showed that esophageal pressure trend during a SBT provided an accurate prediction of weaning outcome.[58] Over the course of a SBT, esophageal pressure-time-product remained unchanged in successfully weaned patients. In contrast, weaning failure patients developed marked and progressive increase in esophageal pressure-time-product (up to 4-fold above the normal value) as a result of an increase in the mechanical load of the respiratory muscles.[58]

Advances in high-frequency oscillatory ventilation (HFOV)

HFOV has been commonly used for decades in neonatal, pediatric, and adult populations.[58] Clinical trials have demonstrated that HFOV is associated with an oxygenation improvement in patients with acute lung injury or ARDS.[59-61] However, the clinical use of HFOV in this population has decreased. Recent studies demonstrated an association between early use of HFOV and worse outcome in terms of mortality in adult[62] and pediatric populations.[63,64] However, several biases have been highlighted in the two pediatric studies regarding the methodology.[65–67] As suggested by Rettig et al, the mortality in patients with ARDS supported by HFOV may be linked to the disease category itself rather than the use of HFOV.[68] Given these limitations and with regard to our clinical experience, we consider, as supported by the PALICC, HFOV to still be a rescue therapy in some children with severe ARDS.

Advances in non-invasive ventilation (NIV)

NIV is defined as the delivery of MV without an endotracheal tube or tracheostomy. NIV comprises both

CPAP and bilevel positive airway pressure (BiPAP) ventilation. NIV is increasingly used in PICUs.[69,70] In the last decade, the potential indications for NIV in critically ill patients have grown considerably, and the performance of this mode of support has greatly improved. In children developing ARDS, NIV can be considered as a first line of treatment in milder disease.[55] Despite the lack of clear guidelines, this mode of support definitely has its place in the treatment of a wide range of pathologies in children, including pneumonia, upper airway obstruction, post-extubation respiratory failure, acute chest syndrome, and asthma.[70]

The use of NIV has recently evolved because of the emergence of high-flow nasal cannula (HFNC). This modality is now available from a number of manufacturers and has been widely adopted in practice. Different mechanisms have been hypothesized to account for the clinical benefits, including washout of the nasopharyngeal dead space, reduction of work of breathing, decrease in airway resistance, and improvement of pulmonary compliance.[71,72]

HFNC has been able to provide a mean pharyngeal pressure of 4 cm H_2 O when used at a flow of 2 L/kg/minute,[73] but this effect is variable. In clinical use, HFNC allows improvement of comfort and tolerance to NIV and reduction of air leak, gastric distension, and skin injuries, especially in younger children. The literature is still poor to identify the specific population that would benefit from this technology.[18,74] The role of HFNC outside the PICU still needs to be investigated, and we currently restrict HFNC use in the PICU.

More evidence is expected from several ongoing randomized controlled trials (TRAMONTANE study, NCT02457013; Hi-Flo study, NCT01498094; HHFNC study, NCT01662544). We believe that, within a few years, the role of HFNC will be better defined and potentially widened.

The optimal interface for NIV in children has recently been discussed as a key aspect in respiratory management.[75] A large variety of devices recently emerged, including nasal, oronasal, and total face masks and helmet. Because mask-fit pressure is spread over a larger surface beyond the nose area, total face masks appear to be more comfortable than oronasal masks.[76] This device was shown to be as efficient as oronasal mask in terms of breathing pattern, gas exchange, and outcome in adults.[77] The helmet is also increasingly used[70] and should be considered as a feasible alternative for NIV in children, as suggested by the results of a recent randomized controlled trial comparing the use of a helmet and a face mask in children.[78] As for total face masks, preliminary data are pointing towards the helmet as an interface to increase comfort and decrease skin injury and air leaks.[79] Finally, to improve NIV success, the achievement of an adequate patient–ventilator synchrony is crucial.[19] Although the performance of ventilators has improved within the last few years, patient– ventilator asynchrony in NIV remains a significant issue. As with invasive ventilation, tools to improve patient–ventilator synchrony during NIV have been recently investigated. Electronic data monitoring and non-invasive neutrally adjusted ventilator assist (NAVA) are feasible and well tolerated in PICU patients with patient–ventilator synchrony improvement.[80,81] Monitoring esogastric pressure offers another way to improve patient–ventilator interaction during NIV. In infants[82] and children,[19] esophageal pressure measurement has been shown to be a valuable tool to assess patient–ventilator interaction and to optimize ventilator settings.

Conclusion

There have been major advances in the management of mechanically ventilating children over the last 3 years. The implementation of this new knowledge in usual practice is a challenge, as advances occur not only in the respiratory field but also in many fields that paediatric intensivists must digest. In such a situation, companies that design medical devices including ventilators and respiratory monitoring platforms play a key role in the application of knowledge. The creation of a ventilation consortium that includes companies, caregivers, researchers, and stakeholders could be a solution to promote knowledge implementation.

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