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Editorial

Lung protection strategy as an effective treatment in acute respiratory distress syndrome

Acute respiratory distress syndrome (ARDS) is a serious life-threatening lung reaction to various forms of injuries that cause hypoxia. It is a devastating injury to the lungs, characterized by diffuse pulmonary inflammation, hypoxemia, and respiratory distress (1).

Its mortality remains between 30-50%, despite early aggressive intervention (2). Regardless of the severe lung injury, pulmonary function in most survivors returns nearly normal within 6 to 12 months (1). ARSD diagnostic criteria include acute respiratory distress, bilateral radiographic pulmonary infiltrates, hypoxemia, and the Pao2 to Fio2 (P/F) ratio is less than 200, in the absence of heart failure (pulmonary artery occlusion pressure (PAOP) less than 18 mm Hg) (1, 3).

ARDS is a severe lung syndrome caused by a variety of direct and indirect issues; therefore, its pathophysiology is so complex. The lungs of the afflicted individuals show severe pulmonary edema, distributed cellular destruction, diffuse alveolar damage with alveolar flooding by proteinaceous fluid, neutrophil influx into the alveolar space, patchy alveolar collapse, loss of alveolar epithelial cells, deposition of hyaline membranes on the denuded basement membrane, formation of microthrombi and disordered repair (1, 3, 4).

The level of oxygen in the blood can stay dangerously low, even if the person receives ventilation support. In patients with ARDS, massive alveolar collapse and cyclic lung reopening and over distention during mechanical ventilation may perpetuate alveolar injury (5). Mechanisms include regional alveolar over distention, repetitive alveolar collapse with shearing (atelectrauma), and oxygen toxicity (2, 3, 6).

Experimental data suggest that atelectrauma is prominent in ARDS. Atelectrauma may be mitigated by recruitment maneuvers (periodic hyperinflations) to open collapsed lung tissue and high levels of positive end-expiratory pressure (PEEP) to prevent further collapse (7, 8). There is considerable evidence that progressive lung parenchymal injury is induced by excessive alveolar distension by large tidal volumes and alveolar collapse in the absence of PEEP. The mechanism appears to be a cytokine-induced inflammatory response, now known as ventilator-induced lung injury (9, 10). During the last decade, there has been a remarkable evolution in the ventilator treatment of acute respiratory distress syndrome. In the 1970s, high tidal volume (VT) and pressures were the rule, and the only recognized side effect was hypocapnia (11). In the 1980s, the negative effects of high pressure/volume ventilation were demonstrated and the concept of “lung rest” was progressively accepted. This led to an increasing use of lower tidal volume in the 1990s, to allow a more gentle treatment of the diseased lung (12). In theory, ventilation strategies that combine low tidal volumes with prevention of atelectrauma will be ideal for lung protection (7, 8).

Positive end-expiratory pressure has been revisited during this period, from the concepts of which PEEP should be adequate to keep open the lung and to prevent intratidal collapse and decollapse (13-15).

Recently, it has been demonstrated that mechanical ventilation by lung protection strategy can be provided in patients with ARDS, resulting in better pulmonary function and higher rates of weaning from the ventilator (5, 16). Therefore, lung-protective strategy should be applied to patients with ARDS who are on a mechanical ventilator (5). As compared with conventional ventilation, the protective strategy was associated with improved survival in 28 days, a higher rate of weaning from mechanical ventilation, and a lower rate of barotrauma in patients with the acute respiratory distress syndrome. Protective ventilation was not associated with a higher rate of survival to hospital discharge (5, 17, 18).

Lung protection was based on a strategy of maintaining low inspiratory driving pressures, with lower tidal volumes versus (vs) traditional tidal volumes (4-6 vs 10-12 mL/kg) and preferential use of limited airway pressure over regulation, with the simultaneous circumvention of alveolar collapse through the use of high PEEP to keep end-expiratory

pressures above the lower inflection point on the static pressure–volume curve of the respiratory system (4, 7).

