Editorial

Airway pressure release ventilation versus conventional ventilation for the management of pediatric acute respiratory distress syndrome: do we have an answer?

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Acute respiratory distress syndrome (ARDS) is a significant cause of respiratory failure in children who need to be admitted to the pediatric intensive care unit (PICU). The American-European Consensus Conference (AECC) and the Berlin definitions of ARDS did not address the pediatric specific practices and comorbidities (1,2). Therefore, the Pediatric Acute Lung Injury Consensus Conference (PALICC) bridged the gap to define pediatric ARDS (PARDS). The definition of PARDS differed from the adult's definition by using Oxygenation Index (OI) to replace PaO_2/FiO_2 ratio, Oxygen Saturation Index to measure the severity of illness, and deemphasized the importance of the radiographic criteria (3).

The management of PARDS has mainly focused on the diagnosis and treatment of the underlying cause and on the attempt to prevent secondary lung injury. Multiple ventilator strategies have been used by pediatric critical care specialists to improve lung recruitment, optimize positive end expiratory pressure (PEEP), and ventilate at a lower tidal volume (TV). Low TV conventional ventilation, high frequency oscillatory ventilation (HFOV) and airway pressure release ventilation (APRV) have been used, but there is a paucity of pediatric literature to show superiority of one mode of ventilation over another. In a prospective, randomized controlled trial, recently published in the *American Journal of Respiratory and Critical Care Medicine* (4), Lalgudi Ganesan *et al.* compared APRV to low TV conventional ventilation in children with PARDS. After enrollment of 52 patients, the study was terminated following an interim analysis showing an increased mortality in patients treated with APRV. Fifty three percent of children who were treated with APRV died *vs.* twenty seven percent of the children who were treated with conventional ventilation.

The authors must be applauded for their efforts to study such an important subject in a prospective randomized controlled manner. However, in reviewing the study, there were striking differences at baseline between the studied groups. APRV patients were younger and had a higher percentage of primary ARDS than their controls. There were statistically significant differences in the severity of ARDS between the two groups. Children who were ventilated with APRV had a higher PaO_2/FiO_2 ratio, and a higher OI than their controls, denoting that the APRV group was at a disadvantage at enrollment. There was no difference in the primary outcome of ventilator free days between the two groups. However, there was a difference in 28-day mortality in patients treated with APRV (RR =3.2), although non-statically significant (P>0.05) but clinically relevant. Even after adjusting for the severity of ARDS, mortality was higher in the APRV group (RR =2.02), which led to the termination of the study.

The authors concluded that there is a trend towards a

higher mortality with APRV. Although this is a significant statement with widespread practice implication, the findings should be interpreted cautiously as there are multiple limitations to the study. It is a single center study, which was underpowered by early termination and unstratified randomization. A future multicenter, randomized controlled, and appropriately stratified trial is needed to determine if APRV is a viable option in children with ARDS. Stratification is paramount for any future studies, to address the potential confounders of Ganesan's study. At baseline, children who were ventilated with APRV were relatively younger, and had a higher severity of ARDS than their controls confounders that would affect morbidity and mortality.

In Ganesan's study, children who were ventilated with APRV had a higher mean airway pressure (MAP) and they were more often spontaneously breathing. Younger children have a greater chest wall compliance than older children. Therefore, for the same pressures, volumes may be significantly higher. And if patients on APRV have increased spontaneous breathing with potentially higher generated TVs, spontaneous breathing might become theoretically detrimental, especially in younger children (those who were randomized to APRV).

Although higher MAPs in APRV might affect the hemodynamic stability by decreasing the cardiac output and renal perfusion (5,6), it has been shown that in children with ARDS, despite a higher MAP, APRV does not affect blood pressure or urine output (7) and can even restore hemodynamic stability faster than conventional ventilation (8).

The advantage of using APRV is to maximize recruitment of alveoli and allow spontaneous breathing thereby minimizing barotrauma. In animal models, APRV has been shown to successfully prevent the development of ARDS (9). In adults, a meta-analysis of six randomized controlled studies showed no significant differences in morbidity or mortality between patients treated with APRV or conventional ventilation (10). The role of APRV in pediatric critically ill patients has always been a debate. Although there have been multiple case reports and case series of APRV use in PARDS, Lalgudi Ganesan *et al.* report the first randomized controlled trial comparing APRV to conventional ventilation in PARDS.

In conclusion, the study by Lalgudi Ganesan and colleagues is very important. It is the first, randomized controlled trial comparing APRV to conventional ventilation. Unfortunately, the differences between the group of patients who were enrolled, and the lack of stratification at randomization have prevented reaching a conclusion and a definitive answer.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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