Intensive Care Med (2006) 32:1925–1927
DOI 10.1007/s00134-006-0407-z

EDITORIAL

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Ventilatory setting in severe brain injured patients: does it really matter?

Received: 18 September 2006
Accepted: 18 September 2006
Published online: 20 October 2006

This editorial refers to the article available at:
http://dx.doi.org/10.1007/s00134-006-0406-0

This work was supported by EEC grants QLCT-2000-00454 and QLCT-2002-001160

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Introduction

The presence of pulmonary dysfunction in severe brain injury is a well known phenomenon. Development of acute lung injury/acute respiratory distress syndrome (ALI/ARDS) occurs in 20–25% of patients with isolated brain injury, both subarachnoid hemorrhage and trauma, and is associated with a threefold increased risk of dying and increased ICU length of stay [1, 2, 3]. *Intensive Care Medicine* now present an elegant physiological study carried out by Koutsoukou and coworkers [4] to assess respiratory mechanics in the early phase after severe brain injury. The authors conclude that on the first day of mechanical ventilation patients with brain damage exhibit abnormal respiratory mechanics. Static elastance and minimal resistance further increased after 5 days in patients ventilated on zero end-expiratory pressure (ZEEP) while it remained stable in patients ventilated with a moderate level of positive end expiratory pressure (PEEP). In the present editorial we discuss: (a) the mechanisms of pulmonary dysfunction, (b) its clinical relevance, and (c) the potential "conflict of interest" between the protective ventilation strategy for ALI/ARDS and the ventilatory settings proposed for brain injured patients.

Mechanisms of pulmonary dysfunction

The risk of developing ALI/ARDS after severe brain injury was identified by poorer global initial computed tomography findings [1] and lower Glasgow Coma Scale [5, 6] (intracranial factors) together with the administration of vasoactive drugs and history of drug abuse (extracranial factors) [2]. Several mechanisms have been postulated as causes of pulmonary dysfunction, including aspiration, infection, and neurogenic pulmonary edema. In the past the occurrence of neurogenic pulmonary edema has been attributed to a hydrostatic phenomenon induced by a massive increase in sympathetic activity [7, 8, 9]; active pulmonary venocostriction together with an altered capillary permeability may contribute to an increase in extravascular lung water. Rogers and coworkers [8] confirmed in a large autopsy database a significant increase in the weight of the lungs but not of other organs in patients dying immediately or within 96 h from isolated brain injury. Recently it has been suggested that after acute brain injury there is both an increased intracranial production of proinflammatory cytokines resulting in a secondary injury to the brain [10] and the release of proinflammatory mediators into the systemic circulation [11]. Yildirim and coworkers [12] reported that ultrastructural damage occurred in type II pneumocyte in a model of traumatic brain injury, suggesting that an acute systemic inflammatory response plays an integral role in the development of such injury by initiating infiltration of

activated neutrophils into the lung [13]. In addition, in an experimental model it has been demonstrated that massive brain injury decreases the pulmonary tolerance of subsequent mechanical stress due to mechanical ventilation [14].

Clinical relevance of pulmonary dysfunction

Koutsoukou and coworkers [4] report that patients with brain damage exhibit abnormal respiratory mechanics even at admission. Interestingly, the authors found that although only one patient met the criteria for ALI in the "ZEEP group," in some patients the PaO_2/FIO_2 ratio was below the normal limit even on the 1st day and further deteriorated during the 5 days of observation. These data confirm that a severe deterioration in PaO_2/FIO_2 after admission in patients with isolated brain injury may be present even in the absence of an abnormal chest radiographic findings [8]. Previous studies have reported varying values of static elastance in patients with severe brain injury, ranging from 13 to 27 cmH_2O/l [15, 16, 17]. In patients with ALI/ARDS we have found a mean value of elastance equal to 24 cmH_2O/l with a mean PaO_2/FIO_2 of 186 [15]. All these data suggest that the main feature of ALI/ARDS in brain-injured patients is the presence of a poor oxygenation accompanied by a moderate increase in the elastance of the respiratory system.

Role of mechanical ventilation

Guidelines for traumatic brain injury recommend: (a) ventilating patients using high tidal volumes to maintain $PaCO_2$ at or above 35 mmHg, (b) treating intracranial hypertension with brief periods of hyperventilation, and (c) optimizing oxygenation applying low levels of PEEP while preserving cerebral venous drainage [18]. The use of high tidal volume and low levels of PEEP may further exacerbate the pulmonary and systemic inflammatory response in patients with ALI/ARDS [19, 20]. In the presence of an established inflammatory process represented by the primary cerebral injury [10], an injurious ventilator strategy may present a further relevant inflammatory stimulus. Moreover it has been shown that the use of high tidal volumes for the first 48 h after ICU admission is associated with the development of ventilator-induced lung injury in patients without ALI/ARDS [21, 22]. The NIH protective strategy is the gold standard ventilatory treatment for patients with ALI/ARDS and recommends ventilating patients with low tidal volumes (6 ml/kg predicted body weight) that lead to plateau pressure lower than 30 cmH_2O [19]. Patients with acute brain injury differ from other patient populations because mild hypocapnia is a key factor of the clinical management. Consequently, all clinical trials testing protective ventilation strategies for ALI/ARDS exclude brain-injured patients because of the tight CO_2 control required [19, 20]. Until further studies are carried out, brain-injured patients developing ALI/ARDS should be ventilated using a ventilatory settings that lead to plateau pressure lower than 30 cmH_2O. An attractive alternative in the early phase after brain injury to guarantee tight CO_2 control may be the use of different ventilator strategies based on lower tidal volumes and higher respiratory rate to obtain similar minute ventilation. More sophisticated techniques such as tracheal gas insufflation [23] and extracorporal CO_2 removal [24] may be considered in the most severe cases of ARDS complicating brain injury.

Application of PEEP increases intracranial pressure (ICP) when the baseline ICP value is lower than PEEP but has less effect on cerebral perfusion when ICP is above the highest applied PEEP (Starling resistor model). In addition, the application of PEEP may affect cerebral circulation by a CO_2-mediated mechanism depending on recruitment/hyperinflation of alveolar units: if alveolar hyperinflation is the predominant event with PEEP, there is an increase in pulmonary elastance and dead space leading to a rise in arterial PCO_2 and ICP [15]. Consequently, even if hemodynamic transmission is minimized because ICP values are higher than applied PEEP, ICP may still be affected by changes in $PaCO_2$. Moreover Caricato and coworkers [17] have reported that the effect of PEEP on cerebral circulation depends from the baseline value of the compliance of the respiratory system. In their present contribution Koutsoukou and coworkers [4] demonstrate that applying moderate levels of PEEP in brain-injured patients without ALI/ARDS prevents the peripheral airway closure and atelectasis without impairing cerebral perfusion. Integration of the various mechanisms proposed in the literature may help intensivists to titrate the optimal level of PEEP to protect the lung without damaging the brain.

Although some controversy persists, it seems that the presence of a neurocritical care team has a favorable effect on clinical outcome of patients and resource utilization [25]. The aim of clinical management in severely brain-injured patients is to improve neurological outcome, but the impact of the brain-oriented therapies on nonneurological systems should be always evaluated: a *multiorgan* clinical approach instead of a *single organ* approach probably represents the optimal way to reach this goal.

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