The nearly maximal alveolar recruitment and aeration accomplished with this strategy were intended to minimize shear stresses in the lung tissue during inspiration (4, 7, 16). The lung protection strategy permitted plateau airway pressures up to 40 cm H2O; however, plateau airway pressures rarely exceeded 35 cm H2O with this strategy (4, 17). PEEP is an essential component of the management of ARDS. PEEP improves hypoxemia and decreases intrapulmonary shunting, and these effects have been the basis for titrating PEEP in clinical practice (19).

A clinical study specifically investigated the incremental effect of high levels of PEEP (17, 19). Researchers demonstrated that, despite the use of high PEEP values (up to 24 cm H_2O) and relatively higher mean airway pressures, there was a lower incidence of barotrauma in the patient treated by protective- ventilation strategy (5, 16, 17, 20). Thus, the protective-ventilation approach may not only improve pulmonary function and oxygenation but also reduces clinically apparent alveolar damage (18).

Studies showed that in the patients who suffer from ARDS treated by lung protection strategy have three important prognostic factors. The mean PEEP (positive end expiratory pressure) used during the first 36 hours, and the driving pressures (plateau pressure-PEEP) during the first 36 hours were the strongest prognostic indicator. All other respiratory variables were of secondary importance. Higher PEEP values and lower driving pressures were independently associated with better survival (5, 21). In preparing this paper, we spoke in detail to more than a dozen people with extensive knowledge of the controversy and various points of view about ARDS and best treatment strategy.

Mechanical ventilation with plateau pressure lower than 35 cm H2O and high positive end-expiratory pressure (PEEP) had been recommended and it seems that high initial PEEP values appeared to be beneficial, even when the plateau pressure value increased, as long as the driving pressure did not change disproportionately. A significant proportion of patients treated by lung protection strategy might have failed to achieve optimal protection against barotrauma with this experimental strategy. This theory was supported by recent computed tomography evidence demonstrating that response to PEEP in a heterogeneous population of ARDS patients was highly variable and frequently led to over distention as opposed to lung recruitment (17, 22).

Thus, the benefits of recruitment maneuvers and higher levels of PEEP for some might had been offset by harm to others, particularly among the relatively few patients exposed to higher plateau airway pressures (4). After a search for underlying cause of ARDS, we recommend using volume assist/control mode for mechanical ventilation according to early use of lung protection strategy by applying adequate PEEP (PEEP set 2 cm H2O higher than the inflection point of the pressure-volume curve of the respiratory system) to support oxygenation avoiding excessive stretching and hemodynamic impairment, low tidal volume to avoid a plateau pressure higher than 35 cm H_2O; lower FIO_2 (below 50-60%) and using sigh (a sequence of three consecutive sighs per minute with the volume such as to reach 45 cm H2O plateau pressure in volume control mode).

We found no evidence of significant harm or increased risk of barotrauma despite the use of this amount suggesting PEEP. In addition, the “lung protection strategy” appeared to improve oxygenation, with fewer hypoxemia related (1, 18, 23, 24).

Application of sigh during lung protective strategy may improve recruitment and oxygenation (21). Introducing three sighs per minute at 45 cm H_2O plateau pressure led to further lung recruitment. We believe that two kinds of atelectasis possibly coexist in ARDS, the compression and reabsorption atelectasis. The compression atelectasis develops immediately because of the increased lung weight, and its anatomic basis is likely the collapse of the small airways at end-expiration. As some gas is left behind the collapsed airways, the transmural pressure required for opening is relatively low (12 to 20 cm H_2O). The reabsorption atelectasis develops when the regional gas uptake exceeds the delivery (23-25).

Although, glucocorticoid therapy is not helpful in the acute phase but may control progression of fibroproliferation in late ARDS so, its prescription is recommended. In contrast, there is no indication for diuretic therapy. Using N-acetyl cysteine and surfactant in the recovery period will be helpful (26, 27).

In summary, the base line of ARDS management is ventilation support and lung-protective strategy known as the most popular strategies. It is defined as ventilation strategies that combine low tidal volumes and relatively high respiratory rate by applying positive end expiratory pressure

in relation with appropriate FiO2 to prevent atelectrauma and hypoxia in volume control mode in a tracheal intubated patient who is connected to a mechanical ventilator. There are considerable evidences that using lung-protective strategy has a significant role in patient's outcome.

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