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Brain and lung: dangerous crosstalk

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Acute lung injury (ALI) occurs in 20–25% of the patients with isolated brain injury and is associated with a poor neurological outcome [1]. Patients with ALI admitted to the intensive care unit (ICU) often develop neuropsychological changes, as do patients recovering from acute respiratory distress syndrome (ARDS) [2]. This implies that there are close interactions between the brain and lung.

The progression of brain injury to ALI is commonly explained by the "double hit" model [3]. After the brain injury, *i.e.*, the "first hit," a catecholamine storm and inflammatory reaction both occur. Inflammatory reactions lead to the migration of neutrophils and activated macrophages into the alveolar spaces and ultrastructural damage to type II pneumocytes [4], while catecholamine release leads to increased hydrostatic pressure and capillary permeability in the pulmonary vessels [5]. The normal lung becomes a primed lung, which is very susceptible to further injurious stimuli, the "second hit." The second hit can be an infection, transfusion, or inappropriate ventilatory setting with a large tidal volume and inadequate positive end-expiratory pressure (PEEP). The potentially injurious ventilation leads to stress and strain in the primed lung and results in alveoli inflammation with neutrophil recruitment and cytokine production; ultimately, ALI develops [3]. Potential risk factors for developing ALI are altered initial brain computed tomography, a low Glasgow Coma Scale score, low PaO_2/FiO, and the use of vasoactive drugs [6].

During mechanical ventilation, stimulation of the mechanoreceptors or chemoreceptors located in ALI lungs generates information that reaches the central nervous system via humoral, neural, or cellular pathways [7]. Risk factors for the development of neurocognitive deficits include the length of ICU stay, duration of mechanical ventilation, use of sedatives or analgesics, increased cytokine levels, hypoxemia, hypotension, and hyperglycemia [8,9].

Protective mechanical ventilation is needed to minimize pulmonary damage, improve cerebral blood flow, and reduce the interaction between pulmonary and cerebral damage in patients with brain injury. We must consider oxygenation, tidal volume, $PaCO_2$, and PEEP for the proper management of patients with acute brain injury on mechanical ventilation [7]. Hypoxemia not only decreases cerebral oxygen delivery but also leads to cerebral vasodilation and increases intracranial pressure (ICP). More than 20% of the patients with severe traumatic brain injury experience episodes of hypoxemia resulting in secondary brain injury. Hypoxemia should be avoided [10]. Whereas a large tidal volume causes pulmonary and systemic inflammation, a small tidal volume increases $PaCO_2$ and ICP. While protective mechanical ventilation with permissive hypercapnia is needed for patients with ALI, tight control of O_2 and CO_2 is needed for the patients with brain injury. One size does not fit all and, therefore, treatment should be individualized. The priority can change over time, i.e., sometimes it is brain over lung and at others it is lung over brain [7]. PEEP has both sides for the patient with an injured brain during mechanical ventilation. PEEP decreases the arterial pressure and cerebral blood flow and it impairs venous return and increases ICP [11], while it can recruit collapsed alveoli and improve oxygenation. To minimize interference with venous outflow, the PEEP should be lower than the ICP [12]. The PEEP should be monitored to determine whether it causes alveoli recruitment or over-distension. If possible, head elevation may be considered and close monitoring of hemodynamic, respiratory, and cerebral parameters is helpful in head-injured patients on mechanical ventilation [13]. In ARDS patients, the prone position might improve oxygenation and reduce ventila-

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tor-induced lung injury (VILI), but it cannot improve mortality. In patients with brain injury, the effects of the prone position on ICP are still controversial. When hypoxemia is a concern, the prone position can be used for patients with severe ARDS and traumatic brain injury [14]. High-frequency ventilation can reduce VILI and barotrauma, and has a minimal effect on ICP. Of note, the $PaCO_2$ should be monitored frequently [15]. It can be considered for patients with ARDS and an elevated ICP who have failed with conventional ventilation. Extracorporeal membrane oxygenation may be another consideration, but it carries a potential risk of cerebral bleeding [16]. In conclusion, the pathogeneses of both ARDS and acute brain injury both involve inflammatory reactions. Protective mechanical ventilation can provide safe oxygenation and maintain brain homeostasis. Clinicians must understand the clinical issues surrounding ventilator management in brain injury.

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